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Depression, Anxiety & Apathy in Parkinson’s and How to Manage Them  
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Dr. Greg Pontone & Dr. Soania Mathur

Dr. Soania Mathur

Good afternoon everyone. My name is Dr. Soania Mathur. I'm a family physician, and also I've been living with Parkinson's disease for now over 20 years, almost 22 years. I have the privilege of serving on the board of directors for the Davis Phinney Foundation. And I have the distinct pleasure of being your moderator today as we all experience. And if we're a care partner, as we watch our loved ones experience Parkinson's disease goes much beyond motor symptoms of tremor, stiffness, slowness of movement. This disease affects us globally, with non-motor symptoms presenting in almost every bodily system. This, in turn, affects us not just physically but emotionally and mentally as well. And these non-motor symptoms, particularly mood disorders, can have a really significant impact on our daily life, our quality of life.

Dr. Soania Mathur

So today we're going to explore further the topics of depression and anxiety in Parkinson's disease, how they are related, how to recognize the symptoms, the treatments that will benefit us both medical and non-pharmacological as well. And we're also going to discuss the topic of apathy, which is a very common and impactful symptom that goes beyond the sort of general fatigue that this disease brings to us. To help us tackle these important topics today's is Dr. Gregory Pontone, an associate professor in the departments of psychiatry and neurology at John Hopkins university school of medicine in Baltimore, Maryland. He's also director of the John Hopkins Parkinson's disease neuropsychiatry clinic. And both his clinical work and research are directed towards neuropsychiatric symptoms in Parkinson's disease, such as cognitive impairment, anxiety, and depression. Welcome, Dr Pontone.

Dr. Pontone

Thanks for having me.

Dr. Soania Mathur

So maybe to get started, we might want to start with sort of defining what the problem is in terms of how common is depression and anxiety in Parkinson's disease?

Dr. Greg Pontone

Well, it turns out that most disturbances of mood are overrepresented in Parkinson's compared to the general population. And there are several reasons for that. One is the biology of Parkinson's itself. So, in addition to depleting dopamine in the brain, it also depletes or perturbs the concentration of neurotransmitters like serotonin and norepinephrine, which are vitally important for mood regulation in addition to dopamine. And so when you think about depression, and I don't mean just being a little down or sad, but what we would clinically classify as depression, about a quarter, 25% of people with Parkinson's will experience a major depressive episode at some point during the illness. And at least half will experience symptoms that are impactful on their day to day life over the course of the disease, even if they don't have a major episode. Now the interesting thing about depression and Parkinson's disease is that it is very often accompanied by anxieties. So much so that I would say that if you're diagnosed or suspect that you have depression, your doctors should also screen for anxiety because they occur together in the majority of cases. Anxiety is also very common, probably occurring in about half of everyone with Parkinson's disease at some point in terms of having a clinically important symptom and a full-blown disorder or something like panic disorder, what we call generalized anxiety disorder occur in up to a third of people at some point with Parkinson's.

Dr. Soania Mathur

And how do these numbers compare to the general population?

Dr. Greg Pontone

So if you look at the world health organization, depending on which category you're looking at, you know, these are all elevated above the general population and elevated beyond that of other neurological diseases as well.

Dr. Soania Mathur

That's interesting actually that it would, it would be such a significant difference, but I mean I think a lot of us have an idea of what depression and anxiety are, but how can they be distinguished from changes that we would normally experience sort of being sad or stressed about our diagnosis of an incurable, progressive illness. How do they differ from just feeling down about things?

Dr. Greg Pontone

Yeah, I think that's probably the most important point here is that the depression and anxiety that we're talking about are to the extent or severity that they interfere with functioning. Whereas you know, you can be down or blue and still function when you're sad or depressed or uninterested to the point where you're actually not completing your day to day activities. That's when it crosses the line and becomes a clinical disorder, and in large part, we think that's because it's biologically based. You know, if you have Parkinson's, you can't just decide to wake up and move better. You know, you need a little help from some medication. I mean, certainly exercise and the things that you do are very important but without that dopamine, you, you know, you're just not going to move well, and the same way when you have a clinical, biological depression or anxiety disorder. it doesn't matter how disciplined you are, how hard you try, how much support you get from your, you know, a spouse or caregivers.

You're going to need a little bit of biological help in the form of medications to fully recover. Now that said, just like the physical problems in Parkinson's being active talk therapy are all really important. But I just want to make this distinction because oftentimes I think, you know, people who are motivated and disciplined their entire lives get depressed and then it's almost as if the community turns on them. And all of a sudden, you're lazy. And that's not the case at all. It's, I mean, a kick in the pants is not going to fix these problems. They're like any other medical condition you need to be treated.

Dr. Soania Mathur

I think that's a really important point because I remember when I was in family practice that stigma attached to mood disorders was so significant that patients would often not come in to get the help they need. And I would tell them, you know, it's like breaking your arm. You wouldn't walk around with a broken arm. You need intervention. So why wouldn't you come in for your mood? But I think there's, unfortunately, that stigma that's attached. But that distinction about what you're saying about how the mood impacts on functioning I think is really important for us to remember. But clinically, how do you diagnose it as a neuropsychiatrist because we have symptoms of depression sort of anyway, when a patient with Parkinson's comes in with slowness and movement or lost appetite or weight loss or energy, I mean all symptoms of depression and Parkinson's. How do you kind of distinguish between the two?

Dr. Greg Pontone

So that's a great question. And that's the key clinical sort of differential is how much of this is a, you know, a symptom of Parkinson's. And how much of this is attributable to the depressive disorder because of that overlap. So, you know, low energy is a symptom of both depression and Parkinson's. So, if you have potentially both, how do you know which one is causing it? And so because we treat depression as a syndrome, we have a threshold of five symptoms or more to meet the threshold for a major depressive disorder. And you know, there are things like sad mood, although you can absolutely have a neutral mood and still have depression. I think that's probably one of the other important points is just losing your sort of motivation or interest in things is sufficient. You don't necessarily need to be sad or tearful to have depression.

In addition to that, people often feel guilty or hopeless when they're depressed. People often have a sense that life isn't worth living or sometimes they become frankly suicidal. I, those thoughts are not normal. I mean, if you get demoralized, you know, you might think that maybe you weren't as successful as you could have been or that you've missed some opportunities. But it's rare for a person who's only demoralized to become frankly suicidal. And then there's another category of symptoms that we call neurovegetative symptoms that I think are very important in making the diagnosis of depression. So, these are things like psychomotor slowing. In Parkinson's, when you move slowly, we call it Bradykinesia. When we talk about depression, there's a symptom called psychomotor slowing or retardation that is very much like Bradykinesia, but it affects even more of the functioning.

So not only do you move slowly, but there can even be what we call speech latency. So I'll give you an example. People who are psychomotor slowed when they're depressed, you ask them a question, you say, Mrs. Smith, how's your mood? And then I always tell my residents, I say, count one, 1000, two, 1000, three, 1000. And then she responds, that's speech latency. So, there's a delay in her cognitive processing and then her verbal response. And that's very characteristic of a moderate to severe depression. A sleep disturbance. Again, that can be the Parkinson's or the depression. But sleep disturbance is very common in depression. In fact, not only is it a symptom of active depression, some people believe that sleep disturbance might be a prodromal or early risk that leads later to depression. Appetite disturbances. So in depression, it can go two ways. The most classic appetite disturbance and depression is lack of appetite and weight loss. But there are a substantial number of people who have what we call it, a typical depression where there they eat almost to comfort their emotional state. They overeat. And those same people who tend to overeat with depression tend to oversleep instead of have trouble with insomnia.

And then, you know, loss of energy. And then poor concentration are also symptoms that can happen in depression and, and the concentration problems and depression can be very severe. In fact, one of our biggest sort of mimics of dementia, not just in Parkinson's, but in the general elderly is depression. So, you can be so profoundly depressed that you appear as if you're demented in terms of your cognitive functioning. But the great news is that if it's from depression, and we can reverse it.

Dr. Soania Mathur

That's amazing. One of our listeners asked a question. They said, “I seem to need a lot of sleep, nine to 10 hours. Could this be a sign of depression or is it PD related issue? I don't feel depressed during waking hours.”

Dr. Greg Pontone

Yeah. So I guess the first caution would be if this is a change from your usual pattern of sleep. So let's say for the majority of your life you've only required six to seven or eight hours and all of a sudden you're sleeping nine or 10. The first thing I would tell you, and you know, I think if, if you have Parkinson's, you know this better than me, although I've seen thousands, it is one of the most fatiguing diseases. So, I would say almost certainly Parkinson's is contributing. It is, I mean, it's like carrying sandbags around all day. And so that could contribute. Depression, as I described, especially atypical depression, you might need more sleep. A sleep fragmentation is another reason. So, even though you're sleeping longer, the efficiency of your sleep could be diminished. So, the reason you're in bed nine to 10 instead of six to eight hours is because when you are sleeping, it's in the lighter phases or the less restorative phase is asleep. And so the thing that we would usually do and when someone who's more than usual is, you know, go get blood work, check your thyroid, have a test for sleep apnea. Right. And you know, maybe even have a sleep study to see if there's fragmentation in your sleep architecture.

Dr. Soania Mathur

Is there a difference between the type of sleep disorder that you get with Parkinson's disease versus depression? And you mentioned the difference.

Dr. Greg Pontone

No, absolutely. So, you know, there's many different ways that sleep can be disrupted either due to Parkinson's or from depression. But one of the most classic things we see in depression is what we call terminal insomnia, which is early morning waking. So, waking before you'd ideally like to, before your alarm clock goes off and being unable to return to sleep. And the classic pattern is you wake, you know, a few hours earlier than you'd like, and you start ruminating, you know, bad thoughts usually. And so that would be one of the patterns. But I've seen it manifest in many ways, middle waking, trouble falling asleep. And then of course, you know with Parkinson's the urinary urgency, some people take doses in the middle of the night. If you take immediate release dopamine before bed, that can be activating. If you don't take some dopamine before bed you can wake up because your ….. And so, I think sometimes journaling why you wake or what's associated with the sleep disruption can help your doctors put together what, which a disorder it might be attributable to.

Dr. Soania Mathur

Do you get REM sleep behavior disorder in depression or is that sort of exclusive to Parkinson's?

Dr. Greg Pontone

Yeah, so there can definitely be what we call a decreased REM latency in depression. Sometimes meaning that you fall asleep and go immediately into REM instead of sort of building toward REM. But otherwise you the REM sleep behavior disorder, unfortunately, that the majority of the time that's going to be associated with something bad, like an alpha-synuclein apathy like Parkinson's or dementia with Lewy bodies. We don't necessarily see that as a symptom of depression.

Dr. Soania Mathur

Okay. You mentioned this, that I think at the beginning about what causes clinical depression and anxiety and why it's more common in PD. Could you elaborate a little bit more? You were talking about dopamine and other neurotransmitters.

Dr. Greg Pontone

Yeah, so this is, you know I want to back up a little bit because what we call Parkinson's disease is probably more than one disease. You know, many roads lead Rome, and I think that's the case in Parkinson's. But even today, you know, we're learning more and more about the genetics of Parkinson's, but the lion's share, maybe 80, 85% is still what we consider to be sporadic Parkinson's. And in that sporadic group of people with Parkinson's, there's a model by Braak. He's a pathologist, and he stages Parkinson's in the six stages. And he thinks that in the sporadic cases, many of them actually start in the gut. We find Lewy bodies in the nervous system part of the gut. And then maybe by going along a nerve called the vagus nerve that feeds sort of the gut and innovates the gut.

Rather these Lewy bodies go into the base of the brain STEM. Okay. And to the ….. and the 10th cranial nerve, which is the vagus nerve. But we find lewy bodies there and then this is where it gets interesting in terms of connecting the depression and anxiety and Parkinson's and why this might happen. So that's a stage one structure is that brainstem and just above that is what Braak calls the stage two structures. They're called, two of them were called the …... So the ….. nuclei produce serotonin, which is crucial to mood regulation. In fact, most of our antidepressants work by increasing the levels of circulating serotonin. The locust rule produces norepinephrine. So not only is norepinephrine a dopamine precursor, norepinephrine is also a brain chemical port for mood regulation. And it's probably the second most popular thing found in antidepressants is norepinephrine.

And we know that Parkinson's affects those two brain areas, right? And depletes them of the norepinephrine and serotonin. And we know both of those are important for mood regulation. And then it's only after those stage two structures that we know are involved in mood, then it goes to the stage three structures which include the substantia nigra and that's where we start to lose the dopamine in Parkinson's. And so there's your trifecta s- erotonin, norepinephrine, dopamine, the three most important chemicals and mood. And we, we're not guessing, we know that probably in the majority of cases of Parkinson's, all of those systems are affected by the disease and the chemicals that are important for mood are decreased.

Dr. Soania Mathur

That might help explain why we think that depression might be a pre-motor symptom for Parkinson's disease if it's in that kind of stratification. That's very interesting. Just to move on a little bit, you described some generalized anxiety disorder and panic disorder, but in general, what are the different types of clinical depression and anxiety? How do they manifest in patients usually?

Dr. Greg Pontone

Yeah. So I guess starting with anxiety cause we've neglected it a little. The most, there's kind of four DSM, so diagnostic and statistical manual anxiety disorders that are well represented in Parkinson's. And so generalized anxiety occurs in about 13% of people with Parkinson's when they have an anxiety disorder. Panic disorder is also up there. In terms of prevalence, not quite what generalized anxiety is. Social phobia is very significantly associated with Parkinson's and some of that is, you know, probably biological, but some of that is also being self-conscious about symptoms and things of that nature. And then the sort of third one that we see quite a bit of that we think might be fairly unique to Parkinson's is a fluctuation. So, ON/OFF dopamine, medication fluctuation, associated anxiety. And so what people typically describe what that anxiety and this might be as is many as a third of the cases of anxiety we see in Parkinson's is that when they take their dopamine, their motor symptoms get better and they turn on.

But then as they start to wear off just before the next dose, usually they get really anxious, and that's the offstage as they enter the OFF state. And we think that unlike anxiety and people without Parkinson's, dopamine may be part of the answer for treating that type of anxiety. Now about a third of people who have any of those anxiety disorders I just mentioned and Parkinson's will have more than one. So again, once you find an anxiety disorder, look for other anxiety disorders, and also look for depression. Now depression, and I think this is important is you know, major depression is the one we worry about. But like I said, about half of people have clinically significant minor depression that isn't, you know, the full syndrome. But what we found is that if you don't identify and treat that minor depression, the risk for a major depression goes way up. And so, you know, our message is always that if you're a little bit depressed, work with your doctors and do something about it because it leads to a higher risk of the bad type of depression.

Dr. Soania Mathur

Right. And that brings me to the question that was also posed by someone who's listening that in terms of your medical treatment, would a neuropsychiatrist or a psychiatrist, a specialist in movement disorders, be sort of better able to care for someone compared to a general community psychiatrist?

Dr. Greg Pontone

Well, you know, that's the argument from my career, but the fact is that not many people do this. And so, you know, I don't think that that's going to be accessible to most people, but I will tell you that a good geriatric psychiatrist, a good neuropsychiatrist, or just to a psychiatrist who's paying attention and willing to work with your neurologist can do all these things reasonably well. The one that's a little trickier is when the anxiety is associated with the ON/OFF fluctuations. But even that I think can be a remedy as long as you make sure that your care team is talking to one another. So, if you have a good neurologist and a good general psychiatrist, I think they can work together as long as they're communicating and solve these problems.

Dr. Soania Mathur

Yeah, communication is the key thing for many aspects of our care. For sure. Can we talk a bit about the treatment, the pharmacological treatment versus the non-pharmacological treatment of depression and anxiety? Are they the same, or do you have to approach each differently?

Dr. Greg Pontone

Yeah, so I'm going to give you the good news first, and then I'll tell you the stuff that we still need to do better on. So the good news is that for depression and Parkinson's, we have great treatments. We have treatments that are at least as good as in the general population, and we have good evidence for those treatments. Antidepressants. The same antidepressants that we use for anybody's depression seem to be effective in Parkinson's disease. I'm going to give you just a few names, and these are names that have the best evidence currently. It doesn't mean that other things don't work. It just means if you were to just choose one as a first choice, these are the ones that have been tried and true in Parkinson's. The first one, it's a, from a trial called sat PD. That was a multicenter trial, including Hopkins is one of the sites.

Irene, Richard actually was the main PI at the university of Rochester. She's an excellent clinical trial. Is that a great put together? A really great trial affects her is the brand name of the medication or …is the generic affects her, is Effexor what's called an SNRI. So it gets a little bit of serotonin-norepinephrine. So your …. and your …., it's got all the bases covered. It's a medication that's been around for a long time. It's generically available and affordable. It's generally well-tolerated and it right now has probably the best evidence of any single agent and Parkinson's for treating depression. And the other really nice thing about Effexor is it's used equally as often for chronic pain. And I can tell you that people that I work with who have Parkinson's pain seems to be a common symptom as well. So, a lot of times you could get a two for one.

Dr. Soania Mathur

Yeah, that's an added benefit for sure.

Dr. Greg Pontone

Absolutely. So that's the best evidence. Now there are other medications that also have good evidence. So the SSRIs, the things like your, your Zoloft, Paxil, Lexapro are all good choices as well. And they might even be a little better tolerated than the effects are on average. They just don't have that benefit for pain. That affects or does either medications like Wellbutrin, many people use that. Unfortunately, it doesn't have the same degree of trial evidence. But I can tell you that anecdotally in our clinics we use Wellbutrin very often. That other advantage of Welbutrin is it doesn't interfere with sexual function. And that can be a big thing because almost all those other antidepressants can interfere with sexual function. And so Welbutrin is a nice option if that's an important thing or if you're one of the people who gets the sexual side effects from the other medications. So, there are all types of little tweaks. But the good news is that most of the antidepressants we have, regardless of class, seem to work well in Parkinson's disease.

Dr. Soania Mathur

And does that hold the same for anxiety? Would you use the same medications for anxiety as well.

Dr. Greg Pontone

So we, we use them. But the problem is, unfortunately that we don't really have any clinical trials directly supporting the treatment of anxiety with medications and Parkinson's. So we have pretty good trial evidence that cognitive-behavioral therapy works well for anxiety and Parkinson's. But we, there aren't any currently you know, try, you know, trials to support medication use for anxiety and Parkinson's. And that's something we're working on. But it's, it's a little difficult because we use a lot of benzodiazepines outside of Parkinson's. Benzodiazepines, which are good antianxiety medication, probably have additional risk in Parkinson's because they might increase the risk of falls. They might increase the risk of cognitive impairment and sedation, and so they might not be ideal, I'm not saying don't use them, but I use them with additional caution in Parkinson's. And then our main treatments for anxiety in the general population are a lot of those same antidepressants I mentioned before. So Effexor is effective for anxiety in many cases the SSRIs are effective for anxiety. They take a long time to work, you know, a month or two before they kick in. But they're generally well tolerated, but we think they've probably missed that fluctuation anxiety. They don't seem to do much to modify that. We need dopamine.

Dr. Soania Mathur

Do you find that considering anxiety and depression often occur in the same patient that if you sort of saw the depression, the anxiety tends to go along as well? Do they go away together or are you left with anxiety at times?

Dr. Greg Pontone

Again, yeah, I think it depends. The majority of the time they'll go to a way together because for instance, if you use an SSRI or Effexor, it's usually equally good for the depression and the anxiety. But if you have one of those more dopamine based ON?OFF fluctuation anxieties though their mood will get better and they'll still be anxious, especially at the end of those or with fluctuations. So it's, it's definitely something to that we need to do more to investigate.

Dr. Soania Mathur

And do any of these medications interfere with any of our Parkinson's medications? Do we have to be cautious about interactions between the two?

Dr. Greg Pontone

So this is one of those things where I'm going to give you a party line answer and then I'm going to tell you what happens in real life. So many people are on a [inaudible] or as elect. It's an MAOI, so mono amine oxidase inhibitor. And so all those brain chemicals that I talked about that are important for the regulation of mood, that dopamine, the norepinephrine and serotonin, that MAOI increases the concentration of those by blocking their breakdown. And so theoretically if you were to use one of those antidepressants I mentioned along with [inaudible] or one of the MAOI, selegiline is another one. It could build up and causes what's called a serotonin syndrome, which is too much serotonin. And that can be dangerous. And if you get a prescription from your neurologist for the as elect and then you get a prescription for an antidepressant from your psychiatrist, your pharmacist is going to send a dirty letter to both of them saying you shouldn't use these together. But I have to tell you that there is a scientific literature in Parkinson's showing that we use these things together all of the time with good, with a good safety record.

Dr. Soania Mathur

That's interesting. A patient's asking is Trazedone no longer considered a choice?

Dr. Greg Pontone

So that's a very interesting question. Trazadone is actually an old antidepressant that is no longer or very rarely used as an antidepressant. It's used as a sleep aid because it's very sedating and we use it at doses lower than we use it as an antidepressant. Its mechanism is pretty interesting. So most of the antidepressants that I, you know, interface with serotonin today are what we call selective serotonin reuptake inhibitors. So they stop the re-uptake of serotonin, which increases the inner synaptic. Serotonin. Trazedone is what's called a [inaudible] or a sari, SSRI. And so basically it's a serotonin agonist, so it's more directly stimulate serotonin, which you know, who knows, may have unique properties. And in fact, some new molecules are coming out that have that serotonin agonist property. So you may see a recapitulation of drugs like [inaudible], hopefully without the sedating properties becoming more mainstream. Antidepressants again. So I wouldn't say there's no role for [inaudible], but for instance, most people it would be to [inaudible] to you as a main antidepressant therapy. So we use it mostly for insomnia.

Dr. Soania Mathur

So you mentioned sort of things coming down the pipeline. Is there a lot of research going on in, in Parkinson's disease and mood disorders?

Dr. Greg Pontone

So not necessarily specifically in Parkinson's disease, unfortunately, but in the general population, new molecules for the treatment of mood that can then be carried over to Parkinson's are coming along all the time. And I have to tell you, every time I give a talk and I tell them about why Parkinson's is such a wonderful disease model for understanding the broken part and mood disorders, they say, well, maybe you can help us find better mechanisms, you know, by what you know of where the Lewy bodies are in the in Parkinson's. And so for instance, somebody just approached me about using ketamine for Parkinson's depression and ketamine. I don't know if you're aware, but ketamine right now is one of the hottest new antidepressant therapies in the nation right now. It works more quickly than our existing antidepressants and it has a sort of novel mechanism. [inaudible]

Dr. Soania Mathur

That's very interesting. We've talked a lot about the pharmacology behind treatment. What are some of the nonpharmacological treatments that you recommend to patient? You mentioned cognitive behavioral therapy for anxiety. Could you maybe describe a little bit about that and maybe some other interventions?

Dr. Greg Pontone

Yeah, so I, I think this is one of those things where I'm not that everything leads back to exercise, but there is great evidence that physical exercise is great for depression and anxiety and cognition. And that's in addition to, we know it's probably the best thing that you can do for your motor function and to slow down progression of the disease. So I guess the first thing I would say is if you're not exercising, why? Because it's going to help pretty much everything that happens here, whether it's, you know, on the mood side or the motor side. So in terms of therapies, cognitive behavioral therapy has great evidence in general for helping mood disorders of all kinds. And so what cognitive behavioral therapy does essentially is it looks at our thoughts and our behaviors. And when we have a sort of self-defeating cycle of thoughts and behaviors, it helps to realign that.

So whether you're actively depressed and there's a biology behind it or you've recovered from depression but you're stuck in bad habits, cognitive behavioral therapy is a great option because we think that when you're depressed that the biology produces what we call automatic negative thoughts. You know, like, I can't do it out, I'll goof it up, I'll lose. And so you're sort of self-defeating and then your behaviors follow that. Well, if I'm going to lose anyway, why get off the couch if you know, even if I exercise, I'm not going to move better. I have Parkinson's. And then you know, you're just in this downward spiral. And so what cognitive behavioral therapy does is it teaches you first to recognize the automatic self-defeating thoughts and then to not let it lead to what truly results in bad outcomes, which is the behavior of not getting off the couch to do what you're supposed to do.

Dr. Soania Mathur

And who can do cognitive behavioral therapy, who, which allied health care professionals or healthcare professionals in charge of that, I guess.

Dr. Greg Pontone

Yeah. So the good news is that it's ideally a, a number of different people can do this. So psychiatrists, psychologists, social workers, licensed therapists. The problem is who can do it? Well, and the one piece of advice I give people is, you know, ideally start first with your insurance provider. See if there's anybody who is sort of certified to give CBT who takes insurance. Sometimes that can be rare, but start at least there you have a list to go by and then don't be afraid to walk in and walk out if the person, if you don't have a rapport with the person, because whether it's cognitive behavioral therapy or a more, you know, psychodynamic therapy, you have to have a rapport with this person cause you're gonna spend more than a few hours in front of them.

Dr. Soania Mathur

Yeah, no, I think that rapport issue is important for all members of your healthcare team. But particularly, I guess someone that you're going to receive counseling from. Somebody asked about TMS or transcranial magnetic stimulation. Is there any evidence or experience with that in depression, anxiety?

Dr. Greg Pontone

And Parkinson's specifically? Absolutely. So I want to address this in a very broad way. So brain stimulation in general appears to be a good and evolving option in Parkinson's disease and outside of Parkinson's. So the first thing I would say is our TMS. I know people who get that on their lunch break and go back to work. And so our TMS is usually very well tolerated. That one little issue with our TMS is, you know, if you stop it doesn't necessarily have an enduring benefit. So you have to get repeated treatments and it's really only good or it's indication currently is only for up to moderate depression. The more severe depressions, it doesn't really do a great job on but I think you're going to see that that treatment is going to evolve. In fact, I think ultimately it may become one of the mainstays.

The other one that we don't talk about much, but I, I think I at least want to put a plugin for is ECT electroconvulsive therapy. And this is sort of a big brother of our TMS and that's basically where we give you enough of a current to induce a small seizure. And it is to this day it's, it's one of the earliest, but to this day it is one of our most effective and fast working depressant treatments known to man. And it's, it's it, this is what people don't realize is that when we have a pregnant woman who's has severe depression, maybe even suicidal, we prefer that over medications because the medications could affect the fetus. Whereas the ECT itself as well tolerated ECT has been studied in Parkinson's, not just for its mood, improving effects, but it's also shown to temporarily improve movement in Parkinson's independent of whether you're depressed or not. And so when I have a patient with Parkinson's who's severely depressed or especially severely depressed with suicidal thoughts, ECT is a great option with the one caution that you have to get anesthesia before each treatment. And so the risk of a confusional state or what we call deliriums a little higher and Parkinson's and so you have to be a little cautious, but otherwise the evidence is there that ECT is a great option in Parkinson's.

Dr. Soania Mathur

It's funny, these old-time treatments, ECT in this case in Parkinson's disease seem it seem to work phenomenally well. Yeah. All these goodies. Just to switch gears a little bit. I'm getting a lot of people that are interested in knowing as care partners what they can do when they sort of notice changes in their loved one's mood. Maybe even before the person with Parkinson's does. What do you recommend to care partners?

Dr. Greg Pontone

Yeah, I think this is tough because depression most often is insidious. You know, it doesn't, it's not like a lightning strike. Like you go to bed fine one night and you wake up the next depressed, it sort of creeps in, you know, just like them, the movement changes, right? First you get a little Twitch in your finger and then the next thing you know you're tripping over your own feet. Same thing with depression. You know, you're a little less motivated, you enjoy things a little last. Pretty soon you say, geez, I haven't been out of the house in a week. And so I think the first thing that a good care partner should do is help bring this to clinical awareness. Like I said, a little depression most often leads to a worse depression later if it's unrecognized or untreated. And the thing is, it's, it's depression often isn't gonna it's not flamboyant. You know, it's not gonna, you know, you're not going to shoot blood out of your nostrils, your, you know, you're not gonna do Hollywood things. It's going to be you just sort of fade away from all the things you used to enjoy. And I think when you see that, you know, get excited, you know, cause they're not going to get excited, they're too depressed to be excited. So make sure that you help them get attention for this condition.

Dr. Soania Mathur

Be an advocate, I guess for your left one I think is important. We talked a little bit and I talked a little bit in the intro about discussing apathy and I think we should maybe touch on that. I mean that's something that's quite common in Parkinson's disease, something that can really be quite insidious and can really negatively impact a patient's quality of life. How would you define apathy, first of all?

Dr. Greg Pontone

Well, I think probably one of the best ways to tell you about apathy is I have so many, most of the patients that I work with, I've worked with for 10 to 20 years. So I have relationships with these people and they tell me all kinds of great stories or their loved ones telling me stories. And the story for apathy that sticks in my head is this guy was really, he had a great sense of humor. And I asked him one day, cause he didn't care, he was apathetic. It was his wife who was all wound up because he did nothing, right? He sat on the couch all day. I asked him, I said, you know, Mr. Smith, whatever his name was, right, do you know the difference between apathy and depression? He goes, “I don't know, and I don't care.”

And I said, kind of that kind of summarizes it, right? You didn't care. And so to me, apathy, most often, the patient isn't going to come to you and complain of apathy because they literally don't care. They don't good things, bad things doesn't matter. And so the example is it's to be the family that comes to you. They don't do anything, you know, it's hard to motivate them. When I do motivate them, it looks like they're just going through the motions. And this woman comes to me and says, you know, the other day my husband's sitting on the couch watching the world series. He's been a lifelong baseball fan. The power goes out, right? Comes back on, but the cable doesn't come out. So he's watching snow and she says, well, I'm just going to see how lazy he is and see how long he sits there watching the snow.

An hour goes by and he sits there watching the snow almost as contentedly as he was watching game seven of the world series. And then it bothered to get up and figure out what was going on. And that's when she knew, she said, something's really wrong here. You know, he was, he couldn't, he wasn't even bothered enough to do this. And so when you look at someone who's depressed versus someone who's apathetic, the first thing you're going to notice is there's very little to no emotion either way. I mean, they might get irritable if you try to push them to do something and they just don't feel motivated. But most of the time they're not going to be, they don't feel guilty about not doing anything. They don't feel sad. You know, they're not, when you come over to them and say, why are you doing nothing?

They're not. It's not because they're sad. They're not going to be suicidal. Apathetic people aren't suicidal, you know, they don't care. So you really have to kind of look for the things that aren't there to rule out the, the depression. I mean, you can have all those things in depression, you know, the lack of energy, the lack of motivation, the lack of enjoyment, which we call anhedonia. But usually with depression you'll also have this negative component of, you know, either irritability or sadness or hopelessness that just isn't there. And apathy. The other really interesting thing about apathy and this is, you know, holds up in the research, is that apathy seems to go in parallel with cognitive decline. So often what we see is that there'll be at least subjective complaints of either memory loss or disorganization along with the apathy.

Whereas with depression, you know, it could have a problem with concentration, but when you treat it, it goes away with the apathy. Sometimes it's there to stay. It seems to track with that. And then the best evidence for treating apathy isn't antidepressants. It's a …. a·ce·tyl·cho·line

esterase inhibitors, which a·ce·tyl·cho·line is what we use when people have dementia or cognitive problems. And that's what apathy has the best evidence for. And so when, when I think about it in terms of mechanism, it seems to be more linked to a decline in the cognitive part of motivation than the mood or what we call an effect of part, which is more with depression.

Dr. Soania Mathur

Right? But that's not to say everyone who experiences apathy will go on to experience dementia.

Dr. Greg Pontone

Not at all. It's just more, it's just on average, more linked with cognitive trajectory and then depression is in general.

Dr. Soania Mathur

Okay. You mentioned a·ce·tyl·cho·line….. inhibitors. What other medications are we using for apathy or are there any,

Dr. Greg Pontone

Yeah, so right now that too, and this is a little tricky, the two best evidence treatments for apathy and Parkinson's are acetylcholine esterase inhibitors. And specifically, this was done with Rivastigmine which is brand name Exelon. It probably is a class effect, meaning that other acetylcholine esterase inhibitors are useful. But the studies were done in Exelon, which is the one that's FDA approved in Parkinson's. And the other ones that show evidence, but they show evidence mostly in a specific case of people who've had STN deep brain stimulation is a dopamine agonists. And so the idea is that in some people with Parkinson's, the apathy could be a consequence of low dopamine and that if you restore don't mean specifically maybe dopamine that hits the D three type of receptor more so than the D two receptor. [inaudible] We think is more involved in mood and motivation and [inaudible] more directly in movement, which the agonists tend to hit a little more [inaudible] that might help apathy. But those are the two best evidence treatments right now for apathy and Parkinson's.

Dr. Soania Mathur

And what about nonpharmacological treatments are, I mean, apathy can certainly interfere with the proactive approach we need to take when it comes to Parkinson's. We need to exercise, like you mentioned me to keep up with their self care routine and so forth. So how can apathy be managed by the patient or the patient's family?

Dr. Greg Pontone

So apathy like I said, you know, because oftentimes it's happening in parallel with cognitive changes. Providing a structured environment is key. So I'll give you an example. So you know you're lacking motivation, but most of the people I work with who have apathy, if you take them somewhere, they'll go along. You know, the depressed person is like nah and irritable and won't get out of bed. But the apathetic person will be like, okay, path of least resistance. You're tugging on my arm, I guess I'll go. And they get there and sometimes they can rise to the occasion. And so what we found is the best outcomes are when you sort of provide a structured a day for the person. And so there are programs, day programs for people with apathy. That'd be great. But even if you're not in a program, you know, just having the care partner or spouse basically say, Hey, on Thursdays we're having lunch with this group of old friends you enjoy. And that really goes a long way. In fact, I can tell you, even though I mentioned those two medications, the best outcomes we've had are when we can motivate the family to really arrange even just a few activities to look forward through during the week.

Dr. Soania Mathur

And that kind of ties into this one question that I've gotten. The person wants to know, they say, so aside from going to the doctor, the person with Parkinson's, how can a care partner deal in the moment with someone who won't do anything like exercise even if they know it could help?

Dr. Greg Pontone

Yeah. Well, exercise. You know, I, my thought about this is if someone was an athlete and they exercised most of their life and then all of a sudden they don't, that's one scenario. But then if there's a person who is sedentary their whole life and now you expect them to exercise because they have Parkinson's, that's a bigger challenge because, you know, even without depression or apathy, if it's not part of your repertoire of behaviors that's going to take some doing. And so, you know, there's is you have to get creative. I have to tell you some of the best care partners or the most creative care partners, you have to incentivize what you want. And so, and I think a good physician, you know, we, we are always taught that persuasion and healing, you know, you, you have to be able to persuade people to see things your way into agree with the evidence if you want to help heal them.

And so I think this is really a negotiation. You have to find something that makes sense in their world, in order them to adopt these new habits. The good news is, is like any habit, if you can get them to do it for a few months, it'll become easier and more automatic. So I always tell people like, I'll fight with you for a couple of months because once we get them on the tracks, that train will chug along by itself. And I think that's the key is as long as nobody gives up and everybody is on the same page, you know, if you get them, the first thing is to get them to agree that they think exercise is important. Persuade them of that first and then you can build the rest around it. But it's, it's gotta be a challenge and it doesn't even have to be that they're depressed or apathetic. It's just like, that'll tell you a story

We all need convincing at times for sure. Another wife has written in a better husband, which I think it's kind of a a situation that a lot of people experience. She says, my husband was diagnosed with Parkinson's two years ago, but looking back, I started seeing his behavior change and chalked up to his getting older. He just turned 64 he doesn't converse much. He feels uncomfortable in social situations. Like he's afraid he won't be able to find the words that he needs to hold a conversation in the group. He's become very unsure of himself. I have to keep the conversation going, no banter between us anymore. What, if anything can I do to help him? What would you advise that care partner other than what you've said?

Yeah. The first thing I would do is get him screened for depression. Cause a lot of times a withdrawal like that, that's a hallmark of depression is all of a sudden, I mean, and you rationalize it, you blame it on, you know, and maybe it's true, you're having a little bit of word finding difficulty and some of that's normal for age. Some of that could be the Parkinson's. But the bottom line is just like I talked about an apathy. You know, the more you withdraw from things, the worse it compounds the problem. And so the two things are get screened for depression and number two, keep them out there. You know, whatever. If every time he says he doesn't want to plant two more lunches, you know, or whatever it is that you like to do a hike in the woods, whatever it is, you have to going. I mean, that's, I mean, it beats the alternative.

Dr. Soania Mathur

So the just for the last few minutes, I just want to go through some of the questions that are there. So it might kind of seem like they're in random order, but someone's asking about light therapy and isn't effective.

Dr. Greg Pontone

Yeah. So one of the experts on light therapy is a gentleman who lives in this area by the name of Norman Rosenthal. And so there is definitely a proportion of people with and without Parkinson's who have a seasonal component to their mood disorder. And it's very profound, in fact, across cultures. I mean, not Western cultures, Eastern cultures. We live near the Amish here in Maryland. We have the Pennsylvania Amish and then the more Midwestern Amish, they actually call the fall and spring, the hanging months because we have seen a seasonal dip and mood, sometimes severe that goes along with people with depression. And even people who don't have depression could still have a dip in mood. And so the best thing you can do is if you've identified that you have that pattern is get as much natural exposure to sunlight as you can and consider light box therapy. I mean this is definitely a nontrivial thing for the people who have it. And I can tell you're working on the inpatient unit here. April and November are some of our busiest months.

Dr. Soania Mathur

Wow, that's interesting. This care partner says that my husband has tried different SSRI [inaudible] all eventually had symptoms of hallucinations. They went away when he stopped using. Is this a common side effect?

Dr. Greg Pontone

Not at all. Yeah. So usually a, the SSRIs should not cause or be associated with hallucinations. I will tell you the one place where that might seem like that's happening. So SSRS and many antidepressants tend to increase the, our awareness of REM sleep and REM sleep is when we have dreams. And so for instance, if these hallucinations are mostly happening at night, it could be that although they're not technically causing more hallucinations, they're associated with vivid dreams that can seem hallucination light.

Dr. Soania Mathur

Okay. Another sort of side effect question. I was just re I was just recently diagnosed with Parkinson's disease before this I was diagnosed with major depressive disorder and was given medication. This increased my movement issues. Could there be a correlation or should I try again? I still feel depressed on a daily basis.

Dr. Greg Pontone

Yeah. So I, I'm going to give you an answer that is supported by the evidence. So there is maybe some evidence that in some people tremor can get a little worse on some of the antidepressants they a little bit, but two things that are really interesting about antidepressants even before you're diagnosed with Parkinson's is one, if you're treated with an antidepressant and then later diagnosed with Parkinson's, on average, the people who are on an antidepressant need symptomatic therapy later than people who weren't on the antidepressants. So it seems to push the need for Parkinson's medications down the road a little bit. So clearly it's doing something and that's controlled for motor severity, meaning that it's not because the antidepressants are having a direct beneficial effect on movement, it's because they're treating the depression. They think. The second is that, and this is something that our studies that we've done at Hopkins show is that people with Parkinson's who have treated depression versus people who have untreated depression function, physically eating, walking, bathing, hygiene at a higher level. Then people who are depressed and so I would say there is a lot of evidence that even if it makes an individual's symptom a little worse, being treated for your depression translates into much better overall functioning both in the short and longterm and Parkinson's and that's been repeated in many studies.

Dr. Soania Mathur

That's very interesting. The next question is what are the alternatives to benzodiazepines to treat Parkinson's anxiety? I think we reviewed some of that, but how bad are they? They want to know.

Dr. Greg Pontone

Well, you know it's funny. I just was out at a conference in Nevada who has one of the top world experts. He's at Harvard right now and he gave two lectures on sleep. And then there was another guy who talked about benzodiazepines. And there again, this is their sort of take home message to us as psychiatrists in general, not, not specific to Parkinson's is maybe benzodiazepines aren't as evil as we thought. And I can tell you this, whether they have long or short term side effects, benzodiazepines will improve most types of anxiety. Benzodiazepines are a medication that works quickly and benzodiazepines are also wonderful for a lot of the sleep disturbances that happen in Parkinson's, including the REM sleep behavior disorder. And so there's many reasons to consider them. The options are unfortunately a slower acting medications like the SSR eyes that can take, you know, four to 12 weeks to even start to work. Now, there are probably the better longterm option regardless and they don't have the downside of the S the benzodiazepines. But I, I have to tell ya, I use benzodiazepines and people with Parkinson's and people without Parkinson's always with the idea that will decrease and eliminate them if we can. Once the, you know, the other medications solved the problem. But I would say this, if you're suffering, don't be too afraid of these medications.

Dr. Soania Mathur

Right. another question is about I guess care partner stress or family stress because you know, that happens just when with sort of everyday Parkinson's disease is, and if you add the mood disorder into it, it can be quite stressful for the care partner. Do you have any words of advice for them in terms of their own mental health?

Dr. Greg Pontone

Well, I have to tell you the rates of depression and care partners are, are higher than the general population as well. So this strain of caregiving for someone with Parkinson's is, is big and you're not as an effective a care partner when you're depressed. And so I always tell my care partners, and they're usually spouses, but sometimes or other family members or partners is if, if you go down the wheels fall off the wagon. And so, you know, self care is not selfish is a phrase that you'll hear often. And I have to tell you, I tell the care partner, I'm like, you know, go have book club with your friends. Go, you know, have dinner with your friends, take however many hours you need to do whatever it is you enjoy by yourself. Because if you don't keep your batteries charged, nothing, you know, the whole everything you're trying to do is going to be less effective.

And so I think that's the main message. And we have a caregiver support groups in our communities, our Parkinson's communities, they're an essential part. In fact, most of the time we schedule them at the same time so the care partner can go to their support group and the person with Parkinson's can go to theirs. And you know, I, I, I think this is one of the things one of my PhD students is working on right now is how can we better a, protect the care partners and utilize them in the care of Parkinson's? And so I definitely think you have to take care of yourself.

Dr. Soania Mathur

That's very important. As we start to wrap up, I'd like to ask you for some parting advice. So, unfortunately I mentioned before people still feel there's a lot of stigma associated with Parkinson's disease and also mental health issues in general. So are there any words of advice that you may have that could help individuals sort of overcome that feeling of stigma?

Dr. Greg Pontone

Yeah, no, I think this is one of the things, I think the stigma is on both sides. It's when you enter medicine as a career, I always used to joke with my colleagues as a psychiatrist, I felt like we were the redheaded stepchildren of medicine. You know, we have the same MD degree, but you know, they say, are you an MD? Or you know, you're a psychologist and nobody would know exactly what you did. But my next thing is, is the brain in Oregon, it's a special Oregon, but it's an Oregon, like any other organ in the body, the harder the kidney is just an Oregon. We know less about

Dr. Soania Mathur

More complicated, actually.

Dr. Greg Pontone

Absolutely the best ….. and in my opinion, and so, you know, I think that's where we, we have to reframe this whole argument is that, you know, Parkinson's is a brain disease. Depression is a brain disease. Parkinson's is mediated by loss of brain chemicals. Depression is mediated by loss of similar brain chemicals. And so the why, why we put it, you know, why one is stigmatizing and one less so I think is you know, a legacy of, you know, Cartesian dualism, this mind body dualism. And I think as we evolve as a species, we're going to realize that while the brain is a very special organ, there's no reason to be embarrassed when it, you know, like if, if you have diabetes, nobody says you're crazy and has all these euphemisms for diabetes, right? I mean how many pet names do we have for mental illness compared to diabetes or high blood pressure? Right.

Dr. Soania Mathur

Very, very wise words. Thank you so much for your insight and expert advice today was really greatly appreciated and thank you everyone for joining us today. I hope you found your time both helpful and educational and we will send you the link. I think Mel mentioned for the recording of this webinar in the next few days so that you can share with others and always remember, you may not have control over your diagnosis, but how you face the challenges that this disease brings into your life, it's really yours to determine. So, focus on optimizing your quality of life, educate yourself, empower yourself, and celebrate your daily victories. And thank you. Once again, Dr. Pontone.