Marie: Hello and welcome to *The Parkinson's Research Podcast: New Discoveries in Neuroscience*. I'm your host, Dr. Marie McNeely, and I've partnered with The Michael J. Fox Foundation for Parkinson's Research to bring you to the forefront of the field of neuroscience to discuss the latest advances and discoveries with leading experts.

The Michael J. Fox Foundation created this podcast for researchers, clinicians, and industry professionals with the hope that these conversations and the resources we share will advance your efforts and partnerships to improve brain health. We're welcoming guests with a range of experiences and viewpoints. The views expressed belong to the guests themselves.

Today, we are excited to welcome our guest, Dr. Beatrix Feigl. Listeners, Beatrix is an Ophthalmologist and an Associate Professor in the School of Biomedical Sciences and Center for Vision and Eye Research, as well as the Faculty of Health, at the Queensland University of Technology. Today, we are going to talk more about her fascinating research on the visual system and the use of light therapy for Parkinson's disease. So, Beatrix, welcome to our show today. How are you?

Beatrix: I'm very well. Thank you for having me. How are you?

Marie: I'm doing great. Thank you. And I'm excited to chat more about you and your work today. Perhaps we can start by learning a little bit more about you. So, Beatrix, can you tell us more about your background and how you found your way to your current position at Queensland University of Technology?

Beatrix: Absolutely. I graduated in medicine and specialized in ophthalmology at the Medical University of Graz in Austria. And then I worked there as a clinician and academic in the Department of Ophthalmology. I focused on treatment of degenerative and metabolic retinal diseases, and I led also the clinical electrophysiology unit there. And besides my clinical work with patients that I always cherish, I also had a keen interest in research, and therefore, I'd also visiting research appointments in Professor Eberhart Zrenner's Department of Neuro-Ophthalmology and Electrophysiology at the University of Tübingen in Germany, as well as Dr. Erich Sutter's Electrophysiology Laboratory at the Smith-Kettlewell Eye Research Institute in San Francisco.

And then my research interests brought me to Australia, where I completed a PhD in degenerative eye diseases and clinical electrophysiology under the supervision of Professor Brian Brown here at Queensland University of Technology (QUT). And so, I'm still here at QUT and I lead my own research program here that focuses on the investigation of retinal photoreceptors. How their function is affected by common degenerative body diseases like macular

degeneration, glaucoma, as well as in neurodegenerative diseases such as in Parkinson's disease.

Marie: Very interesting. And I know a lot of people may not initially think about Parkinson's disease as an eye disease. Was this something that you anticipated you would end up in this area of neurodegenerative diseases when you embarked on this journey of studying ophthalmology?

Beatrix: Not really. So, this is a long journey, and I'm very excited that our research program now can be applied to neurodegenerative diseases, such as Parkinson's.

Marie: Well, I think this is a really cool area of research, and our listeners out there may or may not be very familiar with light therapy. So, can you explain, what is some of the evidence surrounding light therapy and potential benefits for Parkinson's disease?

Beatrix: Absolutely. So, first of all, light therapy is suggested to improve non-motor function, in particular impaired circadian and sleep-wake cycles in people with Parkinson's. And these are very common. And I just wanted to link back here. I'm very much aware that you have covered sleep problems in Parkinson's in one of your earlier podcasts with Dr. Amy Amara last year, but just to give you a quick summary of what kind of sleep problems can occur in Parkinson's and that are usually sleep fragmentation and difficulties in staying asleep, such as insomnia. Patients with Parkinson's also have difficulties or frequently fall asleep during the day — it's called excessive daytime sleepiness — and also REM sleep behavior disorder, where patients lose their paralysis during the dream stage of sleep and move and act out dreams, which can be also very disruptive of their sleep patterns, as well as disruptive to their partners.

So, there's quite a large application of light therapy based on these sleep disorders in Parkinson's. And there are also different kinds of light therapies targeting the eye that have been studied in Parkinson's. So, they can target the retina either non-specifically, and these are referred to as bright light or polychromatic light therapies. And then there are light therapies that are specific to photoreceptors. We also call them photoreceptor directed. And these are the ones we have used in our recent trial, and I know we'll talk about this a little bit later.

But in other words, bright light therapy can be compared to a more broadband antibiotic treatment, if you say so. And the photoreceptor directed light can be sort of more microbe-specific. So, it's a very specific light therapy. And when we're looking at light therapy, most of the light therapies have been done with bright light. And this one specific light is implemented for improving sleep,

depression, alertness, and even motor function in Parkinson's since the early 2000s. So, it's not a new thing.

But most of these studies were very small. They were pilot studies, and they did not use randomized clinical trial designs. And so, in addition to these studies, and as well as the few studies that did do clinical trials, they all implemented different study science using different lights with different color appearances, intensities, different times of the day when they delivered those therapies. They also did not monitor the environmental light exposure that can additionally have effects on the treatment.

And also there were mainly questionnaires as outcome measures and not so much objective measures of how these treatments work. So, taken together, while all these previous studies with bright light in Parkinson's give very important data on its potential positive effects on sleep and even motor function, they need to be optimized and also based on more randomized clinical trials to allow then for a clinical recommendation on what kind of light we should use, when, and how we should use it.

Marie: Very interesting. It sounds like this is a growing area of research. And I'm curious, you mentioned that there are some positive effects of this light therapy that span a variety of different kinds of symptoms or things that people may experience in Parkinson's disease. Are there any negative side effects documented?

Beatrix: Well, I can come back to this later, but there is the ongoing discussion of light pollution and of artificial lights impacting, in general, on our health and well-being. And there's also some early evidence of artificial light actually having negative effects on dopaminergic neurons. So, there is again a growing research area of looking into how bad actually light for us is in general, especially as we drag it out through the nighttime and all those billboards outside. So, there's a lot of discussion around this.

Marie: Very interesting. And Beatrix, I think it's important to note that you have both clinical and research roles. So, can you comment on where we are in the translational pipeline for light therapy? Is this something that you use in the clinic today or is it just being used in a research setting?

Beatrix: We have applied this light therapy only in the clinical trials. We haven't really done that yet in patients with regards to a day-to-day treatment. This is just based on clinical trial outcomes.

Marie: Well, I think that is a really important clarification that this is something that is still being researched, and light therapy is not currently being used as part of standard clinical care for people with Parkinson's at this time. And I think it really

helps to hear more about the background and to get a sense of where we are in these relatively early stages of looking at light therapy for Parkinson's. And I know pursuing this as a potential therapy is based on theory and hypotheses for potential mechanisms of how this could be beneficial. So, Beatrix, can you go into some of the details of what are the potential mechanisms through which light therapy may be able to confer benefits for people with Parkinson's?

Beatrix: Yes, so light therapies targeting the retina, utilize the fundamental role photoreceptors have in regulating our circadian rhythm. So, just to explain what a circadian rhythm is, it plays an important role in synchronizing our behavioral processes with a 24-hour day-night cycle. So, that allows us, for example, to optimize our sleep, our hormone productions, body temperature, and alertness. And the circadian rhythm is set by a central regulator in the brain, a time-setter, or in German it's also called zeitgeber. And that orchestrates the circadian functions in all the peripheral tissues and organs, including peripheral clocks. And it is the retinal photoreceptors in the eye that provide the light input to set this clock.

So, there are other cues, such as food or exercise, but light mediated by the retinal photoreceptors is a major input. Or in other words, the benefit of light therapy is that it is thought to realign a person's circadian rhythm. And this is important because there's evidence of dampening of the amplitude of the circadian system in Parkinson's that is then thought to contribute to sleep problems. And our research also indicates that people with Parkinson's have dysfunctional photoreceptors in the eye, potentially also impacting on the light information that is then eventually sent to the brain.

Marie: I see. And for light therapy, you mentioned that there is this more general bright light therapy that targets the retina and also this more specific photoreceptor-directed light therapy, which is activating certain types of photoreceptors. And I'm curious, for people who have Parkinson's disease who might also have some comorbid vision problems, Beatrix, do you think they may respond differently or perhaps may not respond at all to these different kinds of light therapy?

Beatrix: Well, we haven't really tested this. And again, this would need to be tested in controlled clinical trials. But when we did our clinical trial, we ensured that there were no co-existing diseases that would have impacted on our research outcomes. But we do, for example, know that people with macular degeneration have melanopsin, or a photoreceptor, dysfunction that can lead to sleep problems. Likewise, in people with glaucoma, so they have degenerating so-called melanopsin cells, and I will tell you about these cells a little bit later. They also have sleep problems and problems in their circadian function. So,

there is a link between photoreceptor dysfunction and sleep disruption and circadian disruption.

Marie: And can you share maybe a little bit more of the story of how you got involved in this area of research and perhaps what pieces of evidence brought you to this point of thinking that light therapy, you know, looking at the mechanism, looking at the data at hand, could have promise in Parkinson's disease?

Beatrix: So, we started off from research into eyes, into eye diseases, and came then across Parkinson's disease where we knew that there is also functional deficits. There is problems with vision. There is contrast vision, for example, it can be reduced. And then we sort of thought well, we'll look also into more detail into these so-called melanopsin cells function. And just to give you a bit of a background, there are three types of photoreceptors, or light sensitive photoreceptors in the back of the eyes. These are rods and cones. Most of the people, probably have heard of those photoreceptors, so they are either responsible for vision in the dark and dim light and cones for color vision. But there's a third photoreceptor, the so-called melanopsin photoreceptor.

And these all have different sensitivities, so spectral sensitivities. And all three are important for relaying the light information to the central clock, to this time setter by a specific pathway that is called the retinohypothalamic pathway to synchronize our circadian rhythm. And studies demonstrate that all three types of photoreceptors are required and need to be activated by light in the correct ratio to mediate the full effect of sleep. So, we have been researching into these photoreceptors, in particular in melanopsin cells, for a long time and have developed functional techniques for studying their responses. And I find this very, very interesting, as photoreceptors in the back of our eye are not only important for high-resolution 20/20 vision, they have far more reaching non-visual functions, such as regulating brain functions, including circadian health, and mood behavior, and alertness.

So, that brings me then back again to Parkinson's, where we know there is a problem with the circadian function. So, we thought, let's have a look at these melanopsin cells and how they are involved and is there a connection? And then, just to give you a bit of a background of these specific photoreceptors. The melanopsin cells, they're quite fascinating and unique because they're one of our oldest photoreceptors with the smallest number in the back of our eyes, compared to the millions of rods and cones we have.

And over the past over 150 years, vision scientists believed that vision is solely based on rods and cones. And then we had the first indication of another photoreceptor in the early 1900s when they did experiments on blind mice, and they showed these blind mice that did not have any rods or cones, but they

showed they still had the pupil light response. And as such, had some kind of visual perception, which indicated there must be another photoreceptor, but it took another few decades to really gather evidence. And that was then when they discovered this new melanopsin photoreceptor within the early 2000s. So, it's quite a long story to link back to those specific photoreceptors that play a major role in our circadian regulation, in our sleep-wake regulation, and again, you know, have a very important role also in neurodegenerative disease and Parkinson's.

Marie: Well, Beatrix, these sound like really cool cells, these melanopsin photoreceptor cells. And you mentioned that your lab was developing techniques, actually, for being able to study their function. Can you tell us a little bit more about these techniques and perhaps the process involved in developing them?

Beatrix: Yes. So, just to mention that these cells also in extensive research by other groups, they showed that these melanopsin project to up to 15 different brain areas, including visual and non-visual functions. And some of the most prominent non-visual functions are due to their projections to the circadian clock, mood, and pupil centers.

And that brings us back to our research. So, the pupillary light reflex is a non-invasive and readily available biomarker of their functionality. And this is where my research team and I have co-developed international standards for the measurement of the melanopsin cells in humans via the pupil. So, we developed several different protocols to characterize those cells via the pupil by implementing different stimulation, paradigms, different light, and intensities.

And then we also use those paradigms and apply them in different diseases, such as people with diabetes, or common blinding eye diseases, and in Parkinson's disease, where we then showed that these cells are not functioning very well. So, they show different pupil light reflexes compared to people without having a melanopsin deficit. And we also completed observational studies in people with Parkinson's that showed that the reduced pupil light reflex that was reflecting the reduced melanopsin function was also related to poor sleep quality. And these functional deficits are actually also supported by studies that were later done when they looked into human retinae of people with Parkinson's. So, in post-mortem human retinae, and they showed that these melanopsin cells lose their neuritic arborization and they undergo atrophy. So, that fits very well into the pupil measures we did that showed that they're not functioning well. So, there's also histological evidence of their degeneration.

Marie: Very interesting. And is the number of cells similar in people with perhaps Parkinson's versus people who don't have Parkinson's? Is it just a functional difference? Or is it actually the amount of cells or cell death that's happening?

Beatrix: Yes. So, they basically undergo atrophy, and there is also a reduced number of them.

Marie: Well, I think these are fascinating findings. And I think really pointing to the importance of these melanopsin cells in the proper function of the nervous system. And I'd love to talk about your findings. I think this has been a really perhaps exciting area of research with some unexpected results popping out. Have you been surprised by any of the findings that you're seeing in this area, Beatrix?

Beatrix: Well, I guess one of the things we were really surprised was when we applied our clinical trial and our lights, our photoreceptor directed lights, we found that one of our conditions that was the condition that had the enhanced melanopsin light showed also an improved function of these melanopsin cells through the pupil response. So, we did not really expect that. We thought we'd just boost the cells through this increased light, but we didn't expect that we're actually really functionally improving them as objectively measured through the pupil. So, that was quite exciting results.

Marie: Absolutely. And I'd like to get into some of the details of your clinical trial of this photoreceptor-directed light therapy for people with Parkinson's disease. So, again, listeners, this is the light that is specifically stimulating these melanopsin photoreceptors. So, Beatrix, can you give us the context of what led you to apply for funding from The Michael J. Fox Foundation, which you were ultimately awarded, for this particular project?

Beatrix: So, the rationale for doing this clinical trial was really that previous sort of bright light intervention did not use these biological daylight conditions or conditions that matched photoreceptor ratios that occur during natural daylight, which is really critical when we want a light therapy that mimics the biological effects of sunlight. So, as I said before, this is important, given there is emerging evidence of potential negative effects on dopaminergic neurons of artificial lights that does not match daylight. So, also these previous studies, bright light interventions did not think about the melanopsin photoreceptor degeneration.

So, there was no real targeted, specific approach to these light therapies. And then as part of the MJFF-funded randomized clinical trial, my team and I designed a custom-built light therapy that used sort of new artificial light spectra designed to accurately reproduce the effect of natural daylight on the human eye to control for the biological effects of light on sleep and circadian rhythm. So, these biologically directed photoreceptor-directed lights use light sources, we also call them primaries, that match rod, cone, and melanopsin photoreceptor daylight excitations.

So, these daylight excitations are actually known. So, they are established and based on the International Commission on Illumination Standards. So, this was one of our light conditions, which was basically daylight, which matched all the photoreceptor excitations that occur during daylight. And then we also created another light source with an enhanced melanopsin. So, to take care of the melanopsin degeneration found in Parkinson's disease. So, this enhanced melanopsin light condition enhances the melanopsin photoreceptor excitation while keeping rods and cones balanced, as we say, or similar to daylight excitations. So, this is a method also called silent substitution, and it's a very common method used in visual science to stimulate a photoreceptor type separately from the other. And the beauty of this method is that we can make both lights appear similar (white) while targeting different photoreceptor types; and therefore, we can adhere to double blinding.

And then with these two lights, we developed and designed — and here I want to really mention Professor Andrew Zele who was crucial and fundamental in designing — those lights. We then performed one of, what I believe, the most comprehensive sleep study in Parkinson's where we measured the sleep brain waves, or polysomnography, as well as the hormone melatonin and marked a battery of other subjective and objective sleep and motor function tests in response to these two photoreceptor-directed lights. So, one treatment, or the treatment group, received the melanopsin-boosting or enhanced melanopsin light whereas the control group received the natural daylight.

Marie: I see. That makes sense. And for each of these treatment groups, can you explain what the parameters were of this therapy, and perhaps how it was delivered? What did the experimental setup actually look like?

Beatrix: Yes, so both groups used these lights. So, they were like in an iPad format that could sit on the table next to them. They were advised to use them for four weeks every day for 30 minutes, and we personalized this light therapy based on their natural preference for sleeping at certain times. So, for example, early bird versus night owl. So, we determined their chronotype, and then gave them kind of a time interval where they should use those lights.

And they would usually use them in the morning, based on their chronotype, while they had breakfast. So that light was sitting next to them, and they did not even have to look into it. It was just sitting sort of about 30 to 50 centimeters away, just sending indirectly light to their eyes. And we found that both lights improved their deep sleep or restorative sleep, as measured with our brainwave recordings or polysomnography. And just to give you a background on the deep sleep, so our body goes through several sleep cycles that consist of a very light sleep, then followed by a stable sleep, and then this deep sleep phase, it's also

called N3 or slow-wave. That is then followed by the dream stage. And we go through those stages several times during the night, and it's in particular the deep sleep stage where our body cells regenerate. And we found that this stage showed the most significant improvement when compared to normal age-matched patients.

Marie: Very interesting. And did you get any feedback from participants on what they thought of this light therapy? Was this something that they would be willing to do every day? Is this something that they enjoyed?

Beatrix: Yes, we looked at that here and then we also obviously asked them. And it seemed to be fitting into their normal day-to-day tasks very well. So, we still have some of the participants are knocking on our door wanting to have this light or just participate in other studies with regards to the light because they seemed to really enjoy being part of this trial. So, they had these four weeks of light therapy but there was a fair bit of other things involved, which we kept them engaged with. So, it was, I guess, a quite enjoyable process for our participants.

Marie: Wonderful. And you mentioned that you use this sort of iPad-like device. Is this something that requires special technology? Or is this something, kind of thinking further down the line — if this clinical trial goes well, if we move down to the phase of implementation — could this be easily implemented in perhaps a device that people may already have, or would they need something special?

Beatrix: Absolutely. So, this is something that could be implemented into normal day lamps or down lights. So, it's something that is very easy to implement it.

Marie: And then perhaps the dreaded question about dosing. I think this is very difficult for clinical trials in general, but Beatrix, how did you determine the right dose, or the dose that you would test at least in this particular study? And then maybe on the flip side, how did you control for other light exposures?

Beatrix: Very good question. So, the dose, I think that was something we know from previous studies and literature on the effects of light and sort of a half an hour was kind of the general thoughts that would have effects. And with regards to controlling for the environmental light, our participants also wore a, we call it an Actigraph or an active watch. So, this is a device, it's like a watch that's worn on your wrist, and it measures the ambient light in the environment. So, we made sure that our participants in each group had these watches, and what we found from our trial is that they had both the same level of light exposure, environmental light exposure. So, any effect is really due to the treatment.

Marie: Very interesting. And then can you perhaps go into the details of the results of the study and kind of your interpretation of what they mean and what the next steps might be?

Beatrix: Yes. As I said, we found improved deep sleep in both groups, as well as all the sleep questionnaires scores, like very standard questionnaires, such as Pittsburgh Sleep Questionnaire Index, Epworth Sleepiness Scale, and Parkinson's Disease Sleepiness Scale. So, they were all improved after these four weeks of light therapy. We also had positive effects of mood and quality of life, even motor symptoms improved.

And the improvement was also noticeable by their partners. So, partners of people with Parkinson's rated their partner's sleep better after the light therapy. And while both therapies did not differ, sort of significantly or statistically, and had both effects, there was a greater physiological effect of the melanopsin boosted light, or enhanced melanopsin as we called it, on objective measures such as the melatonin. So, it caused a greater shift, as well as on the melanopsin function, as measured by the pupil light response, as I mentioned before.

So, this made us believe that there is definitely an effect, as we can objectively measure it. And while it was not significantly different from the daylight condition, it might be in the future important for people who have more advanced stages in Parkinson's disease. So, the conclusion of our study was that daylight brought into the homes of Parkinson's — and our Parkinson's patients all had very early stages of stage one and two — significantly improved or is sufficient to improve their sleep and the boosted light may be useful in people with more advanced stages of Parkinson's, based on seeing this significant objective improvements in melatonin and melanopsin function.

Marie: In the group of people that you studied, did they have melanopsin deficits that were measurable even in these kind of relatively earlier stages of Parkinson's disease?

Beatrix: The answer is yes. And we have also seen that in our previous observational studies that the melanopsin function is reduced, and we confirmed this in our participants in this trial. So, they all had reduced melanopsin function, and the enhanced melanopsin group significantly increased this function.

Marie: That makes sense. And then perhaps the next question, where do we go next? It sounds like there were some potentially promising hints of physiological function improvements with this enhanced melanopsin light administration. You mentioned that the sort of dose the time was about a half an hour a day for four weeks. Do you think having a longer exposure time or a longer trial runtime

(more than four weeks) would enhance the effects? Or do you think there's some sort of ceiling that you're hitting with this level of deficits in melanopsin?

Beatrix: Well, it's really hard to say. I guess, we found after four weeks of light treatment, and then we still kept our participants in the trial for another two weeks without treatment, and we still found there were positive effects still going. So, this was something very interesting to see that the improvement continued beyond the cessation of the light therapy. So, if we would have done it longer, I guess maybe there would be a clearer differentiation between the two groups. But what our study also showed is that simple daylights seemed to be sufficient to show improvements in all those functions we measured.

Marie: And then what are your next steps, Beatrix?

Beatrix: In the future, we would like to see these biologically or photoreceptor-directed lights integrated into homes of people who live with Parkinson's, such as in lamps and ceiling downlights. And here we are really open to collaborations within lightening industry partners to make this happen. I guess an unanswered question may be also whether persons experience the same benefits on sleep by spending simply 30 minutes outside in natural daylight every morning. And I believe, based on our study results, the answer would be yes. But strictly speaking, we would need to do another clinical trial to include a study arm where people just go outside and sit for 30 minutes in the sun to see whether this has a similar effect or not.

Marie: That makes sense. And it sounds like The Michael J. Fox Foundation funding for this particular study had a big impact on moving this forward and starting to answer some of these unanswered questions. Can you comment on how it has helped your research?

Beatrix: Absolutely. So, this was a real amazing support. We're very grateful to MJFF and Shake It Up Australia to have funded us in this clinical trial in their Therapeutic Pipeline Program. So, these programs are so crucial in helping new developments out of the ground. And it allowed us also to implement our fundamental research in this first randomized clinical trial. So, without this funding and program, it wouldn't have been possible to bring it to this stage.

Marie: And then is there anything else that you'd like to share about your experience in this clinical trial?

Beatrix: I guess one major thing I would like to say is that we have to consider artificial lights being photoceuticals that should be cautiously applied like a pharmaceutical. And we are bombarded with new light therapies that promise health and well-being every day. And many of these therapies have not been

tested in controlled clinical trials. And this often leaves patients and doctors confused of what to use or recommend. And it might even lead to the oversight of treatments that have been tested in clinical trials. So, there is a need to provide evidence in randomized double-blind controlled clinical trials, although they take long, and they're hard to do, but we are not doing them enough. And I would also like, on that note, to refer to a statement by Paul Feyerabend in his 1981 book *Problems of Empiricism* that also encourages the conduct of behavioral clinical trials in this area.

And his statement reads, “A new treatment is born into a hostile environment. It needs to be kept alive in its infancy. It needs to mature. Scientists should protect early development, not contribute to premature deaths.” And as such, I think our current clinical trial results do not only show that daylight can be beneficial in alleviating sleep disruption, but now also provides a standard daylight control against which new light therapies can be tested in clinical trials. And I believe our results are also an important step towards preventing premature death of new developments, so that they can help people with Parkinson's in the future.

Marie: Absolutely. I think this is so important. And I think you're really pioneering a new area here, Beatrix. So, how do you maybe combat some of those naysayers who may be skeptical of your approach overall after maybe seeing a lot of these untested products being sold or marketed to people who have these diseases?

Beatrix: Well, it's very hard, you know, to see that, and you want to really make sure, because people are confused. They try all sorts of different things. And most of the time, I just tell them whether there have been trials and try to re-ensure that these are safe, or whether there needs to be more research done to actually use those new technologies. Because sometimes they're also quite expensive. So, there has to be good information or conversation between the doctor and the patient of what is out there and what has been tested, and what has shown some benefits.

Marie: Absolutely. And then thinking about, oftentimes with these untested therapies, not only is there the potential risk of people wasting their time, their money and not getting a benefit, but there can also be some detrimental effects. Are there any pieces of evidence or studies that have been done so far that show that any of these light therapies may have problems in terms of impacting the visual system or having any other negative effects?

Beatrix: I mentioned before, there is some animal studies on artificial light on dopaminergic neurons, but otherwise, I'm not aware that there is studies done that actually look into that comprehensively.

Marie: Very good. Well, I think this is an important area for ongoing research. And I think you're in a unique position kind of having this ophthalmology background and working in this very interdisciplinary area of neurodegenerative diseases that have this component of eye involvement or this sort of axis of eye-brain involvement. So, can you comment on what your experience has been like being an ophthalmologist in the Parkinson's research field?

Beatrix: Yeah, this is a really, very good question, because it is so important to have an interdisciplinary approach to make these big steps towards solutions, for example, in Parkinson's. So, as my background is in ophthalmology, I also had to bring on board neuroscientists, vision scientists, psychologists, engineers, including also clinicians that are specialists in motor movement disorder, and sleep scientists. For example, at the Brisbane Mater Hospital, Dr. Daniel Schweitzer and Dr. Lucy Burr, as well as from Sydney University, Dr. Simon Lewis, who are all immensely important for the successful completion of this trial. So, there's a big team with different backgrounds involved, and it's really important to have this, to make these steps towards solutions.

Marie: Definitely. I think these collaborations are critical, but also having the right tools, the necessary resources and other things that you need that can really help move the field forward. So, do you have examples that you're seeing right now of things that are really advancing the field of Parkinson's research or things that are missing that you think could really accelerate PD research?

Beatrix: Well, I think just keeping up those collaborations is really important. Yeah, we always reached out for collaborators in different areas, and that's the most important thing, I believe. Again, we approached Michael J. Fox with our idea, and we were lucky to be heard. And I think having this foundation is a really crucial part in advancing new knowledge and bringing it from the benchtop to the clinic and to the patient. So, that's what we're really grateful for.

Marie: Absolutely. And then thinking about the future, Beatrix, we hinted throughout our conversation that there are still quite a few unanswered questions in your specific research area, but what do you see as maybe some of the biggest contributions that ophthalmologists can make in Parkinson's disease research going forward?

Beatrix: So, I think one of the things that in normal care of people with Parkinson's, often the eye, or the ophthalmologist, or just the discipline itself doesn't really have a role. Or when there is sleep problems, I don't think neurologists would think first of the eye or an ophthalmologist. So, in this area, I think just having assessment, having also this ophthalmological examination, and find out whether there is some contributions. Whether, particularly in melanopsin, the pupil light reflex is a very easy technology to apply. So, we could definitely work together here. And often patients ask, or they need answers as to why things are not working. And

we just need to be ahead of this, and we need to be able to give them an explanation. So, I think as eye specialists, there could be a role just in the normal care of a patient with Parkinson's.

Marie: I think you made some really important points there, Beatrix, that hopefully listeners out there who might be neurologists themselves, or involved in care of people with Parkinson's in some way, you know, can start to think about these things in their daily practice. And we talked about some cool areas that you're working on in your research. What are some of these next steps or maybe future directions for your work specifically that you're most excited about, Beatrix?

Beatrix: Well, as I said before, we really want to bring those lights into homes of people with Parkinson's. And then also, it does not only affect a person who has the disease, there's also a big burden on their partners. And, you know, having these lights around also would benefit their partners to, you know, have better health and well-being, as well as just in general promote health.

Marie: I love it. And do you think that this light therapy could have benefits in other neurodegenerative diseases beyond Parkinson's?

Beatrix: Absolutely. So, it would have benefits. We know already, for example, in Alzheimer's disease, that there's photoreceptor degeneration and dysfunction. Other neurological conditions such as multiple sclerosis, so there's lots of applications of those indoor daylights that could be integrated into homes and help people with these conditions.

Marie: I think that's wonderful. And I'm looking forward to additional research coming out in this area. And I'd love to maybe end with just a statement here of how your work, Beatrix, is bringing us closer to some of these big picture goals in the field of whether it's finding a cure for Parkinson's or in your case, perhaps, contributing to improved therapies for people with PD.

Beatrix: Well, I think our work, while it's not a cure, I think it can help, you know, in just normal day-to-day living and well-being. As we know, our circadian health, our sleep-wake patterns, everything's so important. And just alleviating the sleep disruption, making a person better sleep will make them also move better. So, if it's just an additional support for a person suffering from the condition, and just to make their lives easier.

Marie: Absolutely. And I think it works wonderfully as an adjunct therapy, potentially, where people could add it without having to take away one of the therapies they're currently using.

Beatrix: Absolutely. I agree, yeah.

Marie: Well, Beatrix. Thank you so much for joining us on the show today to talk more about your research and to share your insights.

Beatrix: Thank you very much, Marie.

Marie: Well, Beatrix, thank you again. And listeners, it's been great to have you here with us as well. If you want to know how The Michael J. Fox Foundation can help your research, please visit MichaelJFox.org/researchresources. And you can find new episodes of this show each month on the MJFF website or on your favorite podcast platform. And when you have a moment, please subscribe to our show to make sure you don't miss our outstanding lineup of upcoming episodes. We look forward to connecting with you again in our next episode of *The Parkinson's Research Podcast*.