Zoom in on **Dementia & Alzheimer's**

Bruce Willis Has Frontotemporal Dementia: What Are the Symptoms of FTD?

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Transcript of Zoom with Malú Gámez Tansey, PhD, Norman and Susan Fixel Chair in Parkinson's Disease and Professor of Neuroscience and Neurology, University of Florida College of Medicine

Please note: This transcript has been edited for clarity and brevity.

NANCY LYNN: Welcome to the second episode, Zoom In On Dementia & Alzheimer's, which we're so happy to bring to you to ask questions of the experts. With support from Lily and Genentech, we're able to do this wonderful message, this wonderful series. I'm looking, I'm reading messages and speaking at the same time. I'm joining you from Los Angeles. My name is Nancy Lynn, and I'm a Senior Vice President at BrightFocus Foundation. And I've been in the Alzheimer's field for about 15 years now, providing funding for research, which is what BrightFocus does primarily, is provide funding for research all over the world. And because of that, we have access to fantastic experts from all over the world. And so we want this series to be a chance where you can submit questions ahead of time, or ask your questions live of some of the world's greatest research experts and mentors.

And we're delighted to have an incredible speaker today. So I am really delighted today to introduce Dr. Malu Tansey. She is the Norman and Susan Fixel Professor of Neuroscience and Neurology at University of

Florida College of Medicine, and she is the Co-director at the Center for Translational Research in Neurodegenerative Disease. Translational research is going from basic science into the use of therapeutics. Dr. Tansey's research lab employs multidisciplinary ways to investigate the role of inflammation and immune system responses in brain health and the development of neurodegenerative diseases with particular focus on the gut-brain axis, which I think would be another wonderful episode. Dr. Tansey, we'll have to have you back, on the gut-brain relationship. Her long-term goal is to train the next generation of scientists who can develop better therapies to prevent and or delay these disorders.

So, welcome Dr. Tansey. I'm going to kick us off right away and say what is, and I don't even know if I am pronouncing it correctly, frontotemporal dementia. What is the difference between dementia and Alzheimer's, which is always the number one most asked question in our field? And then, what's the difference between Alzheimer's and FTD?

DR. TANSEY: Thank you very much Nancy and thank you BrightFocus for sponsoring this incredibly important webinar for all of you and for all of us who are committed to being in a world where we don't have to worry about neurodegenerative disease. And I thank you all for your time today. As Nancy said, I am not a neurologist or psychologist, I don't treat patients with FTD or Alzheimer's dementia, but I am in the field trying to understand what causes it, how to delay it, how to prevent it. And as a result, I am very committed to being informed about what troubles the patients and caregivers with FTD. So this is an important process for me as well.

What is FTD or Frontotemporal Dementia? And what are the differences with Alzheimer's? So Alzheimer's as you know is the most common form of dementia in older people. And so when an older individual presents with any behavioral or memory issues, that is the first thing that the doctor is going to consider. However, FTD in terms of what areas of the brain are affected, its your anterior and temporal lobes in the brain, which basically control a lot of the behavior and language that an individual needs to do. And so one of the main differences between Alzheimer's and FTD is that Alzheimer's usually begins with memory forgetting and memory loss. And FTD is more of a behavior, personality changes, and language difficulties.

And so usually the first noticeable differences in FTD are those with difficulty with language, for instance, aphasia was one of the things that was reported by Bruce Willis about a year before they informed us of his FTD diagnosis. And the key difference is, in terms of the memory loss, memory loss as I said is very prominent early in Alzheimer's, much earlier in Alzheimer's than in FTD. But in the advanced stages of FTD it is possible to have memory loss in addition to the behavior and personality and language difficulties that start much earlier in FTD.

NANCY LYNN: And would that be short-term memory loss primarily?

DR. TANSEY: Yeah, so for Alzheimer's it's usually short-term memory loss, like what you had for breakfast yesterday. I can't really remember much that way either. They give you a language test, like a five-word language test, and you just have to repeat as many words as you remember. But it's generally short-term memory loss. Now in more advanced stages in both FTD and Alzheimer's you can have a loss of memories that are long term memories, when you actually don't recognize your loved ones. The other thing to remember is that FTD, as I said, usually begins with loss of speech or language difficulty and the abnormal or anti-social behavior that makes loved ones start to be concerned. And then later in the advanced stages you could have things that look more like Parkinson's because there is a movement disorder component and you could have rigidity, slowness of movement, muscle weakness, and difficulty swallowing, all of which are really characteristic of Parkinsonian features. And the reason there is so much overlap and crossover is because the proteins that are aggregating and glumming up in your brain are basically spreading to different parts of the brain. And so as the pathology affects different sections of the brain, different regions of the brain, you end up having some overlapping symptoms in these diseases. But the critical thing is how did it start? So what were the earliest signs? And that along with the family history, and then, you know, genetic testing, if you want to do that, you can pinpoint more accurately what might be going on with the individual.

NANCY LYNN: Ok yeah, you covered a bunch of my follow-up questions. And you mentioned, my next question that had come in is how is it

diagnosed and how is it most often misdiagnosed? And you mentioned a five-word memory test but how do most people discover they have it and what is the typical age of onset?

DR. TANSEY: Yeah, so that's a great question. So the range of ages is 45-65 but there have been cases as early as 30 and as late as 90. The average is like 58. And so people talk about Bruce Willis being classic because he was 58 when it was confirmed that he had FTD. Now it is most commonly misdiagnosed... 30% of it is diagnosed wrong and the doctors think it is Alzheimer's. 40% of the time it is thought to be a psychiatric disorder because of the behavioral and personality changes. 20% of the time it is misdiagnosed as just depression and 20% of the time it is misdiagnosed as mania. So the important thing, as I mentioned, is to be able to document whether the behavioral and personality and language changes came first, before any of the memory changes, and that would be more characteristic of FTD. And it can be diagnosed, as is said with the questionnaire, behavior accounts from the family, as well as with an MRI. So if there is advanced degeneration of the frontal and anterior or temporal lobes it will show as shrinkage in an MRI.

NANCY LYNN: And do you have to have an MRI to have an official diagnosis?

DR. TANSEY: You know I don't think that you necessarily do in the early stages because there is not going to be a lot of degeneration at the very beginning. But it really will depend on your doctors. If it's clear that you've had FTD in your family and you know they might recommend that you get a test to make sure, that will help them you know nail down a familial FTD diagnosis potentially. And then you would be eligible for clinical trials which I think is the silver lining to knowing whether or not the form of FTD that you might have is genetic or familial or sporadic. It's you know about 50/50. So you don't have to have a family history to have a diagnosis of FTD.

NANCY LYNN: Can you describe the different types of FTD? And also tell us which one Bruce Willis has and I guess what's different about them?

DR. TANSEY: Yeah, so there are three main types of FTD and they are

basically what we call the behavioral variant, then there's the primary progressive aphasia or PPA, and then there's the movement disorders type. And based on the reports it's believed that Bruce Willis has the primary progressive aphasia type. The behavioral variant type is the most common. And, as I said before, every patient can present a little differently but characteristically the behavioral variant presents with more behavior and personality changes. The primary progressive aphasia presents with language difficulties. And the movement disorder type presents more with movement disorder along with some of the you know, personality and behavior, but it's primarily movement disorder. That's usually the one that gives neurologists the hardest time because you know, you want to suspect Parkinson's since a lot of the facial expressions are lost in Parkinson's as they are in FTD.

NANCY LYNN: And we just had a question come in from someone watching on Vimeo – could it be diagnosed from spinal fluid? Because I know that's true in Alzheimer's.

DR. TANSEY: That's a great question. So, so far no we don't have a diagnosis with a biofluid, but there have been some studies looking for potential biomarkers that you could, you know, test for. For instance, if you do have the granulin mutation which is one form of the familial FTD then you basically had a decrease in a protein called progranulin in your body and your fluids. And if they were to test for it, the levels of it might come out low. So that might be a way to confirm, although I'm not really aware that there is an FDA approved CSF fluid for it. So these are all part of the different tests that can be done to help a neurologist make a diagnosis. Along with, as I said, the interview, the memory test and more than likely the MRI. And so, it is hoped that we could look for things that we know are changing during the disease but it's not quite as easy as it is for instance to look at hemoglobin A1C for diabetics or c-reactive protein for people with cardiac risk for instance.

NANCY LYNN: Got it, thank you Penny for that question. I'm going to ask I think two more before I start opening it up to everybody, although everybody can ask as they wish. But some of the questions that came in, then I'm going to get to is there anything that slows it down or stops it,

but I put together a bunch of them. What are the stages? I assume there are different stages of FTD. How fast does it progress? And what is the average lifespan of somebody, from noticing symptoms til the end?

DR. TANSEY: Ok, yeah those are good questions. So let me just extend a couple of _____. If you were to ask what is the lifetime risk for getting FTD for any person in the general population, it's 1 in 742. So it's rare, right. It's less than .1%. Now if you have a family history, and if there is a gene that has been passed on from parent to child, then you are looking at familial forms of FTD. And if you look at people with FTD, individuals with FTD, about 10-15 in every 100, so 10-15% will have the familial form. Which means that 90-85% is sporadic. So that's one argument against genetic testing because the chances that you will have a genetic form are low, right, compared to the sporadic. However, as I mentioned before...

NANCY LYNN: The 10-15% is genetic?

DR. TANSEY: Yeah 10-15% in every...yea exactly. 10-15% of people with FTD will have the familial form. Which means that it is going to be a progranulin mutation, a C9orf mutation, or a tau mutation. If that is in the family, then the child of a person with familial FTD has basically 1 in 2 chances of inheriting that gene. So one of the things about that is, you know, we always think that knowledge is power and you want to make sure that you know, you know, the risk if you do have these in your family because there's a lot of clinical trials that you could potentially enroll in in a pre-manifest, so young, young you could enroll and they would learn a lot from you. And they might be able to put you in a trial where you can delay or prevent the development. So I think that's, you know, an argument for the power of knowing, if you want to know.

In terms of the stages, so what are the stages? So again, it progresses differently in different individuals, but in general, you end up with, you know, a few very mild cognitive changes. Not like the ones you typically see in Alzheimer's. But the primary initial stages are changes in behavior and personality. So some people will classify that as inappropriate behavior in public, some times like no filter kind of thing, language difficulties, right. And so those are the real primary stages. So those are the first three stages: mild cognitive changes, changes in behavior, and language difficulties. And then you get to the fourth stage and fifth stage,

which are basically that these symptoms are now impacting your quality of life. You, you know, shy away from going into public, start isolating yourself. That tends to make people irritable, and you know, get this cabin fever type thing. So then you start having mood swings and more personality changes. And then at stage six, it's the memory loss that you typically see earlier in Alzheimer's. And then finally, severe cognitive impairment and a general decline in health. So those are the main seven stages.

As far as how fast does it progress, so again, every patient is different. My lab, for instance, is interested in does inflammation in your body contribute to a faster progression and if so, how could you lower that inflammation in your body. And so we typically think of things like good diet, and you know, moderate exercise, in addition to the things that we know help the behavioral symptoms of FTD, which are occupational therapy, speech therapy, you know, engaging in sort of a stimulating environment. And so most studies that have looked at how fast it progresses, it is a steady decline that tends to be a little bit faster than what we think about for Alzheimer's. And so you end up with a loss of social contacts, cognitive deficits, inability to speak and that isolates a lot of people, you know, people with aphasia. And then of course you end up, you know, being very dependent on a caregiver or a facility over the next 6-9 years. So the typical lifespan if you will of someone who is diagnoses with FTD is somewhere between six and nine years from time of diagnosis. And you know the important thing is we want to focus on not your lifespan, but your health span. Nobody wants to live long, if you are not enjoying good quality of life and you know, feeling healthy. So in our field, we've started to think about not lengthening health span but finding ways to improve the quality of life so it's really a health span, not a lifespan.

NANCY LYNN: Right. I'm going to insert, ask Jennifer's question here before I start to ask about how to mitigate the effects, which you started to talk about. But Jennifer writes, can someone have both FTD and EOA, and I don't know Dr. Tansey if you're familiar with EOA, so if you are, would you explain it to us?

DR. TANSEY: Yeah, it's early onset Alzheimer's. Is that right Jennifer?

That's what you are thinking? Ok. So there is some overlap in all these diseases, right. So sometimes when someone gets diagnosed with Alzheimer's and they start developing, you know maybe they have a positive amyloid and maybe it's known that they are really declining in cognition and memory, they may start with movement difficulties. Just because they have Alzheimer's, doesn't also mean that they have Parkinson's. So these diseases can coexist. But I don't think that...so because Alzheimer's and FTD don't have a very defined genetic etiology they're basically multi-causal, right, especially because there is 90% that are sporadic, same for Alzheimer's, then it is entirely possible that there is overlap. And early onset Alzheimer's tends to also be linked to a genetic predisposition, so genes like presenilin one, amyloid precursor protein genes that are very, also very uncommon, maybe 5-10% of all Alzheimer's cases are due to a single gene that you inherit. Same as with FTD, 90% of the cases of Alzheimer's are sporadic and 90% of the cases of Parkinson's are sporadic. So when I say that, I want to make sure that you understand that I'm not saying that they're not inheritable. There is a component of heredity but we don't really understand or know what all the gene or gene variants that are increasing that risk. Ok so, we are still trying to figure out are there more genes that predispose you in addition to these very rare mutations that account for up to 10% of these cases.

NANCY LYNN: And Jennifer, if you want to ask any follow-up questions, please feel free.

DR. TANSEY: Let me just add that the commonality of the overlap is about 10%. So 10% of people with Alzheimer's also have another mixed dementia or Parkinson's. And so it's entirely possible that you may also have, you know, features of both and you know there are other causes of dementia, like vascular dementia that are also considered to be a comorbidity if you will with some of these disorders.

NANCY LYNN: And you know I think it would be interesting perhaps to do a future episode just on diagnosis, because it seems so common, it's so difficult to get a definitive diagnosis. And I know Robin Williams was first diagnosed with Parkinsonians and all kinds of stuff and depression and drug use and he had Lewy Body Dementia. And then Linda Ronstadt who did a movie recently, they thought she had Parkinson's. She has something called PSP. So even when you are famous and wealthy and you

know even if you're not a rural under resourced person, it's so difficult to get a diagnosis.

DR. TANSEY: Yep, no absolutely. And you know we talk about how the incidence is increasing and that could be true, because we are living longer, right. In addition, we've gotten better at diagnosing. So if you get better at diagnosing, and then you are living longer, it's going to seem like oh my gosh we have an epidemic, right. And in a way, you know, it is because we are living longer. And so if you are good and take care of yourself and you don't have heart disease, you're going to live a long life. It's a privilege not afforded to many. So I think this is why we focus so much on the quality of life because we don't want you to have a long life unless it has, you know, a good quality in health.

NANCY LYNN: Well and so that brings us to, and I don't know whether this would apply specifically to FTD or to a whole group of the different types of dementias or dementias with different causes, but are there any drugs that help the symptoms or slow down the progression of FTD? And are there drugs that can make it worse?

DR. TANSEY: Yes. So that's a good question. Because sometimes it's misdiagnosed as Alzheimer's, the first line of intervention in someone that has Alzheimer's is typically what we call acetylcholinesterase inhibitors, right. That's because you are losing acetylcholine, which is a neurotransmitter that helps with brain, you know, impulses, brain transmission. And when you have a little bit of that left they inhibit the enzyme that breaks it down to make sure you have more around in your nerves. And so acetylcholinesterase inhibitors are typically given to people with suspected Alzheimer's. But they can be very disruptive and bad for people with FTD.

NANCY LYNN: So can you just say the names of some of those drugs so that..

DR. TANSEY: Sure. So the more common ones are galantamine, donepezil, and rivastigmine. And they go by different names whether you are using the generic or the trade name. But the important thing is to not just go to a general practitioner if you suspect these issues. I would

definitely find a neurologist and in particular a memory clinic, right, if you are having memory issues. The memory clinic will be able to tell the difference between an Alzheimer's and an FTD. And I think because of the fact that you could get misdiagnosed, you don't want to take that chance. So one of the big pushes in the US and around the world is to educate primary, you know, general practitioners with how to spot these things because really they are not the experts, right. But they are the detectives, they get the first report, and it's really critical that you know you get seen by a specialist.

So acetylcholinesterase inhibitors, not good for people with FTD. Now what is there available? So there is still no know cure for FTD or Parkinson's, the only thing we have more recently as you've all heard is the amyloid immunotherapy, the aducanumab, the lecanemab, that are coming along that have shown to slow down the decline in early Alzheimer's. Okay, so that's the only thing we have right now. But it's a win. It's kind of a miracle, because we haven't had anything ever and I think we will all remember 2023 as the year where we finally started making a dent in how to stop the progression of these diseases that are so similar. So I think that discovery is going to help us with FTD and Parkinson's.

And so what do we do if we don't have a cure? So the important thing is to manage the symptoms, right. So if you have behavior, speech and movement symptoms the best thing to do is to try get you know speech therapy, occupational therapy and then to be able to stimulate the individuals with activities, right. Moderate physical exercise, maybe some you know memory games or puzzles, and good sleep. So sleep has been underrated for all this time. Sleep is the time that these glummed up proteins get removed from your brain. So if you don't get enough sleep, you get more accumulation. And this doesn't start in your 50s or 60s, it actually is going on your whole life. So the best advice that we can now give people in their 20s, 30s and 40s is to get enough sleep. And of course people in their 20s and 30s think you know, that life is going to go on forever and you know, people in college you know pull all nighters and things like that. It's not a good thing. So at any rate, at any age, quality of sleep is really, really important. And they recommend anywhere like

seven to eight hours. People that sleep more than that actually have an increased risk for dementia. So we don't really know why. It may be because the passing up on that extra hour of stimulation in isolation. So that's what we do, occupational therapy that will help them you know, how to get dressed, how to you know, deal with others, how to improve their swallowing, their communication, and physiotherapy with you know a physical therapist to help with movement difficulties because you don't want anybody to be exercising if they are unstable.

NANCY LYNN: Yeah, this brings up a lot of questions from me, but you also...since I know you study gut brain connection and you talked about inflammation, is there any, is there more evidence on diet in terms of helping FTD?

DR. TANSEY: Well so there's no evidence that any diet actually is able to slow down the progression of any neurodegenerative disease. What we do know is that good gut health in important so that you don't have a leaky gut. And a leaky gut results a lot times from a bad diet, you know too much sugar, too much fat. A leaky gut obviously comes from IBD or Crohn's. It could also come from exposures from the food you eat. You know, pesticides and things like that. So the important thing is to realize that a good diet, moderate exercise, and sleep, to reduce the stress and kind of you know, reboot and recharge your batteries -- as my 90 year old father likes to say -- that's really important. And we do know that with good gut health, and you know, vegetables and fruits and things that are not highly processed, and not a lot of canned food, that tends to give you better gut health and we know that that health is important for that brain for gut brain health. So, if you have good gut health, you're likely to have better brain health. But so far there have been some studies with the Mediterranean diet, for instance, and very few, you know, studies that need to be replicated. They have shown to improve some of the balance issues in Parkinson's patients. That was some of the work done here at UF, and of course people are trying, right. People are trying all sorts of things. One possible way in which that could have helped Parkinson's patients, for instance, is that they suffer from a lot of constipation and potentially because some Parkinson's may start in the gut right with the glummed up

proteins. And so one possible reason why a Mediterranean diet might help them is because if you're less constipated, you're going to be more likely to exercise, right. And so, it could be related to that effect.

NANCY LYNN: Oh, that's so interesting! Why do people with dementia crave sweets?

DR. TANSEY: Hmm, yeah. So that's a good question. That's actually one of the common behavior changes that are, you know, seen and manifested in people with FTD, and it's got to do with the fact that in the brain, in the areas that are being affected, there's a change in one of the neurotransmitters. And it's called serotonin. And serotonin is sort of you know, one of the things that that make you happy, and you know, comfortable. So it's thought that it's an altered way of making yourself, you know, feel better with comfort food, and so you crave sweets, and you eat a lot of candy, right. So, if that is something that is manifested in a patient, it's a good idea to mention that to the doctor, because there might be ways to modify the serotonergic system, to be able to modify those cravings.

NANCY LYNN: Interesting. I was traveling a little bit when the Glen Campbell movie was being filmed and Glen used to get a piece of chocolate cake for dessert when he was in assisted living, and he would eat the piece of cake ask for another one he would literally lick the plates. And I just I was always so fascinated.

DR. TANSEY: Yeah, I mean we have to be really careful, though. Right? Having a sweet tooth is not the same thing, right, and I don't know if those behaviors were, you know, insistent with that, you know an FTD change, but this would be like bags and bags of sweet candy, right. So, it's more than just having dessert every day, or you know I don't want to worry people about that. So it's, you know, it's an unusual craving for a lot of sweets.

NANCY LYNN: Thank you for clarifying that. I wanted to go back. You mentioned Leqembi, which we talked about last month, Donemana, which has come out with some data. Do we know yet whether these drugs may slow progression and improve or slow down the rate of decline of activities of daily living in FTD as they have been shown now to do for

Alzheimer's related dementia.

DR. TANSEY: Right. So that's a really good question. The fact that all these neurogenerative diseases have the aggregated protein in common gives us a lot of hope that the immunotherapy positive results for early Alzheimer's with lecanemab in particular will be able to translate into FTD, and Parkinson's, and ALS, right. Because the idea now is to make sure that those proteins never get aggregated. And so the antibodies that are being used to slow down the progression are those that are binding up those proteins before they glum up, and if they bind them up before they glum up, then you don't have this plaque or aggregated protein accumulation. And so the thing that needs to be done is to figure out, okay, if it's not amyloid Beta in FTD, what is it? So it's likely to be TDP 43 or Tau, and there's a lot of research going on right now with those kinds of approaches for antibodies against them, so that we can give them, you know, very early. So I'm very hopeful that because there's a lot of common mechanisms underlying the causes of what we know are many of these diseases that we will be able to benefit from that. The lecanemab results are very hopeful because they included a lot more people with diverse ethnic and genetic backgrounds. One of the problems we have is that a lot of times the studies are only done in Caucasians, and in that is a problem. So, we need more diversity in our clinical trials. The other thing about lecanemab, it was given, you know, early and it was given to people with, you know, early early signs not advanced. As well as that antibody is able to detect an earlier form of the protein that's going to aggregate. So if you can imagine this as sort of a process, there's lots of different forms. If you have an antibody that recognizes the early stages of the misfolded protein, you have a better shot at arresting the progression than if you target, you know, a more aggregated form.

NANCY LYNN: So if I'm understanding correctly, it would not necessarily be a straight line to try to do clinical trials of Leqembi or donanemab in people with FTD because it's a different protein?

DR. TANSEY: Exactly. That's right. You would need to target the exact protein that's aggregating. So in the case of Parkinson's, you do have some amyloid, you do have some TDP 43 in the aggregation, you know,

pile in Parkinson's, but the majority of it is synuclein. In FTD, it can be TDP 43 or Tau. But there's different forms depending on whether it's the familial or the sporadic.

NANCY LYNN: Do men get FTD more than women?

DR. TANSEY: Yeah, it seems to be a little bit more common, maybe twice as common in men versus women. And we're not really sure why that is, you know. It's possible, it's the opposite for Alzheimer's, and so it's possible that some of the changes related to estrogen and other hormones and menopause are protecting, you know, against FTD in women, and not so much against Alzheimer's in women. So the sex differences is a really important area of investigation that is really not that new, if you believe it. But most of the studies in most places have been done with white males, and so, as women start to participate in clinical trials, and you know they go in and see the doctor and see care, then we're learning that there are some really interesting and important sex differences that that will give us clues about, you know what's going on.

NANCY LYNN: I'm smiling, Dr. Tansey, because I chatted to everyone "Am I asking the right questions? Please feel free to chime in." And of course, these questions were all submitted by all of you. So I hope they're the right questions. I just don't want anyone to be shy if you have specific questions. Someone wrote in, can a brain injury kickstart FTD?

DR. TANSEY: Yeah, that's a good question. So there is some evidence to support the idea that the biggest non-genetic risk factor for FTD is traumatic brain injury. Now, if you know a little bit about Parkinson's, Parkinson's is very common in boxers. The biggest factor risk factor other than age for Parkinson's is a head injury. And so we look at that, and we say, well, that's really interesting. Why would a head injury, or TBI be a risk factor for two very different diseases? And so with my bias in hand, we think part of that is the inflammatory response that you have after the head injury, and then that persists for many, many, many years and decades. And what happens is that glummed up protein that should be removed is not removed because the immune cells that are in charge of vacuuming up the house are now kind of lazy and sick as a result of that chronic inflammation. So what dramatic brain injury does, and any chronic

inflammation in your brain, it kind of makes these professional vacuum cleaners kind of, you know, lazy and dysfunctional. And we believe that's one of the things that contributes to more protein aggregation in a risk for neurodegeneration.

Now, why, it would be FTD versus Parkinson's may have more to do with your genetics and other exposures. We know that exposures to pesticides, and you know various things are very closely linked to Parkinson's, and not so much to FTD. And so that's why we think that a brain injury that goes on for many, many decades in terms of inflammation may be a risk factor.

And we worry about long Covid, to be perfectly honest with you, because long Covid is likely to be more related to ongoing inflammation, chronic inflammation, long after you know your Covid respiratory virus is gone. And so studies to monitor people with long Covid are ongoing and I think it's going to be one of those things that we're going to have to contend with, you know, decades from now in people. So you know, the lighter or milder infections may not be as associated with that.

NANCY LYNN: You're making me think because about boxers and football players and CTE...

DR. TANSEY: Chronic traumatic encephalopathy

NANCY LYNN: So is there a relationship do we think between FTD and CTE? Because and also I'm thinking, because they both have intense symptoms of agitation, and actually, someone wrote our people with FTD violent? And I believe that is one of the agitation symptoms. And then I'll follow that up with, because there was a recent FDA approval. Are there any drugs available for agitation and these mood issues?

DR. TANSEY: Yeah, that's a good question. So CTE is more associated with repetitive head injury. So football, players, soccer players, rugby players. And the repetitive nature of that is what we think leads to chronic traumatic encephalopathy. And that's why you know, it's not just a head injury, a falling off a horse, right. But the interesting thing is that CTE definitely is associated with aggregated protein. It's tau right? And tau is

one of the things that also aggregates in FTD. And so I think there is the connection, but the CTE connection is more to repetitive as opposed to a single, you know, big traumatic brain injury.

In terms of agitation, people with FTD are not violent per se. They basically could become agitated if you approach them and surprise them. And so you don't want to misinterpret that. And so a person with FTD could, if provoked, become kind of agitated and violent. A person with Alzheimer's will also become agitated sometimes, if somebody you know surprises them and they can be combative as the disease progresses. There are medications to deal with agitation, and I think that those are some of the important conversations to have with your doctor. They have some side effects. So I think it's, you know, it's certainly something you want to consider if the agitation is too much. It is common for older individuals to be agitated more in the evenings. So you know it's called Sun Downing, or Sundowner Syndrome. And so physical activity and natural lights are really good to make sure that, you know, you don't have these episodes of agitation.

NANCY LYNN: You wrote something that really intrigued me so I'm going to ask the question here: what are the three things never to do with your loved one if they have dementia? And I'm sure there are more than three.

DR. TANSEY: Yeah, I'm sure there's more than three. So I you know, I think, the things that are more critical is that you don't want to agitate them right? You don't want to argue with them. You don't want to say, you know, well, you know you're flat out wrong, or that's wrong. Right? Because that's like what people call poking the bear. Nobody likes that. So you know, not pointing out when they are wrong about something, or if you're going to do it, doing them in a very gentle and, you know constructive manner. Also arguing with them is, it's kind of a losing proposition, right? Because their ability to speak and communicate is already affected. And so you don't want to put them at a disadvantage and feel even worse about it.

The other thing to do is remember that, you know, all these disorders have a component of memory loss. And so you don't want to see, you know, if they've remembered something or forgotten something that's something

that you know, kind of upsets them. And if they've had a traumatic loss or an event that you know has profoundly affected them, you know, loss of a loved one, I wouldn't bring that up, right. And any topic that upsets them, I would just stay away from. The idea is to make sure that you know you are treating them like you know, human beings that deserve you know respect and consideration, and you don't treat them like a child. Because a lot of people do do that. They sort of talk to them like they're, you know, 5-year-olds, and maybe they start speaking, you know, loudly or shouting at you. But I think it's important to remember that, you know, but for the grace of God they're alive. So it could happen to anybody, and I think it's important to have the dignity and respect for them.

NANCY LYNN: And so I've seen many friends argue with their parent with dementia, and correct them, and argue. So when my grandfather walked around saying, "Where's Francis? Where's Francis?", when Francis had died several years before from dementia, what is the, I'm not going to say the correct way to respond, but what is a way to respond that is most helpful for the person with dementia?

DR. TANSEY: Yeah, you know, I think it's clear that they know that it's happening, especially in the early stages. And most parents, I know my mother felt this way, don't want to be a burden to anybody. And so I think the important thing is to remember that living to old age is a privilege, not afforded to all, and you need to walk away and step outside, count to ten before you say something that might be hurtful because you don't want to add to that right? You want to make them comfortable. You want to appreciate them and love them and focus on the positive aspects of the fact that they're still here. And we can still benefit from their love and their wisdom.

NANCY LYNN: And so, if your loved one is asking for someone who's long dead, or, as in the case of a friend of mine, whereas she was looking for her cat all the time, who had passed away, you're not a terrible person, if you say we're going to see her later on, or the cat is resting. That perhaps that's okay.

DR. TANSEY: I think that's okay, because you definitely don't want to say anything that's going to upset them even more and they may be more

accepting just to say, "yes later" or "not now" or you know "let's look at pictures." Sometimes looking at pictures is sufficient, because in their mind, you know, they just saw them. And then maybe they'll dream about them, and that may be sufficient.

NANCY LYNN: And music, which I'm just thinking would be a wonderful association.

DR. TANSEY: Music is fantastic. Yes, music has a very interesting effect on people with dementia. Any kind of dementia. It's linked to lots of memories that can make them feel really, you know, alive.

NANCY LYNN: Happy. Yeah, I'm going to read this. There's a wonderful question in the chat from Marcy Byler. I hope I'm pronouncing correctly. My 88-year-old mother-in-law has some form of dementia, we've not pursued a specific diagnosis. At this point, we have felt that it is most important to keep her as comfortable and happy as possible and thought the testing for diagnosis would be uncomfortable and frustrating for her. Is there a reason to pursue diagnosis in patients with advanced age? And I will say we got a lot of questions about, you know, the medications that are symptomatic, you know. Is it really worth having people take these medications? But I really like this question, is it worth getting a diagnosis in a person with advanced age?

DR. TANSEY: Yeah, no. So this is a really perfect question. And it's important that you know that we talk about it. People feel the same way about cancer or anything that's terminal right? Things that we don't have a cure for. And so I would say that it's definitely not required that you pursue a diagnosis. The most important thing is to keep them comfortable, and you know them best because they are your family members. So I can only say that, you know, if my 90 year old father were to start showing signs of anything, I would probably not put him through the ringer. I would keep him comfortable. I would, you know, ask him if he wants to go and find out, you know, a diagnosis? Then yes. But I think the important thing is, you know, what do you do with that knowledge? And so one thing that you can do with that knowledge is to make your family members aware that there's now a family history of X. And once you know that I am absolutely 100% confident that we are going to get there to the

point where we will be able to identify and enroll people with genetic predisposition into clinical trials that will prevent the development of this these diseases. I'm 100% sure that will happen. Maybe not in my lifetime, because I'm already 60. But it's going to happen. And so if you want to think of the information as knowledge is power and I could provide this information of a definitive diagnosis of X, it could potentially help your children and grandchildren in the future if they start having, you know these similar things. But the most important thing for the here and now is clearly to have them be comfortable, and you know them best.

That's I think that's wonderful. Wonderful answer and a great question. Thank you, Marcie, and I'll also point out that you would not necessarily have the same answer for someone younger, and in very early stages, who may be eligible to participate in a clinical trial, or do interventions that could help slow the progression, and things like that.

Unfortunately, we have 1 min left, and the time just flies by. So first, I wanna thank you. Dr. Tansey, and I do hope you'll come back and talk about the gut brain access and everyone thank you so much for your time. Roger, could we put up the follow up slides here, and, thanks to all of you, very much for participating and you're submitting your questions and being here. It's wonderful to see people's faces. It's very helpful for those of us in the field who really wanted help provide some of the information.

If your question was not answered today, or if you're dying to know about a topic that we have not addressed, you can email reply@brightfoot.org and that would be really wonderful. Next month we are doing "Is Alzheimer's hereditary? Genetics and Dementia" with Dr John Hardy. And I was thinking that after that perhaps we would return to the differences between the new breakthrough drugs because since last month when we talked about Leqembi another one had has come, has had a data readout that we've had information about it. Another drug donanemab, which we did mention in the prior episode, but by the summer we may have a full approval on one or more of those drugs. And so I thought, if everyone agrees that it would be of interest to focus in on what are the differences? Who can get it? What's the situation with CMS? and go back to that.

But let's see, here are some expert articles that BrightFocus has online.

And I'm sure Dr. Tansey has quite a few more. So if you're interested in getting copies of these articles or other resources, please email info@brightfocus.org or call the number on the screen (855) 345-6237. But we will be emailing everyone who registered a copy of this program to watch and resources, printed resources.

And let's see, do we have any more slides left? Oh, yes! And so next month, June 22, "Is Alzheimer's hereditary? Genetics and Dementia" with Dr. John Hardy, who has a wonderful accent. And I'm again going to thank Dr. Tansey, who teaches professionals and the public like us in both English and in Spanish, which is so necessary. And I'm just thrilled to have had you today, and I thank you so much. I'm going to end today like I did last month and say, hug or call the people that you love often and thank you so much for attending. And we'll see you next month. Bye!