



Live Well Today Webinar Series:
Medications for Non-Motor Symptoms in Parkinson's
Recorded on November 10, 2021
Davis Phinney Foundation

Leigh Cocanougher (Education Program Manager, Davis Phinney Foundation):

Hi, welcome everybody. We are here today with Dr. Aaron Haug to talk about medications for non-motor symptoms of Parkinson's. We're so glad that you're here with us today. We want to first thank our Peak Partners for 2021 Adamas, Amneal, Kyowa Kirin, and Sunovion. Thank you for supporting all our educational content and making it possible for us to provide it to our community for free. So I'm going to quickly introduce Dr. Haug and then I'll turn it over to him. Dr. Haug attended undergraduate at Creighton University and earned his medical degree at the University of Kansas. He completed his neurology residency as well as a fellowship in movement disorders at the University of Colorado, including a year as chief resident and his primary medical interests include Parkinson's tremor and other movement disorders. So Dr. Haug, thank you as always for being here and I will turn it over to you.

Aaron Haug (Neurologist, Blue Sky Neurology):

All right. Thank you very much, Leigh. And thank you everyone for joining us for a discussion about the medical treatment of non-motor symptoms in Parkinson's. This is a big topic. Sometimes people will talk about Parkinson's like an iceberg and the tremor, the stiffness, the slowness, that's kind of the tip of the iceberg above the water, but then there's a lot of non-motor symptoms that are happening underneath the surface. So who's excited to talk about constipation? That'll be one of the topics we talk about as well as a number of others and let's get into it.

So I'll be breaking non-motor symptoms down into a few major categories. And we'll talk about each of these in turn. Autonomic symptoms, we'll talk about what that means. Sleep, mood, and thinking, and then a couple of other important things as well. So sometimes it can feel like this, all these people really seem to have it together, and I still have no idea what's going on. And these informational sessions are to try to demystify some of this, to kind of build up our vocabulary and language surrounding these things to make it easier to talk about. And also just to know what might be related to Parkinson's that you might not have even been aware of. At the same time, it's important to note that not everyone will have all the symptoms that we're talking about here. And that's why in the future look for some shorter videos where we talk about maybe one symptom at a time. So, you can really hone in on the issues that you have, and maybe not pay so much attention to symptoms that you're not having, but by identifying the symptoms and knowing that there are treatment options, the goal as always is to improve quality of life. So it's tough to make predictions, especially about the future, said Yogi Berra, works great for quotes like that.

So in a separate webinar that we've done earlier, that you can find through the David Phinney site and through YouTube, we talked about the medications for motor symptoms, and some people found it

helpful to kind of have this bird's eye view of these are all of the medications that can help with tremor and stiffness and slowness. One of the things that's notable is that neurologists, movement disorder specialists, we're the experts on these medicines. A lot of other doctors may have never heard of some of these medications, but as we started to talk about non-motor symptoms, there are other experts that may know more than your movement disorder specialist does about the treatment of constipation or lightheadedness or depression. As neurologists and movement disorder specialists, we have the ability to recognize and treat these things but we will sometimes recommend that you get other experts involved.

So now, this is kind of that same overview slide, but for non-motor symptoms. And you may notice kind of right off the bat, that the font is quite a bit smaller. There are a lot of possible symptoms and a lot of possible tools in the toolbox. And so this can kind of feel like a whirlwind tour of the options that are available and any one symptom, any one medication potentially could have its own hour-long lecture. And so it's not really possible to be exhaustive about being very detailed and prescriptive about this much for this reason, for this long, all of these things are to kind of raise awareness about there are different options, but in terms of specifically treating the symptoms that you're dealing with, kind of have this as a list of things that you might want to discuss with your prescriber, but please do check with your prescriber about any specifics.

Okay. So as we go through this, of course, this talk is to focus on the medications, the ones that I mentioned just on that prior slide, and we'll get to in some greater degree of detail, but of course, a lot of motor symptoms and non-motor symptoms have non-medication options that are important to consider for treatment. And so one of my patients once wore this shirt into the office, Exercise... I thought you said, extra fries, because exercise is one of the things that often has benefits, not just for the physical symptoms, but also for many of these non-motor symptoms. So I'll be mentioning these non-medication options for non-motor symptoms as we go along as well.

Okay. So the first category is autonomic symptoms. Let's get into this. So the autonomic nervous system, when you hear autonomic, you can just kind of substitute the word automatic. So this is the part of the nervous system that controls things that we can't really control voluntarily, how quickly our gut processes our food, what our heart rate's doing, what our blood pressure does when we stand up, and Parkinson's can affect the autonomic nervous system in a variety of ways. So I promised it, here it is right off the bat, we're going to talk about constipation. This is an extremely common symptom in Parkinson's. Some studies say 98% of people with Parkinson's may suffer with this to some degree. And so this can either be that the bowel movements are hard or that they're infrequent, or you feel like you don't get completely empty. And this is important, not just because it's uncomfortable to be constipated, but there's also clinical experience that shows that if a person is constipated, their Parkinson's medications, their Carbidopa-Levodopa in particular may not work as well.

This is because Carbidopa-Levodopa is absorbed in the first part of the small intestine in the gut. And if your whole gut is backed up with bowel movements or poop, or we use these different terms, BM, these are all synonymous. If you're all backed up, then it can make your medications not work as well. And so it's a good worthwhile goal, not just to have a bowel movement once a week, as some of my patients

unfortunately tell me, I'm glad they tell me, it's unfortunate that's what's happening, but really the goal is to have a bowel movement every day.

So the treatment of constipation, that's talk about some of the options. So in the non-medication world, exercise, the more you move your body, the more you move your bowels. Hydration, shooting for eight, eight-ounce glasses, 64 ounces, two liters of water, rather non-caffeinated beverages throughout the day can be helpful. A warm drink in the morning can sometimes help get the gut moving. Classically, this is somebody who has a cup of coffee and is able to have a bowel movement, but it just is the warm temperature that often triggers that. Dietary fiber is an important consideration, shooting for at least 30 grams of fiber over the course of the day and breakfast cereals are often a good time and way to increase your fiber intake. Probiotics are an area of increasing interest and there are some specific probiotics that have been shown to be beneficial for Parkinson's in a variety of ways. So that's an interesting topic, and probiotics potentially can be helpful for constipation as well. Then here's an interesting little trick that will also come up in a moment when we talk about drooling, but having sugar-free gum, the sugar-free aspect of this, it's often a sugar alcohol that makes the sugar sweet like sorbitol, and that has an osmotic effect on the gut that can cause things to move. So having a few pieces of sugar-free gum throughout the day can sometimes be a helpful trick for constipation as well.

So let's shift into talking about the medications for constipation. The vast majority of these are available over the counter. So it's mostly a matter of having some roadmap of what to get and how much of it to try to use. So the two major categories of medications are stool softeners and laxatives, and this is a little bit crass, but maybe that makes it memorable. Think of this as the mush and the push. So we don't want the bowel movements to be hard little rabbit poops, but we also want the gut to move. And so it's often a stool softener and a laxative together that work better than either one does alone. So stool softeners, there's really only one it's Docusate, or the brand name of it is Colace, it's usually a little red pill like this. This is really the only stool softener out there.

And stool softeners are not at all habituating, and it can be taken as little as just one pill once a day, every day, or as much as three pills every day. Laxatives, osmotic laxatives that help draw water into the gut and keep things moving include polyethylene glycol and milk of magnesia. These are medications that if you read the fine print on the bottle, it'll often say don't take for longer than such and such without consulting your medical professional. Well, certainly do consult your medical professional. We don't want the pendulum to swing towards diarrhea and get dehydrated and so on, but people often do need to take a laxative with a stool softener every day, even multiple times a day, Miralax, for example, people will sometimes take as much as four capsules, two in the morning and two in the evening, and eventually are able to dial in a dose where they take a little bit every day and are able to facilitate having a bowel movement every day.

If it's been a while, 2, 3, 4, 5, 6, 7 days since you've had a bowel movement, that often takes a while to get cleared out. And if you have a blockage, you can sometimes have kind of leakage around the blockage when you're first starting to take a laxative, which is not something anybody wants, but you kind of need to get cleared out and start from a blank slate. And then you can stay on top of it rather than always trying to play catch up. So laxatives, daily or as needed. So another category of laxatives are

stimulant laxatives. These are not so ideal to use every day. Gastroenterologists will sometimes talk about people even without Parkinson's can have a lazy colon and taking excessive amounts of stimulant laxatives can make the colon lazier, which of course we don't want. So these are kind of a plan B if a person has a few days without a bowel movement, so more suited for as needed use, and these include Dulcolax, you sometimes have to read the fine print because Dulcolax brand does also make Docusate, stool softener, or sometimes they'll put them together, but Bisacodyl is the stimulant laxative that's in most formulations of Dulcolax.

And then Senna or Senokot is available as a pill. And it's also available in another formulation, which is as a tea, which some people are pretty pilled out. And so having a non-pill option is nice. There's also, Bisacodyl Dulcolax that comes in the form of a suppository and Fleets Enema is or again, if it's been a few days or if you're needing to have that initial kind of clean out, sometimes those tools can be helpful with that.

A couple of other tools in the toolbox, these are usually not necessary. These are prescription medications for constipation. These can also be expensive, but Linzess and Amitiza, are a couple of these options, I'll mention it towards the end, pain as a symptom in Parkinson's. And although opiates narcotics are in most cases better if avoided, some people are on those for various reasons, whether it be back pain, or some other pain and opiates can induce their own constipation. And there are medications specifically for opioid induced constipation, like Movantik, that can make a huge difference in that circumstance. If we've kind of gone through this long checklist and have tried a number of different things, then occasionally consultation with a gastroenterologist, a GI specialist would be warranted as a next step.

So another gastrointestinal symptom another gut symptom is nausea. It's important to note that nausea is more likely if you're constipated, if you're eating and there's nowhere for the food to go, then that can make you nauseous. Nausea is also one of the more common possible side effects of dopamine medication. So carbidopa levodopa will sometimes cause nausea. So just a couple of things to mention here regarding treatment. One is that the nausea medications, Zofran, or Ondansetron is the main anti-nausea medication that's advisable to use if a prescription medication is needed for nausea. If Carbidopa-Levodopa is identified as the source of nausea, then there is standalone carbidopa by itself without the Levodopa, which is the old brand name Lodosyn and is a surprisingly expensive medication, but additional carbidopa with each pill of Carbidopa-Levodopa can sometimes help to reduce that associated nausea. A note of caution that there are several other anti-nausea prescription medications, Reglan, Compazine, Phenergan, and these should be avoided if at all possible among people with Parkinson's, because part of how these medications treat nausea is by blocking dopamine. Of course, we're trying all these other things to get dopamine into your system, the treat the motor symptoms. So Reglan, Compazine, Phenergan, should be avoided if possible, because they blocked dopamine.

So another gut type of symptom is at the upper end of the GI tract, and this is the possibility of drooling. So the reason that some people with Parkinson's drool is because they don't swallow as often as spontaneously as they normally do. We think that the amount of saliva production is actually normal, but the saliva just isn't being taken down as normally as it should be. Combine that with the fact that

people with Parkinson's will sometimes have a forward head position or a forward trunk position and a mouth full of saliva with the forward position leads to drooling. So treatment of drooling can be either of a two-pronged attack, either increase the swallowing or actually do decrease the amount of saliva that's being produced. So some treatments in this respect, probably the simplest thing, the nickel and dime solution is to keep something in your mouth. This will trigger you to swallow more often, and sugar-free chewing gum, sugar-free hard candy can be quite helpful situationally to reduce drooling in this way. And as mentioned earlier, sugar-free often has a sugar alcohol like sorbitol in it, which can have some anti constipation effect.

There are prescription medications, pills that can help to reduce drooling. Glycopyrrolate is one of the main ones of these. I'm not a big fan of this medication, because part of how it helps with drooling is through what is called an anti-cholinergic effect. And anticholinergics also have side effects besides dry mouth, which we're kind of trying to achieve in this case. It can also cause dry eyes, make constipation worse. It can make people feel fuzzy. So it sometimes is useful, but it's not something that I draw upon very often. Another tool in the toolbox is to use a certain eyedrop. Atropine eye drops in a non-conventional manner. So these drops, which might otherwise be used for glaucoma or something else, you can put one or two drops underneath the tongue, and it will dry the mouth out for an hour or two at a time, which can be helpful situationally.

The most effective kind of most powerful treatment that can be used for drooling is to do injections of some type of botulinum toxin like Botox or Myobloc into the salivary glands. If you eat sour candy and you get that pucker right here, that's the parotid gland squeezing to crank out more saliva. And so you can do injections of these medications there and often another gland underneath the chin here. This is done every three months and can be quite effective for reducing drooling during that three-month period. So let's move on to talk about another autonomic symptom. We've talked about the GI tract. Now let's talk for a moment about bladder symptoms. So what often happens in Parkinson's is that there's a sensation of overactive bladder. This may manifest as a sense of needing to urinate urgently or more frequently than normal. The bladder pictured here is basically a big ball of muscle.

And among some people with Parkinson's, that muscle is irritable and it can clinch and that makes you feel like you need to urinate right away. And so the main thing that we try to do is calm the bladder muscle down. So there are a number of medications that can be helpful in this regard. I just mentioned that some anticholinergics can have some undesirable side effects. These are more peripherally acting anticholinergics that will have more of an effect on the bladder and less of an effect on the brain. And some of these anticholinergic medications that can be helpful for overactive bladder are listed here with old recognizable brand names like Detrol, Vesicare, Sanctura, these are now all available as generics that are more easily accessible than they might've been 10 years ago. Another note of caution, Oxybutynin is another overactive bladder medication. It's the least desirable one, it's cheap, which is good, but it does have more of the possible side effects, including more cognitive fuzziness than some of the other ones do. So the other options are preferable.

So I mentioned some of the possible anticholinergic side effects, especially for Oxybutynin, more than the other options. A couple of, maybe one other option here for overactive bladder is a medication that

came out a few years ago that works in a different way. The bladder has these Beta-3 receptors and this medication Myrbetriq by stimulating these receptors accomplishes the same in that it calms the bladder. This medication probably has fewer side effects because it's not a so-called anti-cholinergic medication, although it does have a possible side effect of hypertension, raising blood pressure. That's also so far available as a brand name medication so it is more expensive. Beyond these things, which your Parkinson's specialist or your primary care doctor may be able to help with. If it gets beyond, you know, a couple of these tools then often a consultation with a urologist will be appropriate.

So another, a genital urinary symptom is to talk about erectile dysfunction. This is a not uncommon symptom among men with Parkinson's. And the first thing to consider is that certain other prescription medications used for high blood pressure like beta blockers, or some most antidepressants have erectile dysfunction as a possible side effect. So it can be an effect of Parkinson's, but it can also be a side effect of certain medications. So if this is a problem, then consider that potential impact and discuss with your prescriber, whether something might be adjusted in terms of beta blockers or antidepressants. And then there are the usual suspects for the treatment of erectile dysfunction. Some of these medications are now available generically, so you don't see them advertising during football games and baseball games, as much as you used to. So this is Viagra, Cialis, Levitra, a brief note here that these medications, although now generic can sometimes still be expensive. And if you've not ever heard of goodRX, goodRX.com, this is a free thing that allows you to compare prices among different pharmacies, and also to print out a free coupon that allows you to use this coupon kind of as your insurance, rather than actually using your insurance. And they can bring the costs down by in the case of some of these medicines, 98% of a cash pay price of \$400 a month, and then a goodRX price of \$10 a month. It can make a big difference.

One main note of caution for these erectile dysfunction medications is that they work by dilating blood vessels. And so be aware that that can cause other blood vessels to dilate also, which can make your blood pressure lower and cause lightheadedness. Beyond those medications again, consulting with the urologist would likely be the next step because there are some other more advanced treatments that may be available. So another autonomic symptom, we're getting towards the end of the autonomic category is orthostatic hypotension. So this is two big words that basically mean your blood pressure goes down when you stand up. And this happens a little bit to everyone, with or without Parkinson's. I stand up and my blood pressure drops five or 10 points. Then my blood vessels tighten up to accommodate for that. So I don't really even notice it. It happens in a second, but among people with Parkinson's that tightening up response is lost due to autonomic dysfunction.

And so the symptoms that can occur with this are lightheadedness, even fainting. A couple of other less commonly recognized symptoms include something called Coat Hanger pain. So the big muscles in the back of the neck and the shoulders, they require a lot of blood flow to function and to be happy. And if your body is kind of a tube of water, when you're lying down, your heart has kind of an easier job. It's just pumping blood horizontally, but then you go upright, your brain doesn't get enough blood flow and you can feel lightheaded. Maybe your shoulders don't get enough blood flow and you get this aching pain in the shoulders. And you can identify that this may be the symptom Coat Hanger pain related to low blood pressure, because if you then lay back down, the pain goes away almost instantly. So those are some symptoms that can relate to orthostatic hypotension.

The way to check for this at home is to get an upper arm blood pressure cuff. You can get usually for 30 or 40 bucks at the store online and lie down for five minutes and then check your blood pressure and your heart rate, write it down and then stand up for two minutes and check again. And what's normal is if the numbers are within 20 points, that top systolic number, maybe it's 140 when you're lying down, it's 125 when you're standing up and that's okay, but if it's dropping 30, 40, 50, 60 points between the lying down and the standing up position, then that may be enough to cause symptoms. And that's why we might treat it.

So again, one of the first steps here is to think about are medications that you're on for something else, maybe for years, you've had a history of high blood pressure. Now, as Parkinson's goes along, maybe the game is changing. And if you're on blood pressure medications, maybe those could be lowered. And that's something to talk with your primary care doctor or cardiologist. And so your medications sometimes have unintended consequences. So we found a bunch of these clogging your arteries, their cholesterol pills. So how to treat some of the symptoms that can happen with orthostatic hypotension, stand up slowly, that's probably the most basic thing to do. Compression stockings can be helpful. In the solidarity, I've got these pictured here, kind of blue compression stockings on myself, which also leads me to realize that the person in the top picture here is having an unrealistically easy time, putting their compression stockings on. And so you might look online for five or 10 bucks, you can get these things which are called donning gloves. They're covered with little rubber bumps and make it easier to grip the socks. You can pull it on. I had to put these on to pull my compression socks early this morning. So that's potentially a worthwhile investment donning gloves, like putting on gloves, D O N N I N G.

Other ways to mitigate the impact of orthostatic hypotension is to make sure you're staying well hydrated, again, shooting for at least 64 ounces of water a day. Maybe not just water in this case, but also electrolyte beverages, Gatorade, or something else to increase your electrolytes because sometimes we'll actually, instead of doing what doctors normally tell people, which is to eat a heart-healthy diet, low salt. If orthostatic hypotension is a big issue, then we start saying, drink more water, eat more salt. If you have any heart issues, of course, that's something you would want to check with your heart doctor on.

So then some of the medications to treat orthostatic hypotension, fludrocortisone, or Florinef is a medication that causes your body to hold on to more salt and water. So it kind of fills the tank. Midodrine is a medication that constricts blood vessels. So it squeezes the tank. Droxidopa or Northera is a medication that's basically the precursor to norepinephrine, the same way that levodopa turns into dopamine Droxidopa turns into norepinephrin, and this helps to keep the blood pressure up. Another medication, this is a little deeper in the bag of tricks is Pyridostigmine or Mestinon. This is a medication for a disease called myasthenia gravis. And what this medication does is increase the amount of acetylcholine, this messenger that communicates from nerves to blood vessels. And this can sometimes be quite helpful for raising blood pressure and causing a more normal response to position changes. So one or more than one medications from this list can be considered. These medications almost always would be started only after a person is down titrated and even gradually taken off of any blood pressure lowering medications.

So that's the autonomic category of medications, and that's a big one. A lot of those symptoms are some of the most bothersome symptoms that a person with Parkinson's might have. So again, as we now shift into talking about sleep, none of this is meant to be an exhaustive discussion of any one of these symptoms. Any one of these symptoms could have its own lecture, but kind of generating some ideas about things that might be helpful for you to discuss with your prescribers. So, as we shift into talking about sleep, we'll talk about a few main categories, including insomnia, daytime sleepiness, restless legs, and REM behavior disorder. So insomnia can mean, of course, either difficulty falling asleep or difficulty staying asleep. And actually that difficulty staying asleep is particularly common among people with Parkinson's. This may be due to physical motor symptoms of Parkinson's like stiffness, if your medication is wearing off during the night, difficulty repositioning due to bradykinesia, that can happen during the night. Tremor, likewise, there are also just some chemical changes in the brain that happen as part of Parkinson's to make insomnia more likely. And so let's first talk a little bit about the non-medication options for the treatment of insomnia.

Most important is good sleep hygiene, which doesn't mean take a shower before bed. It means optimize some behaviors surrounding the sleep habit that can improve your chances of having a good night's sleep. So during the day, exercise and make sure that you're exposed to bright, natural sunlight. As it gets to bedtime, no screens before bed, no news before bed, certainly not in bed and a relaxing bedtime routine. One that I find helpful is no clock watching. So rather than saying, oh, I've got four hours and 52 minutes until my alarm goes off, now four hours and 51 minutes, instead just make a commitment to not look at the clock and that will give your brain one less thing to fixate on that might make it easier to fall back asleep.

If you've been in bed for 15 or 20 minutes, and it's just not happening, then get up, do something boring, so again, not something that's going to agitate or excite you like the news or an exciting show. What's something pretty boring and then get in bed and try again once you're sleeping. The other thing that's helpful and that's recently been disrupted as we've gone from daylight saving time back to standard time is that it's important to set a consistent wake up time seven days per week, a consistent bedtime is also helpful, but it's really that consistent wake up time to let your body kind of know what it's supposed to expect and what you want it to be doing.

So medications for insomnia, over the counter medications, there's not a lot that I'll recommend for Parkinson's for any reason, but over the counter melatonin is something that can be helpful for people with Parkinson's for insomnia and for something we'll talk about in just a minute. So melatonin can be quite helpful, often starting with three milligrams in the evening, and maybe going up to as much as 15 milligrams an hour or two before bedtime, and then prescription wise, the main tool that we'll use is clonazepam. So this is a benzodiazepine, its old brand name was Klonopin, and clonazepam is a more powerful sleeping medication. Both of these can help you fall asleep and stay asleep.

Some antidepressants are what are so-called sedating antidepressants. These are mainly trazodone and mirtazapine. Mirtazapine, also known as Remeron. And so these medications are sometimes used just for insomnia in people with or without Parkinson's. But if a person is dealing with some depression or

anxiety as well, then trazedone, mirtazepine, these can sometimes help get two birds with one stone. Another note of caution, diphenhydramine over the counter, which is, it's what Benadryl is. It's what is makes the PM in Tylenol PM and Advil PM, best to avoid this. Again, this medication diphenhydramine has what are called anti-cholinergic effects. And so I have some people who say, ah no, I don't really take anything for sleep. Well, I take two Benadryl every night, and I can't understand why my memory has really gone downhill in the last year or so that I've been doing that. Well, there's a straight-line connection between those two, diphenhydramine can cause foginess as well as dry eyes, dry mouth constipation. Another note of caution, Ambien, and Lunesta. These are common prescription medications for insomnia. They can worsen dream acting out, which we'll talk about in just a minute. But people with Parkinson's generally should avoid those medications.

So the flip side of insomnia, often hand in hand with insomnia is daytime sleepiness. So either an increased need for sleep during the day in general, or in particular sudden, uncontrolled need for sleep falling asleep while you're eating, falling asleep while you're talking to someone, that excessive daytime sleepiness is an issue that can sometimes arise. So addressing the insomnia, if present is the first step in treatment, if you haven't ever had a sleep study, you might talk to your primary care doctor about having a sleep study because sleep apnea is common among people with Parkinson's and if that's present, then treating it to can be quite helpful for improving daytime alertness. It's important to realize that rest and naps are okay. Some people say, oh yeah. If I would just take a 20-minute nap in the afternoon, I would feel pretty good, but I don't want to do that. And just to kind of reframe and say, well, if it's that or another pill, maybe it's better to take that 20-minute nap.

And then re-evaluating Parkinson's medications, especially as it pertains to those sleep attacks, that's an issue that's more likely with the family of medications called dopamine agonists, ropinirole, Requip, pramipexole, Mirapex. And so if you're having sleep attacks, then potentially using less of those medicines and more of something else like Carbidopa-Levodopa if needed. So how can we treat the daytime sleepiness itself? Well, one of the most widely used drugs in the whole world is caffeine and caffeine can be useful as a tool for treating daytime sleepiness, best to keep it before lunchtime throughout the morning. If you take it much after lunchtime will start to cause insomnia and contribute to that underlying issue. We will sometimes think about using stimulant medication. So methylphenidate, which is Ritalin can sometimes be helpful. This is a schedule two controlled substance, which has some logistical hassle factor issues that go along with it that can sometimes be helpful or Modafinil, Provigil is a medication originally used for excessive sleepiness among people with sleep apnea but can sometimes be helpful even in the absence of sleep apnea.

So another sleep related issue to talk about is so-called restless legs. And I like to point out that there's maybe at least two different things people mean when they say restless legs, they might be referring to what we actually call restless leg syndrome, which is an uncomfortable sensation in the legs that you feel like you need to move the legs. This tends to be worse in the evening, worse when you're lying down. About 80% of people with restless legs, will also have what are called periodic limb movements. This is when the legs move of their own accord. So the legs will actually jerk or have some other sort of complicated movement that can last up to a few seconds. And it tends to occur by the clock like every 20 or 30 seconds as you're lying there this movement happens. So that's a periodic limb movement disorder.

The treatment of both of these things tends to overlap, restless legs and periodic limb movements. And actually the medications that we use to treat Parkinson's motor symptoms may also help with restless legs. So dopamine agonists levodopa will sometimes help with these symptoms. Other medications that we might use specifically for restless legs include Gabapentin, which also has positive effects for treating pain. And then clonazepam can help restless legs and jerky legs in addition to being mentioned earlier for the treatment of insomnia. In some cases of severe restless syndrome we will refer, we'll end up using opiates or narcotic medications. As mentioned earlier, this is not a course of first resort, kind of a last resort because they make constipation worse. There's the hassle factor involved, they may cause some fogginess, but in very severe cases of restless legs, we will sometimes use opiate medications.

So another thing that can happen during sleep is dream enactment. So we call this REM sleep behavior disorder. REM stands for rapid eye movement which tends to be when you're dreaming. And so normally when we dream, we don't move. Our brain has a safety mechanism in place to paralyze your body when you're in REM sleep. But among people with Parkinson's, this safety mechanism is sometimes lost, and people can act out their dreams. This might be as benign as sleep talking, but it could also be punching and kicking. It can lead to falling out of bed or other more dramatic behaviors. And so there's some practical treatment considerations, move sharp things away from the bed, maybe pad corners of the nightstand if you were to fall out of bed, put something soft next to the bed pillows, or even an extra mattress, maybe put a bed railing along the side of the bed.

And then bed partners will sometimes even need to sleep separately to keep both people safe so that no one's taking a left hook in the middle of the night and then medications for REM behavior disorder. That again is these familiar suspects of melatonin and clonazepam, which both can be very helpful for shutting down this dream enactment behavior. All right, we've covered a lot of ground already stand up stretch, get the blood flowing if you're lightheaded when you stand up, think about using some compression stockings. All right. So we'll shift gears into talking about mood and thinking, depression, anxiety, cognition, which means thinking or memory. So my other psychiatrist only charges a nickel says Charlie brown here.

So let's talk about depression. So depression is a low mood, a blue mood, maybe manifesting with decreased interest in the things that you normally like to do. And it's common among people with Parkinson's and it's often unrecognized. The reason it might go unrecognized is that some depression symptoms overlap with Parkinson's symptoms. So less facial expression can be part of Parkinson's. And if somebody says, oh, well, that's just how their Parkinson's looks in their face, they might overlook if it might be a sign of depression. Low energy can happen with either depression, Parkinson's, or sleep can happen, depression can happen in Parkinson's. And so the key is feeling depressed. If your mood is low or blue, if you're feeling down more often than not over the course of the past couple of weeks, and that's the criteria that we use to diagnose depression.

So the treatment of depression, we'll talk about medications briefly, but moving your body and also kind of faking it until you make it. There's this term out there called behavioral activation. When you're depressed, you don't feel like doing anything, but if you just start doing something, the activity itself can

have a treatment effect. Exercise, kind of to double down on the prior point, if you can get yourself to go for a walk or be more physically active in an exercise focused way, there's evidence that that helps depression and then talk therapy. There's some research that shows that talk therapy, cognitive behavioral therapy is as good as medications in some cases for depression.

So let's do talk about medications though. Depression is a chemical issue in the brain often and moving your body, being active can help to improve the release, increase the release of some of the feel-good chemicals that our brains are in charge of making. But if there's really a more severe serotonin deficiency, or maybe it's related to the dopamine deficiency, then medications can have a powerful treatment effect for the treatment of depression. Among the medications that are used for Parkinson's motor symptoms it's notable that the dopamine agonists, ropinirole pramipexole can actually have some antidepressant effect on their own. And sometimes these are even used among people that don't have Parkinson's as a kind of later line treatment option for depression. The most widely used medications for the treatment of depression are the selective serotonin re-uptake inhibitors. So your brain is making serotonin, but maybe it's not as much as it should be. And these SSRIs allow your brain to use more of its own serotonin. So these are the medications like fluoxetine, Prozac, sertraline, Zoloft citalopram, Celexa, escitalopram, Lexapro, paroxetine, Paxil, all of these medications can be helpful. And these medications are well-known because among many people they are very well tolerated.

There are many other prescription antidepressants, bupropion, venlafaxine, duloxetine, trazodone, and mirtazapine were mentioned earlier because they can sometimes help with sleep. And so this slide could have a lecture of its own but be aware that there are options out there. And if one doesn't help another one may still help. Anxiety often goes hand in hand with depression. And for some people with Parkinson's anxiety can be their worst symptom. Anxiety and tremor can often create this negative feedback cycle where the anxiety makes the tremor worse, and the tremor makes the anxiety worse. So disrupting that cycle by treating anxiety in one way or another is important. So maybe even more so than for depression, anxiety can often respond to non-medication options, exercise, talk therapy, meditation can actually be very helpful for anxiety. Meditation is about changing your relationship with your thoughts. Nobody can stop their thoughts, but if you can attach to your thoughts less than meditation is kind of a way of training yourself to do that.

Every time you find yourself getting caught up in your thoughts to take a step back and go back to focusing on your breathing or your heartbeat or something other than thoughts, then every time it happens that you get caught up in thoughts, which we all do about every seven seconds or so, just go back to thinking about the breath. The medication treatment of anxiety overlaps a lot with the medication treatment of depression. So the same list of SSRIs. I think here I switched to the brand names instead of the generic names, other prescription medications, again here, I listed the brand names for some of these, instead of the generic names, clonazepam, which was mentioned several times in the context of sleep can also sometimes be helpful for anxiety. Although if you're taking it during the day, the sleepiness or fuzziness that can occur as a side effect, just be aware of that with a note of caution.

So we'll start talking about memory. Don't tell anyone, but I actually forget lots of things. So cognition is the term that we'll use to kind of encapsulate thinking and memory and among people with Parkinson's there can sometimes be an issue with recall. So unlike other diseases, like Alzheimer's where if you think of your memory like a filing cabinet and Alzheimer's people will kind of lose the ability to put new files in the file cap, in Parkinson's the files are still going in, but it can be harder to recall that information. And so having a cue or a trigger or a reminder can be helpful, but this spontaneous recall issue, tip of the tongue phenomenon, is a common symptom. There can also be issues related to what's called executive function, which means things like decision-making and planning. So these are the types of function that tend to be somewhat more effected in Parkinson's than they might be in other diseases like Alzheimer's.

So the treatment of cognitive symptoms, again, exercise is mentioned here as well. What's good for your body is good for your brain. Mental activity, people will often ask about puzzles, crosswords, Sudoku. I don't know that those things are something that you have to torture yourself with, but if you enjoy doing them, then anything that keeps you mentally active, anything that's not watching television, basically whether it's reading a book or doing puzzles or learning about things, learning a language, learning an instrument, all of those forms of mental activity are like exercise for the mind. And then also social activity. There's been obviously a huge obstacle to this during the pandemic but being socially active is good for the mind.

And then reducing sedating medications. I just spent all this time talking about medications that can be used for insomnia, but if a person is finding that they're more fuzzy during the day, we sometimes strive for a compromise between getting good sleep because insomnia will cause cognitive symptoms, fuzziness, slowness, but trying to balance that with potential sedating effect of medications, and again, avoiding diphenhydramine if at all possible. So you need more activities, start with some light dusting of your exercise equipment. So mood and thinking exist on a spectrum. There are some changes that are just part of the normal aging process. There's a gray area in between called mild cognitive impairment. And then if thinking and memory issues are severe enough that they're impairing a person's ability to be able to live alone then that's the functional definition of dementia. So normal aging, dementia, and this gray area in between that we call an MCI, mild cognitive impairment.

The medications that we use for cognitive impairment have been studied in mild cognitive impairment and in dementia and for a variety of reasons, they haven't really proven to be helpful in mild cognitive impairment. We will still sometimes use them, but the medications have more proven benefit among people that do have dementia related to Parkinson's or otherwise. And a couple of these medications are cholinesterase inhibitors. This choline, acetylcholine has been mentioned in a few contexts, diphenhydramine is anticholinergic and can make memory worse. These medications rivastigmine, Donepezil are procholinergic by inhibiting this cholinesterase enzyme. And this can help with thinking and memory. Another medication is Memantine or Namenda, and these can sometimes be used together.

A symptom that can sometimes occur, typically in more progressed stages of Parkinson's is hallucinations. Visual hallucinations refers to seeing something that's not there. And that's the most common type of hallucination when this issue does occur. People might have an illusion like thinking

that a pattern on the wall is a face or they might actually see things that aren't there, like people, figures or animals or children. And if this is bothersome, if it's frightening, then there are medications that can potentially be helpful. I brought this up with one of my patients last week, who was occasionally seeing small children, wasn't bothered by it, could tell what was real and what wasn't real. And he said, what frightens me is that you're going to tell me to take another medication. And so we're balancing out, you know, what do we need for quality of life? So the same cholinesterase inhibitors that were mentioned on the prior slide can also help to reduce hallucinations. And then there are some medications that are called anti-psychotics. Psychosis is the term for seeing or hearing things or believing things that aren't real. And so anti-psychotics may include Quetiapine, which is Seroquel, a more expensive brand name, only medication is Nuplazid, which can be helpful for reducing hallucinations. And then a medication generally only managed by a psychiatrist because some blood monitoring is necessary is Clozapine, Clozaril. Other anti-psychotics should be avoided if possible, because part of how anti-psychotics function is by blocking dopamine, which can make the motor symptoms of Parkinson's worse.

So Haldol, Risperdal, Abilify, Zyprexa, Geodon. Sometimes these are a necessary evil if the hallucinations are severe enough or if there's agitation, but those medications should be avoided if possible. So a couple of other important things as we are wrapping up here, pain is a common and often unrecognized symptom in Parkinson's. It can be hard to sort out, even for me as a Parkinson's expert. Well, does your back hurt because Parkinson's is causing you stiffness or is it because you have some wear and tear from having lived with your back for 70 years? So tightness can be a way that Parkinson's pain can manifest. There's a specific symptom called dystonia, which refers to a forceful contraction of muscles. Often the ankle kind of causing the foot to turn in and causing cramps in the calves or in the bottom of the foot and pain, dystonia, these sometimes occur with motor fluctuations.

So when your medication wears off, maybe the symptoms are more likely to occur. In which case adjustment of Parkinson's medications can sometimes be helpful for pain. Other things that can be used for treatment for pain. We'll talk about non-medication options, stretching, massage, warm baths, things that feel good for your body. Obviously, it can help to reduce these symptoms sometimes. As far as medications, generally over the counter pain medications like acetaminophen and ibuprofen are acceptable for people with Parkinson's as well. And that may be all that's needed. There are a few prescription medications that we will sometimes consider Gabapentin, which is Neurontin is widely used for neuropathy. It can be helpful for other kind of nerve pains. A similar medication is pregabalin, which was Lyrica as a brand name. And then as has been mentioned a few times avoid narcotics, if possible. I didn't mention it here, but fluoxetine, an antidepressant, Cymbalta is its old name is a medication that can help depression and anxiety and potentially also pain.

So the narcotics have these potential issues of long-term dependency or worsening of constipation. If a person has dystonia like the foot turning in, then botulinum toxin injections, which were mentioned earlier for drooling, Botox or these other toxins can be injected in the leg muscles or other areas if pain is focal to that area, or if the dystonia needs to be treated because it's otherwise impairing leg mobility while walking or other symptoms like that. One last maybe fairly minor symptom to mention but it can be quite bothersome is Seborrheic dermatitis. So this is the medical term for dandruff. And some people with Parkinson's will develop this seborrhea, seborrheic dermatitis between their brows and in the



creases along their nose. And it can be kind of socially impactful to have that issue. And so there are a number of treatments that can be helpful.

Sunlight exposure actually can reduce seborrhea, anti-dandruff shampoos can be rubbed onto the affected areas besides just in the hair. And these are things like Selsun and Head and Shoulders, Neutrogena T Gel, there are either over the counter or prescription medications available that are an antifungal Ketoconazole cream, or sometimes just a low dose of steroid, a hydrocortisone cream can be helpful. I mentioned sunlight exposure can help with seborrhea. I don't have a slide on it here, but melanoma risk is increased among people with Parkinson's. And so, regardless of whether you're getting a lot of sun, if you have at any point previously in your life, you should see a dermatologist once or twice a year for a skin check. So this has been a whirlwind tour. We've covered a lot of symptoms in the autonomic category, as well as sleep, mood, thinking and a couple of other important things. So thank you very much for your attention and we'll have further information forthcoming in the future. Thank you very much.

Leigh Cocanougher:

Thank you so much Dr. Haug. We want to thank again our Peak Partners, Adamas, Amneal, Kyowa Kirin, and Sunovion, we'll see you all again soon.

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