



Victory Summit: Sleep

Sleep, Light, and Neurodegeneration

Davis Phinney Foundation

Note: This is not a flawless, word-for-word transcript, but it's close.

Melani Dizon (Director of Education, Davis Phinney Foundation):

Okay. So, I'm really excited to welcome you here today. We're going to talk about sleep and light and neurodegeneration, and just that conversation, I feel like just that conversation that Polly had with Davis is going to give us 10 hours of content. There's just so much to talk about or related to sleep. But as we said, you know, everybody's bio is in the program book and Sam posted the link a little bit earlier. So, I don't want to read your bio word for word, but I would love to hear from you about what you're doing and how you got interested in sleep and movement disorders, and where you're sort of research and experience has brought you

Aleksandar Videnovic, MD (Associate Professor of Neurology at Harvard Medical School, Director of the Division of Sleep Medicine at MGH, and Director of the MGH Program on Sleep, Circadian Biology, and Neurodegeneration):

Good morning, everyone. It is really my great pleasure to be with you all today. And this is the first program that I'm doing with the Phinney Foundation. I'm very excited about that and would like to applaud to all of your efforts and for bringing such a great PD community together. These are such a worthwhile and much-needed effort. And it is wonderful that I have this opportunity to be part of this today.

Melani Dizon:

Yes. And I will say, I have to tell you this because when I was putting this together and I was talking to our friends about sleep, you were at the top of every person's list. So, I was like, well, how have we not had him on this to this day? So, I'm really thrilled to finally have you on with us.

Aleksandar Videnovic:

Oh, this is very kind, there are many colleagues who do this line of work. And but this is, this is very kind. Your comments are very kind just to briefly introduce myself. I'm a neurologist, I'm a movement disorder specialist. And also, I specialize in sleep medicine. I work at Massachusetts general hospital in Boston. Prior to my work at my general hospital, I was in Chicago at Rush University Medical Center and subsequently at Northwestern. And how did I develop interests both clinical and research interest in sleep? Well actually that dates back when I was a fellow in movement disorders from two, and at that time, really a lot of my patients would come to see

me, and they would complain about excessive daytime sleepiness. It was a time and dopamine agonists, which many of patients who join us today, I'm sure are still using are in the focus of medical and scientific PD community because of those associated issues of sleep attacks and sleepiness.

And this was really very debilitating to my patients at that time. I developed interest in that area, how, what can we do to help them? And everything else is in the past. I remain in that field of work with some additional aspects as well. But I really dedicated a lot of my both clinical and research work to the intersection of sleep and Parkinson's disease. And I'm sure we will have an opportunity to talk about this today during this interactive session.

Melani Dizon:

Yeah, absolutely. Well, thank you so much. One of the things that I know that I want to give to our audience today is this ability to kind of be a fly on the wall in a conversation with a doctor, they very rarely probably will never get 60 minutes with their doctor to talk about sleep. The one topic that can really impact absolutely every single area of their life. So, I want to give them that today. So, we'll get started on that. One of the things I want to start with though is just to, for some people that are, you know, maybe recently diagnosed with Parkinson's and they're hearing a lot of different things about, you know, some people never sleep, some people sleep too much, you know, some people have terrible dreams, some people don't love to just kind of start out with a level set and say, what is happening in the brain of somebody with Parkinson's that is impacting sleep. Why is this such a problem? And we know that it's a big sort of prodromal symptom, right? Why is that?

Aleksandar Videnovic:

Well, the process that leads to eventual development of Parkinson's disease starts decades before the onset of a tremor or balance problem, or one arm doesn't moving much as we walk, right? So, this is the process that starts 20, 30, 40 years before these symptoms emerge. And those changes in the brain are occurring very, very gradually. And these areas that are affected by these changes that are causative of Parkinson's disease, do not necessarily start in the areas that are important for movement, right? Parkinson's disease is a movement disorders. Simply those areas can start in brain regions that are very relevant for the regulation of alertness and regulation of sleep. And as this pathology progresses it'll affect different regions of the brain in different patients. So, therefore, the onset of sleep problems and the type of sleep problems that patients may develop throughout their journey with Parkinson's disease will be very different. And one aspect that we always share with our patients that there are no two Parkinson's patients that are fully alike and similar and similarly sleep problems are, we know very ubiquitous in patients with Parkinson's disease, but may affect very differently our patients with Parkinson's disease. So, changes in sleep are simply occurring, in Parkinson's disease because they affect the areas of the brain that are relevant for the regulation of sleep and alertness.

Melani Dizon:

Great. So, let's I think it would be great. There are a lot of topics that everybody wants to talk about, and I want to make sure that we get to them, but let's start with one of the most common questions we get, which is what is the difference between sleepiness and fatigue?

Aleksandar Videnovic:

Yeah, that's a very good question. And the way I try to explain it is fatigue is really a lack of energy, right? You just really feel very fatigue. You feel like you want to lay on the couch all day long. You're really exhausted if you try to get up and do some things, fix the lunch, go throw the garbage out, et cetera, or do any activities, you just feel exhausted, right? You just have a lack of energy. Being sleepy is a little bit of a different phenomenon. And you just really have this urge to really fall asleep. You just need to close your eyes, and you're just going to easy breath to sleep, even eating lunch or breakfast, or so one can just nod and often fall asleep with fatigue. However, one of the pointers that I like to tell my patients if you are fatigued, and if you lay on the couch, you will not necessarily fall asleep.

You can feel exhausted, but even if you try to sleep, you may not be able to fall asleep, sleepy person. They don't even need to lay down. They can fall asleep, even sitting in a, in a, in a chair or at breakfast table. So, I think this is how we can differentiate between these two phenomena, which can overlap, right? So, both of these can coexist at the same time, but the same time they are different. They are really different aspect on a symptom spectrum, right? We are talking about very different symptoms. And in my experience, fatigue is much more challenging to address. Sleepiness can be a very problematic as well, but there are things that we can think about what can be really the because of that sleepiness and how we can intervene with fatigue, which affects majority of our patients. At least almost all of them. If you look at the entire lifelong journey with Parkinson's disease frequently, it's a large unmet need frequently. We can't do much to pinpoint the because of it. And therefore, we are not great as with treating it

Melani Dizon:

Right. And so sometimes when you are, well, we're going to talk about different ways to treat sleepiness and different sleep issues. But sometimes if you're you might very well figure out a way to get this person to sleep. And so, they don't have the sleepiness, but they might still struggle with that fatigue during the day. And that's going to be a sort of different mechanism that you have to treat. Okay. So, I know one of the fields that you're really very interested in and is circadian biology. Can you talk to us, what is circadian biology, and you know, why do people with Parkinson's need to know about it?

Aleksandar Videnovic:

Yeah. Yes, Mel, this is an area of that we have really worked a lot on. And well, circadian biology is the area of biology that is interested in the study of our internal timing of what we call circadian system or circadian rhythms deep in our brain. We have about 20,000 nerve cells that function like that function as our internal clock, our internal timer, all of us have it, right? And that internal timer that is located in the brain is the conductor for all other clocks that are distributed all over our body, all of our organs, our heart and kidneys and liver and stomach, they all have their own clocks. And this mechanism gives our organism the sense of time. And this central clock that is located in the brain, coordinates the function of all of these other clocks across our body.

And why do we need to have this timing system this internal time? Right. Well, we live in the earth and the earth rotate around the sun. And as a result of that, we are exposed to dark and light cycles and these dark and light cycles control our lives, right? They influence the social function and any other function for humanity. It is really that internal clock that signals our body and our organs and tells us, wow, the Dawn is just approaching, and let's synchronize our body so that we can get up, that we can have energy moving, and that the flow of food is appropriate, and the blood pressure goes up. And all of those things that are really very important for us to live on this 24-hour scale and to function as a human during the daytime and during night.

And the circadian system has been present and is present in all organisms on the planet. So, it's evolutionary very important biological phenomena, right? When we talk about sleep, the rhythm and the circadian pacemaker is very important because it really helps times our, our behavior it signals when we should go to bed, it helps us stay awake during the daytime. And it helps us stay asleep at night where we shouldn't be asleep. The significance in Parkinson's disease is such that we and others have demonstrated that that clock is not ticking correctly in patients with Parkinson's disease the strength of that clock and oscillations of that time, timekeeping signal seems to be dampen in patients with Parkinson's disease. And that can have a negative downstream effect on all of the other organ systems, which are really necessary for the appropriate functioning of us, of humans.

Right? And the last piece that is important to understand one can ask, well, this clock is deep in our brain, right? How does that clock know when it's going to be the dawn and when the light is going to come out and when the night, when the dusk is coming, right? Well, the clock receives the signals from the outside world. And the most important signal is light, is sunlight. So that's the most important synchronizing agent because that light from the environment and from the sun hits our eyes and then special cells at the back of our eyes directly transmit that light. It's like a highway that goes from our retina, from our eye directly to our circadian pacemaker. So light is very important, and we can talk more about that. How do we implement that in the daily lives of patients with Parkinson's disease, but even other activities that are non-photic stimuli, not related to light stimulation can help synchronize that internal clock with the outside world.

For example, physical activity can be great for telling us for keeping our internal time or strong and on time, even timing of meals throughout the daytime can serve as a good signal to our internal timing system to keep it, to keep it function properly and work properly. So, I hope that I brought this concept a little bit closer to the audience. I think this is a relatively novel research direction. And I would leave it at this, and we'll see if we'll have more questions as the conversation evolves.

Melani Dizon:

Yeah, absolutely. I know we'll come back to it, but just so that I understand, is it because of your meal timing and your exercise timing, how are those impacting your circadian clock? Is it because you if you are getting it on a routine, you're teaching your clock basically like you're teaching your internal clock, and is it, well, if you exercise at the same time every day, or you have your meals at the same time every day, that's, what's going to do it. But if you're all over the map, you're still going to, your kind of going to mess your clock up a little bit.

Aleksandar Videnovic:

Exactly. That is just right. Just think about traveling to the different time zone when we go from, when we go from east coast, let's say we travel to India, it's going to be a huge shift. When we arrive to India, we're going to be reversing our biological daytime for the nighttime. And it's going to take a long time for the, for the clock who is not used to this cue from the environment. And it's not used to be awake at that time when it's supposed to be the nighttime in, in Boston, for example, it takes long time, right? So, think about those aspects, like a jet lag problem or issues with seasonal depression that can occur. Why does that happen? Because the lighting cycle from outside world is changed and in the winter, the days are shorter. And that light that now does not get to stimulate that internal timing is reduced, and that can affect, for example, mood in this case. And we know that patients with Parkinson's disease frequently suffer from a mood problem. So, I think they have a really great opportunity to better understand the importance of that timing system for, for general health. This is relevant to all disciplines of human health, not only Parkinson's patients, but it's really important for our community of Parkinson's disease. First of all, because this is very dear to us, and there are potential interventions that we can employ to improve our function really through using very easy non-pharmacological intervention without a lot of side effects.

Melani Dizon:

Yeah. I think the interesting thing about this topic, that's getting a lot more sort of prime-time news these days. I think the interesting thing is probably for most of our lives, we've just thought, oh, well, that's just, it's just what it is. There's the clock is the clock and it's light and it's dark. And there's nothing that we can really do. That's like a that's bigger than we are able to do anything with, but what you're saying is no, that's not true. And we have, we have control. We have a lot of things that we action that we can take and hopefully will get into

some of those specifically as we talk about treatments. So, another question that we get a lot is what can you say about the difference between sleep-related issues that are Parkinson's or age-related? Like, do they look different? And, you know, a lot of people are said, I don't know if it's just because I'm getting old or because I have Parkinson's.

Aleksandar Videnovic:

That is a great question. And I would just say that there is a great overlap between Parkinson's disease and is disease of aging. And all of us is the age will experience some issues with our sleep cycle. Our sleep is going to become a little bit more fragmented. Our deep sleep, which enhances memory formation is going to be reduced as we age, but generally aging population should still be able to achieve good sleep. Other things that are happening with aging and sleep is that comorbid sleep disorder starts to occur, increase. And then if you have an aging as we all hope to do, if everything goes well, if your aging gets complicated with Parkinson's disease, you have a double hit when it comes to your alertness during the daytime and nighttime sleep. And I would just look at Parkinson's issues as it being much broader than normal aging, but super imposed on what normal aging does to sleep and sleep in us during the daytime.

Melani Dizon:

Okay. a lot of times we'll hear, you know teenagers, they should be getting 10 hours of sleep and but that, you know, as you get older, you need less and less sleep. And we think old people don't really sleep that much like, or is there, is, is that true also for, for people with Parkinson's or is that absolutely not true? Like everyone should be getting a certain amount whether you have Parkinson's or whether you're 18 years old,

Aleksandar Videnovic:

Well, we all need to get sleep, right? if we just don't get sleep right, we simply would die, right. If somebody restrict your sleep, we will not survive. So, sleep is really essential function for, for, for survival. Many studies have done to investigate how much sleep is needed and how, how much is enough. And we like to say that anywhere between six to eight hours of sleep in general for the general population should be enough. Some studies have demonstrated that having less than six hours and more than nine hours may have some negative consequences for, for help for Parkinson's patients for decades, we have appreciated this phenomenon, which is known as sleep benefit effort. We hear over and over from our patients that their Parkinson's disease is not as problematic the day after goodnight of sleep. And we hear that even responsiveness to some PD medications may be enhanced after goodnight of sleep.

And I believe there is a biological explanation for that because dopamine metabolism, dopamine being one of the major brain chemicals involved in Parkinson's disease through being deficient in this disease state metabolism of that dopamine may be dependent on how well our sleep is consolidated. So, if we have a good physiological state of five, six hours of sleep, the

majority of this is really uninterrupted, uninterrupted, and good of a good quality. It may be that the dopamine availability may be enhanced and therefore the following day, it can be a good day for us. So, this is a phenomenon that is known and for, for decades and something that many of our patients report, that's why we try to emphasize good night of sleep, especially in the Parkinson's disease population.

Melani Dizon:

Great. Okay. So, let's talk about different types of sleep disorders. And so daytime sleepiness, I just want to go through a little bit of, like, what does it look like? How does it show up for people? If they could say, oh, you know, it's real sleepiness or drowsiness, sleep attacks, Reem sleep, behavior disorder, restless legs, insomnia, and then any, anything else you think we should talk about? So, let's, let's start in with the daytime sleepiness and drowsiness. What, what are people what's happening to them, and what

Aleksandar Videnovic:

Sure. The patients really it's simple, right? The patients will just doze off and will have to take many naps. And they are feeling very spaced out and go for a social event because they just feel that they cannot maintain fully their alertness. Frequently though patients will not be aware of it. So, this is important to point. And if I have a caregiver or a spouse next to the patients, as I ask is how is your daytime? And they would say, great. And I see the caregiver nodding the head in a different direction, and patients are frequently not aware of them nodding off as they eat food at mealtimes or how much they spend dosing off in a so far watching while watching TV or reading sleep attacks are a little bit more dramatic sleep attack.

Are these episodes where one transition from full wakefulness to sleep very quickly, and that can happen even within 30 seconds? Sometimes patients do not even have warning signs of transitioning from full wakefulness to full sleep. And these are obviously very dangerous because there are situations where safety of the patient their loved ones or others on the road, if they're driving, maybe, maybe in jeopardy. And this became very heated topic in the field in early nineties, when the initial description of sleep attacks was reported in individuals who were taking and started to be treated with dopamine agonists like *Texel* and or *epi*, and these agents have up to 30% chance of causing excessive sleepiness and somewhat smaller percent of provoking sleep attacks. So that's why we cancel our patients when we start these drugs and monitor them on a regular basis after they have been treated with these medications, which are important medications to have in, in our doctor bag, but they can come with this potentially very troublesome side effect. So, this is really what excessive sleepiness is, and the causes are really very numerous of the successive sleepiness. And we can dive into those as well if you want, but in terms of the definitions of these two entities, this is what I would, what, what I would say about how, how we define sleepiness and sleep attacks.

Melani Dizon:

Great. Yeah. So that note to care partners or friends or family members of people who are starting those drugs definitely keeping an eye on that super important. Is there in your research, have you found, is there if somebody is it because people are not getting the sleep or can they actually have a, a good night's sleep and then they're still facing this

Aleksandar Videnovic:

That's excellent question. And it's this latter scenario. One would think, oh, this must be because I have a terrible sleep. And that can be through, in some cases, patients may have undiagnosed sleep apnea, waking up all night, not realizing that. And of course, they're going to be sleepy the following day. That's one of the Cardinal symptoms of obstructive sleep apnea, but also patients may have a very good night of sleep and have a lot of challenges with staying awake during the daytime. That can be a result of certain brain areas that are important for controlling alertness when we are awake that are being affected by the disease, but also maybe a result of maybe underlying depression and anxiety that are not being treated or medications that are maybe causing drowsiness during the daytime. There are many possible explanations. So, one home take message that I would have for, for everyone who is on this call today is we all should including email and myself, and we all should pause and ask ourselves, how is my sleep?

How often do we think about that? Right? How is my sleep being my alertness during the time? Good. Can I try to improve that? I bet you that a lot of us, if not the majority of us really doesn't or hasn't asked this question recently, and this is really very, very critical. It's a similar question that we should ask for. How are my meals? How is my nutrition being my physical activity? Good? Do I keep connections with my friends and with my family? What is my social network? Because I heard someone said something recently, which really strike me. He says, we want to go travel to the moon, and we don't know how to eat properly. And we don't know how to sleep well on the planet third. And we want to go to the moon. It's just really some, we have not capitalized on these important pillars of health and only we are in control on these major pillars of health.

And yet we have put too much effort on the chemistry and all of these pills expecting that this chemistry that we put in our body needs to fix this. And sometimes we need pills. Don't hear me wrong, but we'll be able to do so much better if you pay attention to these other aspects that are solely in our control. Right? And so, I went off charging of target a little of tangent a little bit, you know, I'm on tangent here, but, but this is a really important message, right? This is maybe the most important message that I would have to relate to anyone who is on this call, including myself. I am terrible for some of those aspects that I just mentioned. So, I should, I should take notes from what I'm saying today for my own purpose.

Melani Dizon:

Right. okay. So, let's, let's talk about RBD, REM sleep behavior disorder. What is it, what does it look like? How does it show up for people?

Aleksandar Videnovic:

This? Well, we shouldn't supposed to have our favorite disorders, right? That's wrong.

Melani Dizon:

Right. That seems wrong, right?

Aleksandar Videnovic:

This is so important. This disorder is so critical. And let me explain why it is critical. And so many levels. When we go to sleep, we oscillate through stages of sleep. And two major stages are REM sleep and non-REM sleep, right?

And this disorder is called REM sleep behavior disorder. So, this tells you that it's going to happen as we sleep. As we enter into that REM sleep. Something is not right in this disorder, right? Well, what is not right is the fact that when we entered REM sleep, and if we have REM sleep behavior disorder, we do, we are not paralyzed during that REM sleep. What I'm trying to say, normally, as we sleep and as we enter REM sleep, during that period of sleep, we cannot move. Our muscles are paralyzed. Only breathing muscles are working. And in this condition REM sleep behavior disorder, our muscles can move, right. Well, why would they move right? If we are asleep, doesn't make sense. Why is that important if our muscles can move if we sleep? Well, it's important because there is a second part. Second, second side of the coin of that disorder.

And that is that in REM sleep, we usually dream dreams are associated with REM sleep. And in this disorder for an unknown reason, there are action-packed, very aggressive, frightening dreams that are occurring, going to attack us, or we just really want to escape the fire or not even aggressive dreams. We just want to jump into the pool. We are sitting standing at the edge of the swimming pool, and now you can act out your dreams because remember you are not paralyzed as you move to this REM sleep, in this disorder. And as a result of that, if you are dreaming that you are ready to jump in a swimming pool, you will jump out of a bed on a hardwood floor of your bedroom. Or if you try to defend yourself, you're going to punch your bed partner, or you're going to choke your pet that sleeps next to you.

So, the disease is very important because it can cause substantial injuries and sleep interruption, both to the patient and to the pet partner. And it is also important because we know that individuals who only have that sleep disorder are at increasing risk of developing Parkinson's disease or other Parkinson's related conditions down the road. So, it's important to improve and treat this disease so we can minimize the impact on sleep and safety of our patients. But the disease has become so important that these individuals who only have these

sleep disorders will now become ideal target population to study interventions, aim, to slow the progression of Parkinson's disease, because it may take decades between the onset of these weird dreams and behaviors and night until the signs of Parkinson's disease show up. So, we have an unprecedented opportunity as disease as these new disease-modifying therapies become available to intervene earlier, have a chance at an earlier stage of neurodegeneration to be more successful in, in arresting that process. So, this is what RBD is.

Melani Dizon:

Right? So, when you let's say you actually get somebody, a patient who has RBD or comes to you and says, I'm having these issues with sleeping and I'm acting things out, there's no other Parkinson's related anything. They haven't been given a Parkinson's diagnosis, but you see them having REM sleep behavior disorder. Is there anything that you can do now? Like, what is it, are you doing anything that is not you know, exert like anything that's pharmacological that you can actually do for those people now? Because I, once I once heard a doctor tell me it was a hundred percent that the people who have RBD actually is how far off is that seems I've never heard a hundred percent before with anything.

Aleksandar Videnovic:

Yeah. Well, you should have not heard a hundred percent because it's not hundred percent and the numbers are, are very variable.

Melani Dizon:

That's excellent.

Aleksandar Videnovic:

The treatment question first, we need to treat the symptoms to minimize the chance for injury in terms of preventing the risk of developing neurodegeneration. We have increasing number of longitudinal research projects and consortium, including RBD consortium, where we can enroll patients and do a yearly detailed assessments so that we can track eventual progression of their disease and get them ready for this disease-modifying trials. And one intervention that we will that we build a proposed to these patients who have even only RBD is a vigorous exercise regimen. I know that you have here later on from my dear colleague and expert in the field, Dr. Amara about importance of exercise when it comes to sleep and other aspects of Parkinson's disease. But we know that the exercise from many studies may be enhancing health of these nerve cells that are producing dopamine. And while we can't tell them, this is for sure going to be helping, we can say that there is excellent rationale for you to engage in a vigorous exercise program in order to reduce the chance of developing one of these disorders down the road. We hope to have a inter interventions that are going to be soon launched that are going

to be focused on prevention of development of these or progression of these neurodegenerative diseases in the RBD population, per se.

Melani Dizon:

Okay, great. Well, so we talked about acting them out as sleep talking. Somebody asked to sleep talking related to this, is it part of,

Aleksandar Videnovic:

Yeah, not necessarily. So important message here at this point is to say that not everything that looks and sounds like RBD is RBD, right? Because we can't alarm the public because everybody is going to once or twice a life as something maybe similar to this, what I just described, for example, sleepwalking or isolated sleep talking are completely different phenomena from brain behavior disorder. Patients with RBD usually do not leave bed. They do not walk around the house. There may be overlap with sleepwalking and REM sleep behavior disorder. So that's why it's important that if one has any suspicion or concern that this may be re behavior disorder, that you reach out to your provider, you find the sleep specialist knowledgeable in this area. And so that you can settle this issue because really important message is not everything that sounds that looks like RBD is RBD.

Melani Dizon:

Okay. Is sleepwalking and sleep talking a thing that people Parkinson's experience more than the general population, or is that not tend to be?

Aleksandar Videnovic:

We do not encounter that frequently.

Melani Dizon:

Okay.

Aleksandar Videnovic:

Sleep talking maybe, but sleep, sleepwalking is mainly disease of our children and early and adolescent adolescence. To certain extent, we try to overgrow this problem is the age.

Melani Dizon:

Okay. Okay. Can we talk a little bit about restless leg syndrome?

Aleksandar Videnovic:

Another sleep disorder? And this disorder is classified as a movement disorder of sleep, and that is a condition usually which starts to creep up in the evening hours, as one is relaxed and sitting on a couch watching TV or reading. And then there is this irresistible urge in legs. Usually sometimes arms as well, that that urges us to move, right? We, there is this unpleasant sensation, you know, maybe like water running down the down, our, our caps, or maybe some bugs crawling, and we just need to move. And then we get up, we move around. That goes away. We come back, we sit down, it comes back in few minutes again. So, this is a prototypical description of restless leg syndrome. Now interface of RLS in Parkinson's disease is very similar. And I would argue that we don't even know the prevalence of how common restless leg in par or restless flags in Parkinson's patients is because it is really hard sometimes to distinguish what are symptoms of Parkinson's disease.

And that can really be our RLS mimics. There are many mimics of RLS and therefore a lot of patients will say, I have RLS. And at the end of the day, it's not going to be this. It's going to be maybe rigidity that gives patients that uncomfortable sensation. That is, that is relieved as they get up and walk. It can be nocturnal like cramps. Some patients will have peripheral neuropathy. So, it's really important to think carefully, is this restless legs, is this something else? And the good news for patients who have both is that we treat, we use the same medications that we would use in the treatment of Parkinson's disease to manage restless leg syndrome. So, there is a silver lining there, but, but this is, I'll leave it here so that we have more time maybe for some other questions and answers. I leave it here when it comes to restless legs.

Melani Dizon:

Okay. Okay, great. Yes. I know people are going to have questions are already asking them and then insomnia.

Aleksandar Videnovic:

Insomnia, inability to fall asleep to stay asleep or to sleep enough early morning awakening, right. Or combination of any of these three symptoms, very common problem in Parkinson's patients, the most common, I would say, and specifically, what is common it's fragmented sleep. I think if we are if we are to address the largest unmet need among patients with Parkinson's disease when it comes to sleep, I think it is really fragmented sleep. Patients will easy fall asleep in majority of cases, but then an hour after hour or after three hours, they will, they will wake up and this is going to, they're going to fall back to sleep. And this is going to continue throughout the night. And I would say that a lot of our work has really targeted that sleep fragmentation. What can we do to try to consolidate the sleep of our patients being that being the largest problem in my opinion?

Melani Dizon:

Okay, great. Well, we'll definitely get into that. One of the questions we do get is, you know, people will write to us, talk to us about their sleep issues and they want to know when does a, you know, just sort of general sleepiness, fatigue, insomnia, when does that rise to the level of a sleep disorder and that they should, you know, raise their hand and say, I need some real specific help here.

Aleksandar Videnovic:

Well, I would suggest that the patients talk to their loved ones, their caregivers, their, their spouses, their children they may learn very valuable information, how their sleep is. They also may have a lot of insight, to begin with. And if the quality of life is really impaired and affected by their inability to sleep or inability to stay alert after you ask your, that yourself, that question, it's important to start with a self-assessment, I think it's time to approach a physician or a light field professional and talk about these issues.

Melani Dizon:

Yeah. And it could be great to the minute you start thinking about it, start tracking it and have your, if you live with somebody, sleep with somebody, have them start tracking it with you so that you can go with a lot more data. Okay. So, I would love now to take each one that we talked about and then talk about the different treatments pharmacological non-pharmacological that are working. And certainly, I'm sure light therapy will fall, fall into that. So, let's talk about daytime sleepiness and sleep attacks. What, what is typically,

Aleksandar Videnovic:

So, I probably, Mel, what I would say first, it is really important first to get a good, better, good understanding before we jump onto treatment, right? Because obviously, it is important to diagnose appropriately primary sleep disorders, right? It is important to find out if somebody has sleep apnea or if somebody has restless leg syndrome, or if somebody has RBD, right? Because these are categories of sleep disorders, which are very clearly defined, and we can diagnose them. If you take a look at sleepiness, for example, or sleep fragmentation, you really don't know what's causing those because apnea, restless legs, and RBD, they can all be causing this sleepiness and nighttime sleep fragmentation, right? So, it's really important to take an opportunity and not miss the primary sleep disorder that may be main driver of these issues with sleep and an alertness.

It's also very important to pay attention about. And this is uniform across all of these, all of these sleep problems. That's why I'm mentioning this. Now. It is important to understand whether one is depressed or not because that has a huge impact on alertness and an ability to sleep at night and an antidepressant or behavioral therapy to improve mood can be really very helpful in these cases. Similarly, review of medications, it's also very, very critical because if someone is taking a lot of sedating medication during the daytime, or if they take medicine that

have alerting properties close to their routine bedtime, that's going to make them unable to be awake during the daytime or fall asleep at night respectively. Right? So, these are some basic grounding principles that one can, that one can try to employ.

Melani Dizon:

So let me speak to that a second. So, if you had somebody come to you and they're kind of talking about all these different sleep issues that they're having, might you say, Hey, let's get you assessed by a, you know, a neuropsychic psychologist or psychiatrist or something like that first to see if there's depression, or is this something that you're going to do an assessment there and then be like, oh, okay.

Aleksandar Videnovic:

Yeah, I may do assessment. If I feel that there is untreated depression, I may treat depression. If I feel that they may need a sleep study to see whether they have sleep apnea, we're going to run that test. You're going to get that answer quickly. I may adjust some of their medications and tell them, please do not take amantadine too late in the evening. Or you are taking too much of clonazepam during the daytime for the management of anxiety. Can we manage your anxiety in some different way? And if they have sleep attacks, I need to do something with dopamine agonist and tell them, we're just going to need to reduce this drug and see how we're going to manage your symptoms of Parkinson's through some other mechanism. It's a really complex conversation that we need to have with our patients. And as you mentioned in a 30-minute visit, follow-up visit with the provider, there is so much that needs to be discussed and sleep frequently gets neglected and pushed to decide. And so that's why I'm advocating that our, our participants today dissect this and think a little bit more carefully about how they approach it,

Melani Dizon:

Right? When you mentioned sleep apnea for a sleep study where, what is the value? What are, what can a sleep study tell somebody, what is it not good for? What is it good for?

Aleksandar Videnovic:

Yeah. Well, the sleep study can tell us what the sleep continuity is, sleep fragmented. It can tell us what's the oxygen supply during the nighttime, whether, whether what's the breathing pattern do we stop breathing every 30 to 60 seconds, which we sometimes see, and that causes a small arousal that we are not even registering. And one can have hundreds of these throughout the night, not realizing they're happening. We can also take at the leg movements and see, are there are a lot of leg movements we can even detect tremors at night as individuals are sleeping. So, sleep study is a very useful tool in assessing sleep and picking up on this diagnosis that we have a specific treatment, like putting a C P a P mask for individuals who

have obstructive sleep apnea, which can improve their cognitive functioning during the following day, which can have a positive effects and alertness overall quality of life, be a good for heart health in addition for to brain health. So, we can do a lot in, in the sleep arena to improve not only PD-related symptoms, but also to maximize the potential for other problems that can come down the road.

Melani Dizon:

Okay, great. Alright. So, the marching orders, or for everybody to pay attention to their sleep, their patterns what they're doing have a friend, a care partner, somebody who lives with you, somebody who spends a lot of time with you to share what they notice, what they see and then, and talk to their doctor and let's say, okay, I've gone to my doctor. We've been able to parse out what is, what let's talk a little bit about some of the strategies that somebody can employ. And then some of the, maybe some of the drugs that are being, being used, and I'd love to talk about melatonin and light therapy, because these are, these are common, common questions, and people have many questions about what they can do with those.

Aleksandar Videnovic:

Sure. So just for the sake of time, if you had the chance to hear Mr. Phinney talk about his approach to sleep, I almost felt, what am I going to talk about that? Because after his feedback that he has provided to all of us today, so all of these are great ideas, and I would like to endorse all of them. I am going to touch upon on light therapy on melatonin. We used to call it sleep hormone, right? It is it is available for purchase over the counter. It is relatively benign substance medication; however, you want to call it and what it does, it can help with the sleep consolidation. It has a Subic property, and I think it's a good, relatively benign medication to try if someone has a problems with maintaining sleep, assuming that other primary sleep disorders and other causes that can be addressed have already been addressed.

Right. I think melatonin is a great choice. Melatonin is also a great choice for the management of sleep behavior disorder because it comes out those dreams and this dream enactment. And it's my treatment of choice when I initiate therapy for patients with REM Sleep behavior disorder, whether they only have RBD or they have Parkinson's disease. And RBD together, we have done a lot of work with light therapy and are currently actually completing a nationwide clinical trial on light therapy and its effect for its effect on sleep fatigue and some other manifestations of Parkinson's disease. And if you, if you heard me speak about the circadian system, I told you that the light is really that connection between our body and our brain and outside world, right? And it is really important that we expose ourselves to enough amount of bright light during the daytime.

Why is this important in patients with Parkinson's disease? Well, it is important that Parkinson's patients are prone to not getting enough light during the daytime. And why is that? A lot of Parkinson's patients do not get enough outdoor exposure. There are mobility limitations. There

are mood issues. I feel anxious. I don't care. There is apathy. I don't want to go out. You name it. He also said that Parkinson's is a disease of aging. Our eyes are changing as we age our lenses that are part of our eyes are becoming yellow. We are developing cataracts. All these are barriers to light getting into our brain. And finally, our retina, which is a part of our eye on the back of our eye. It's important for our vision has a lot of dopamine normally, but that dopamine gets lost in retina. Similarly, like it gets lost from the brain and it is that dopamine that is critical for our eyes, ability to process that light from outside world.

Therefore, you are hit on so many levels. Why our brain, if we have Parkinson's patients is not getting enough, enough light? And therefore, we have with other groups worldwide have started to do systematic study of a phototherapy of a light therapy in which we provide the supplemental light exposure to our brain, trying to strengthen the function of that clock that is deep in our head. And that I said is really directing functions of our body so that we can maximize our health and optimize our behaviors. Right. And light therapy is really, it's really like a drug. If you think about it, right, you need to know when to do the light therapy, how long to expose yourself to the lights. Do you need to do it once a day or twice a day? And also, there are all kinds of light, especially in the modern society, which light is right for me.

Right? And so, it is really not straight. Unfortunately, it is not straightforward either. I can't tell you what is going to work for everyone, but I can give you some tips, do not do bright light very, very early in the morning, or for sure, very late at night, because then you're going to shift your normal natural times when your body wants to wake up. And when it wants to go to sleep, sometimes it's a very useful, so someone who on the other hand sometimes do so we need to time it right, for a person who cannot stay awake past 7:00 PM and would like to go to bed with spouse at 10:00 PM. It can make more sense that they do that just before that 7:00 PM mark to push their bed cycle later on. But if someone really normally goes to bed at 10 and starts doing their light at nine 30 or 10, they may not be able to fall asleep until midnight.

So, we need to be very, very careful. That's why I say, and I like to say, if you expose yourself in the mid-morning about an hour, two hours before you wake up, and if you don't expose to yourself to light for about two to three hours before bedtime, I think you are in a safe zone, right? You want to maximize the bright sun that is out there because that strength of that light is going to be as good, even maybe better than what you can do from the light boxes. And frequently, I get a question. How long is enough? If I have a light box, I will say, if you do it 30 to 40 minutes a day, I think it's a good start. And don't get too with colors. Everybody says, oh, I'm going to have this green blue spectrum, et cetera, just get a good, bright, light, white, bright light, and start with that and see what that can do for you.

So, I'm going to pause here. So, I gave you a lot of tips. I gave your ideas, why light is important, gave your idea why you likely are not getting enough light. And I gave your idea how to use light and will soon report on this clinical trial and hope to do many more trials based on what we find from this study. And hopefully, the light therapy is going to be beneficial. Not only for, for sleep.

It can improve mood; anxiety we'll see what effects it may have on a cognitive function. Think about it. It's an easy intervention it's widely available. It doesn't have side effects for most of the time, as long as you get too used to it and use it properly again, you may use like inappropriately. So, I just don't want you to start going and buying and ordering on Amazon light boxes today. Just take a, take the time to educate yourself a little bit about it. And maybe we can have a session about, about light in the future through this, through this type of programming as

Melani Dizon:

Well. Oh, I hope so. I am already, I have a million more questions and I just saw the time. So, I would love to yes. Invite you back so we can have a lot more Q and an around this sleep-in light therapy. I do want to ask one quick question though, because I know this is something that people often ask when it cut. Like, so the light therapy, the timing is important. What about melatonin? Somebody said, do I take it right when I want to go to bed? What, how is it going to help me with my clock? What, what is the best time to take that

Aleksandar Videnovic:

Great question. I usually advise patients to take it 30 to 40 minutes before intended bedtime. There are some other applications of giving melatonin, try to help patients who are owls or larks to become a little bit more to the norm, but that's too complicated for Parkinson's patients who want to take it for poor sleep or to treat RBD. Just take it 30 minutes before bedtime start with a three milligrams. If you cannot, five, three-milligram tablets, you can go to five milligrams, see what that dose does for you, and then discuss it with your, with your physician, what the next step should be.

Melani Dizon:

Okay. Well, thank you very much. Yes, you have an open invitation to come back whenever I appreciate everybody's questions. I hope we got to a lot of them. I know we missed some, but we do actually have a lot of information. We have some information on light therapy. We have lots of information on RBD so we will be sure to share those with you in the recordings and in all of the emails that we send later. So that you can catch up on that. Thank you again so much for being with us. And I hope that we get to talk to you again soon.