DR. KHOSLA: Thank you for joining us for Talking Sleep, a podcast of the American Academy of Sleep Medicine. I'm your host, Dr. Seema Khosla, medical director of the North Dakota Center for Sleep in Fargo.

Mount Sinai researchers have conducted one of the first studies to show the acute effect of obstructive sleep apnea on Alzheimer's disease biomarkers, demonstrating that untreated OSA may increase the risk for developing neurodegenerative disease.

Here to talk to us today about the study is author Dr. Andrew Varga, associate professor of medicine at the Icahn School of Medicine at Mount Sinai. Thanks for joining us, Dr. Varga.

DR. VARGA: Thank you so much for having me.

DR. KHOSLA: So tell me about this study.

DR. VARGA: So we were really interested in understanding the acute effect of sleep apnea on Alzheimer's disease biomarkers and markers of neural injury. And so we embarked on a study in which we recruited subjects who have known severe sleep apnea at baseline, but who are also very adherent to treatment of their apnea with a PAP machine that we know by virtue of download from their from their PAP machine and had them come on to different nights to do sleep studies. One night in which we asked them to use their PAP machine at the pressures that are therapeutic as they ordinarily would at home, and then a separate night in which we asked them to discontinue their PAP machine two nights prior to coming into the lab so that the record at night represented their third night off PAP. And we expect that they would have recapitulation of their severe OSA on that night.

DR. KHOSLA: Was that hard to convince them to do?

DR. VARGA: No. And generally not. Yeah. You know. Yeah. No is the short answer.

DR. KHOSLA: I imagine I would get a lot of pushback if I asked some of my patients who are adherent and severe to do this. I think I would get a little bit of pushback.

DR. VARGA: Yeah, usually when it's relatively short term, people don't have too much of a problem with it.

DR. KHOSLA: That's fantastic. So keep going.

DR. VARGA: Yeah. So in this context, you know, we had people complete blood draws before and after sleep, right? So essentially right before sleep and then and then immediately after and the idea was to then, you know, analyze that collected blood for overnight change and proteins that are related to Alzheimer's disease and neural injury. And in particular, we looked at beta

amyloid 42 and 40 isoforms, levels of total tau and levels of this protein, neurofilament light, which serves as a marker for neural injury.

DR. KHOSLA: Oh, so that's interesting. I don't know that I've heard of neurofilament light before.

DR. VARGA: Yeah. So neurofilament light is an axonal protein that gets released in response to neural injury. It's something that's not completely specific to Alzheimer's disease. So for example, you can see it go up in other disorders like multiple sclerosis. But the Alzheimer's field has been, I would say, fairly interested in this is a biomarker because it tracks very closely with Alzheimer's disease progression. So as people progressed from, you know, being cognitively normal to having mild cognitive impairment or MCI to then bona fide Alzheimer's disease, levels of neurofilament light, both in the spinal fluid and in the plasma, increase very reliably. And in addition, there's some evidence suggesting that even in cognitively normal people, there is an inverse relationship between your levels of neurofilament light and cognitive performance, such that, you know, kind of higher baseline levels of neurofilament light seem to predict, you know, worse cognitive performance, even if you are cognitively normal.

DR. KHOSLA: Oh, that's really interesting.

DR. VARGA: Yeah.

DR. KHOSLA: So how is this different from previous research?

DR. VARGA: You know, you can you can approach the interaction between, you know, sleep apnea and Alzheimer's in a lot of ways. You know, some of it's been based on, you know, non-objectively measured assessments of sleep apnea, right? So by questionnaire by self-diagnosis. So, you know, having, you know, actual objective measurement was, I think, important here. The other I would say one of the main differences is that, you know, much of the work has, you know, really assessed cross-sectional associations between apnea and biomarkers at sort of one timepoint or looked at longitudinal associations between having a diagnosis of sleep apnea that's in most cases untreated and looking at how that impacts longitudinal risk. But this was, you know, I think, a real first attempt to understanding what's happening very acutely and what's happening sort of dynamically over the night, right from the beginning of the night to the end of the night, either on or off PAP.

DR. KHOSLA: So who are the patients that were involved? I mean, are these sort of anybody that you found that had severe sleep apnea or were they maybe genetically preloaded, you know, felt to be at higher risk for Alzheimer's?

DR. VARGA: Yes. So these were subjects who were recruited, you know, essentially from a sleep clinic who are you know, the main entry criteria was essentially that they have severe sleep apnea and that they they use PAP on a on a regular basis to treat it. Outside of that, there were no other special sort of inclusion criteria. So no, they were not specifically, you know, selected for having any increased Alzheimer's risk like, you know, carrying isoforms of APOE4 or things like interesting.

DR. KHOSLA: Oh, interesting. Okay.

DR. VARGA: Yeah, they, you know, they were, you know, we did not want people that had other sort of neurologic or psychiatric disorders. So, you know, they were excluded. But that was pretty easy to, you know, to figure out really early on.

DR. KHOSLA: And so then was their criteria, you know, I'm guessing they had to be well-controlled, right. And did they have to have maybe been on PAP therapy for years or months?

DR. VARGA: Yeah, we required that they be on PAP therapy for at least two months. So it could be, you know, relatively recent. But just, you know, someone who's really documented that adherence. And, you know, we used, you know, the general Medicare sort of criteria for adherence, you know, 4 hours or more per night for 70% or more of nights.

DR. KHOSLA: So you attach on some biomarkers. And I will be the first to say this as a pulmonologist. So, you know, you're rattling off these biomarkers and so in my brain, I kind of think of beta amyloid and I think of tau associated with Alzheimer's. But is that correct or am I am I wrong? Am I thinking about something else?

DR. VARGA: No, that's correct. I mean, those are I would say the primary pathologic proteins and Alzheimer's disease. And, you know, fortunately for our field, you know, they're able to be measured in a variety of ways. I would say historically, those biomarkers have been measured and in spinal fluid, because that's the fluid that's most proximal to neurons. You can also measure those biomarkers with PET imaging. I will say that while each of those things is highly useful and interesting, they're also a little bit complicated, right, in the sense that PETs kind of very expensive, requires exposure to a radio ligand, and collecting spinal fluid, you know, requires that you put someone through a lumbar puncture.

So we became very interested in this idea of sort of assessing these biomarkers in the plasma. That's something that has historically been a bit challenging to do, mostly because although these, you know, amyloid and tau biomarkers exist in plasma, they exist in very tiny concentrations. And so using, you know, classical, you know, sort of elisa measurements of these proteins was really challenging and you could not meaningfully measure concentrations of things like amyloid and tau in the in the plasma until you know maybe about somewhere between five and ten years ago when this what's called Simoa technology came out, that's an acronym that stands for single assay molecule MO array, Simoa, that is more or less a fancy allies, but it has without getting into the nitty gritty of it, just the ability to detect, you know, like picomole, really tiny…

DR. KHOSLA: Oh wow.

DR. VARGA: …concentrations of proteins in the blood. And so sort of once that became available, people started really looking at, you know, these Alzheimer's biomarkers and in plasma and started there's been a whole number of papers over the years showing that, you know, these can be measured in really meaningful ways. Right. That, for example, that is measured in plasma in that they do correspond to disease progression. Right. As you clinically progress from, you know, normal cognition to marker of impairment to full blown Alzheimer's

also that they correlate to a reasonable degree with the other measures of these biomarkers. Right. So that the plasma levels of these biomarkers do in fact correlate with, you know, imaging biomarkers, right, by PET imaging or in the spinal fluid.

So it's been a lot of work suggesting that, you know, these you know, you can really do this or you can really meaningfully measure these biomarkers in the plasma. And it really means something.

DR. KHOSLA: So so then so then we've sort of established that measuring these biomarkers in the plasma correlates to other imaging. And so we believe it. Right. So what, what happened with the study then. What, what was the result.

DR. VARGA: Yeah. So kind of to me in results, right. So of the four biomarkers that we looked at, we saw that there were significant overnight change differences in two of the biomarkers and neurofilament light and then beta amyloid 40. So when you went off PAP neurofilament light, this marker of neural injury increased relatively overnight off PAP as compared to when you're treated and in addition, we saw that beta amyloid 40 actually decreased off PAP relative to being on treatment and we did not observe changes in beta amyloid 42 or in total tau. So the real big changes were in this neurofilament light protein and beta amyloid 40.

DR. KHOSLA: So what does this, what does this tell us then.

DR. VARGA: Yeah, so I think the interpretation for neurofilament light is a little bit more straightforward in the sense that, you know, we think of it as this marker for neural injury and what we see is that it's, it's increasing overnight, right, when people go off PAP, right. In comparison to when they're treated on PAP. And so the interpretation there I think is relatively straightforward, which is that this is some of the first evidence showing that acutely induced, you know, sleep apnea creates some level of neural injury. Right. That can be measured with this neurofilament light.

DR. KHOSLA: So that that sounds kind of scary to me. So how should I you know, when you say that, I'm like, oh, my gosh. So does this mean that when I have a patient that is like going fishing for a weekend and doesn't want to take his CPAP? Should I be worried about his brain health?

DR. VARGA: Right. So, I mean, I think that we would probably encourage people not to take breaks from using their PAP machine. That's said, I mean, I think it is common for people to do that. And, you know, I mean, I think we want to, you know, not scare people. I mean, I think that this is evidence suggesting that there's some, you know, neural injury that happens. But I don't think there's necessarily evidence that this is, you know, irreversible neural injury. Right. So this may be more like a bruise, so to speak, that we don't know whether. Right. That this is, you know, something that's going to be permanent or. Right. Or whether this is something that, you know, just represents an injury that is going to then recover over time. So, you know, I think that it's just another piece of evidence suggesting that it's probably not a great idea to take too many breaks from your PAP machine. But I wouldn't go over the top with the threat that you're going to become permanently brain damage from that.

DR. KHOSLA: Well, because I think that's I think that's it. Right. I think we need to be realistic about what our patients, you know, are doing and how this fits in with our lifestyle and how do we appropriately inform them of this potential risk. And I love that analogy of it may be a bruise, right? This may not be permanent damage. But, you know, we you know, we don't know. And so if we can minimize the time off of CPAP, you know, the other thing that really strikes me about this is that this is a lovely research study on the importance of treating obstructive sleep apnea that doesn't have a cardiovascular endpoint. Right. This is more cognition.

DR. VARGA: Yeah. I mean, I would say that, you know, there's lots of reasons to treat people that have apnea. You know, many times people have, you know, acute symptoms. Right. I mean, snoring, sleepiness, etc.. It's obvious, right, that you should you should treat them. We I think as a field we've had the idea that, you know, even if someone is asymptomatic, that they should probably be treated. That supposition, I think, was based a lot on these ideas, that apnea was bad for your cardiovascular health. Right. That your predisposition to hypertension and to potentially, you know, you know, things like myocardial infarction or cardiac arrhythmias. So there's been a really big focus and I think, you know, less focus has been placed on, you know, sort of memory outcomes and neurodegenerative risk outcomes. But I think the literature on this is is really growing. And I think this is starting to be something that I mean, I certainly discuss more frequently with with my patients in the clinic. And I would imagine that, you know, many sleep physicians are perhaps starting to as well with theirs.

DR. KHOSLA: So so when you were looking at patients, did you select only sleepy patients or non sleepy patients like was that any part of the process?

DR. VARGA: Now that was there was not a specific a primary inclusion or exclusion.

DR. KHOSLA: Oh, that's interesting. So you've done a lot of research related to obstructive sleep apnea and cognitive health. And you kind of separate I hear you separated into two things, right? You talk about memory and then you talk about cognition. So help me understand what you're referring to for both. On both of those.

DR. VARGA: Yeah, sure. I you know, I think that there's the you know, the ability to learn new facts today and remember them tomorrow. Right. Is something that I call prospective memory. Right. And sleep apnea seems to impair that. Right. And that's, I would say, an important adverse consequence of having apnea is that you have this reduction in prospective memory. And, you know, there was a really great clinical trial that was published last year by my colleague Ina Djonlagi at Harvard that showed that if you take people with newly diagnosed sleep apnea and test them in this prospective form of memory. Right. And this study in particular was a word pair task is memorize word pairs before sleep and then get asked them again in the morning. Right. That people with apnea do worse on this rate as compared to people that don't have apnea. And then she did a small but nonetheless really bona fide randomized clinical trial of PAP for the treatment of OSA. And in those people randomized to PAP when they repeated this overnight memory test several weeks later, you know, did much better on it and were performing at levels that were comparable to people that didn't have any apnea at all. Whereas the people that were assigned to, you know, sort of watchful waiting and no treatment in the interim really had no

change. And so, I mean, personally, I find that like really interesting and exciting. I mean, it shows that, you know, PAP is doing something for perspective memory. But the thing that's, I think, important to to note is that whether that is true or not is something that possibly is dissociable from the risk of sleep apnea on subsequent cognitive decline and in developing something like Alzheimer's disease.

In other words. Right, whether PAP does or does not immediately improve your prospective memory is theoretically dissociable from whether PAP is going to over long periods of time, kind of protect you and slow your if you are someone who's predisposed or predestined to getting Alzheimer's, whether using PAP is going to slow that trajectory. Right. And, you know, we think they're sort of related in the sense that, you know, people that are predestined to develop Alzheimer's disease, I mean, start by having some prospective memory deficits, but then over time, it actually converts to including retrospective memory deficit.

So not only are you having difficulty remembering new items or new things from life, but the things that you have remembered, right? Like your first grade elementary school teacher's name and stuff. This like way back in the past, that starts to fade also, right? That's what I call retrospective memory, right? So all I'm saying is that it's important to think about these things in potentially dissociable ways.

DR. KHOSLA: See, I think that's so interesting. And again, as a pulmonologist, I have never consider that as to, you know, I just sort of lump it all in as, you know, brain stuff. I don't really think about it. Right. Is this is a distinct process that is like you're seeing dissociable from the other.

DR. VARGA: Yeah. So I just yeah, I think that's important to keep in mind.

DR. KHOSLA: So how did you come up with the idea for doing this study?

DR. VARGA: Yeah, this study has a kind of a great back story, which is that I was attending something that's called the International Symposium on Sleep and Breathing, which is a small meeting that occurs roughly every two years and last occurred in 2019 in Finland. And I met Jonathan Jun there, who's an associate professor at Johns Hopkins, who also does sleep apnea research, but in a really totally different domain. He was really interested in sort of sleep apnea effects on metabolism, especially on the way you metabolize things like fatty acids and glucose and things. And so he had subjects who were coming in for this PAP withdrawal paradigm where his primary question was to address, you know, to what extent PAP withdrawal ended up impacting, you know, these other metabolic aspects of things.

And I said, you know, that's such a great paradigm. And, you know, we've had these interest in understanding, you know, acute effects of apnea on an Alzheimer's risk. And I explained to him that, you know, there is this sort of new technology, right. That allowed us to kind of meaningfully measure these Alzheimer's biomarkers in plasma. I said, you know, what do you think about, you know, sharing these samples?

And he said, yeah, that's a great idea. Let's do it. And so I said, okay, that's really cool. And also as part of this dinnertime conversation in Finland, was my colleague at Mount Sinai, Dr. Korey

Kam, who also has related interests in understanding associations between sleep apnea and Alzheimer's disease. And so Korey and I got back to the to the States and we put our heads together and we said, you know, we should we should write a grant, you know, to do this and to get some money to actually, you know, analyze some of these samples that Jonathan has and so Cory and I worked together and submitted a grant proposal to the American Academy of Sleep Medicine Foundation, who have a focused projects grant mechanism that some that's actually grown at the time that we applied for it. It was sort of a $20,000 grant. I think it's now grown to $40,000. But in any case, you know, we applied for this and we were fortunate enough to get this funded by the American Academy of Sleep Medicine Foundation, which was really fantastic. And that gave us, you know, the needed funding to be able to do the analysis on these plasma samples and so, Jonathan, you know, arranged for transfer of the samples from Johns Hopkins to Mount Sinai then we use the AASM Foundation funds to run the analysis.

DR. KHOSLA: And I know if you go to Finland, I love how you had to go to Finland to meet him.

DR. VARGA: Yeah, yeah. It was great. And then and then we and then we hit the sauna afterwards.

DR. KHOSLA: Oh, of course you did. I love that. So let's take a short break and we'll talk more about your research in just a moment. You're listening to Talking Sleep from the American Academy of Sleep Medicine.

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DR. KHOSLA: Welcome back to Talking Sleep. Our guest today is Dr. Andrew Varga, and we're talking about research suggesting that untreated sleep apnea may increase the risk for neurodegenerative disease.

So you're hanging out in the sauna. You're talking about biomarkers. How long did it take for you sort of from start to finish to complete the study?

DR. VARGA: I mean, it took probably three years, really, right? I mean, this thought the meeting was in 2019. We probably wrote and submitted the grant in 2020 and probably did much of the work of it in 2021. And then once we had the results, kind of wrote it up and things and it just got published in June of 2022. So yeah, so from start to finish, like I said, just shy of three years.

DR. KHOSLA: But so did you have access then to their PSG beforehand? Meaning, you know, I'm kind of wondering if there is something within that PSG that may be predictive.

DR. VARGA: Correct? Yeah. So we had the PSG data from both nights that they completed. Right. So their teir night that was on PAP when, when sleep was presumably pretty ordinarily consolidated as well as the, the night that we asked them to discontinue either their two nights ahead of time in which, you know, apnea was present and pretty rampant. And so yeah, you

know, unsurprisingly, right off now, people had, you know, pretty severe sleep apnea. I think the the 4% on average in this group was was around 60.

DR. KHOSLA: Oh, wow.

DR. VARGA: And we had access to, you know, at least some of the standard sleep physiology measures that come out of a scored report. Right. So things about sleep stages and measures of hypoglycemic burden. And so this part of the study, we were interested in understanding, you know, whether or not there were significant predictors of these overnight changes in either neurofilament light or beta amyloid 40, which were the two biomarkers that we saw significant changes in between conditions.

And so we ran some analyzes looking at whether any sleep physiology predictors existed. And we found, in fact, that measures of hypoglycemic burden as measured by the time spent with an oxygen saturation below 90%, as well as measures of sleep fragmentation, which included the number of sleep stage transitions were both significant predictors for the overnight change in neurofilament light, this marker of neural injury, We did the same thing for beta amyloid 40 but we didn't find any significant predictors for that one.

DR. KHOSLA: Oh, so that's interesting. So they weren't necessarily both impacted the same way.

DR. VARGA: Correct.

DR. KHOSLA: Oh, interesting. And so intermittent hypoxia and sleep fragmentation, which I mean, makes sense.

DR. VARGA: Yeah, it makes sense. I mean, I will say that you know, our primary hypothesis was that we would hit on some marker of hypoglycemic burden as a potential predictor for neurofilament light, because we really thought that it was more likely that the you know, the intermittent hypoxia is what's really sort of, you know, injuring neurons and leading to that release in neurofilament light. Whether the sleep fragmentation is also, you know, really physiologically a predictor, I think we need to so kind of work on an answer a little bit.

I mean, I think the reason I'm questioning it a little bit is because although we saw that sleep stage transitions was a significant, significant predictor, we didn't see the other markers of sleep fragmentation that you might expect would be would be more important, like like the arousal index or something, right? We didn't see that as a predictor.

So I think, you know, like I said, work is still ahead of us, us and the rest of the field to kind of suss this out a little bit, but.

DR. KHOSLA: That's really surprising to me, you know, because when I think about sleep stage transition, right? I mean, when you have all these arousals, you know, you see that somebody sleep is super fragmented and choppy. You know, in my brain, I think I think about, you know, cognition in those patients and sleepiness and that sort of thing. And so it's interesting what you're describing.

DR. VARGA: Yeah. I mean, I think, you know, I don't know. I think sleep stage transitions are interesting as a marker of sleep fragmentation, but you would sort of expect that they would potentially go along with things like arousal indices. Right. And it's and and like I said, the fact that those kind of dissociated in terms of the prediction for for neurofilament light makes me kind of question a little bit how that is physiologically fully relevant.

DR. KHOSLA: Right. And so what I was wondering is did you have access to like their initial diagnostic study, which I'm guessing now thinking about it, that would be pretty hard to do. But, you know, I just wonder if that was part of what you analyzed. But it sounds like it was the two, sort of the pre and the post.

DR. VARGA: Yes. I guess my my honest answer is that I'm unsure whether we had access or not to the original diagnostic study. If we did have access to it, it was not something that we really used as part of the study. Rather, we used the the data that we collected from the study is like on that two intervention nights that we.

DR. KHOSLA: Yeah, that makes sense.

DR. VARGA: We actually had.

DR. KHOSLA: That make sense. So, you know, we've had a lot of conversations around CPAP and cardiovascular outcomes, right that AHRQ report came out and it said, well, we're not really sure CPAP is helpful for cardiovascular outcomes. Right. And does this type of data that you're sharing with us, how does this reframe maybe how we should be looking at outcomes?

DR. VARGA: Yeah, absolutely. I mean, I think, you know, we need to be thinking about outcomes across, you know, many organ systems. You know, I'm a neurologist, so obviously I focus a lot on kind of brain outcomes. And I think those as you pointed out, have been kind of under underrepresented a bit. But there's even other ones, right? I mean, there's there's endocrine outcomes. There's other organ system outcomes. And so I think we do need to kind of get beyond a sole focus on cardiovascular. But even beyond that, I mean, I think that, you know, we need you know, we need, you know, more studies and more research. Right. I mean, just as an example, you know, this particular approach that we took shows an effect of acute PAP withdrawal, but it sort of raises kind of the obvious question, which is the opposite true? I mean, can you take someone that is newly diagnosed with sleep apnea and actually put them on PAP and show that if they kind of meaningfully use PAP over some time, that you can, you know, reduce this measure of neural injury. I mean, that's something that remains to be to be seen.

DR. KHOSLA: Michel in the research project can't exactly. But you're right. I mean, I think that's just it. You know, we when we listen to our patients and they're like, yeah, I feel sharper. I don't have the brain fog. I, you know, I can remember things again, you know, to me in my brain, I'm marrying that with Oh, well, yeah, it means you're not hypoxic anymore in your sleep is better. And so it would be interesting to see if that's actually true or for that's just sort of wishful thinking on my part.

DR. VARGA: Yeah, absolutely. And I mean, that needs to be done in all sorts of ways that are some of which are more easy or easier and others which are not right. I mean, I think, you know, randomized clinical trials are often considered the gold standard, right? By which we judge. Right. The effect of a treatment such as something like PAP. But, you know, those are often hard to do. Right. I mean, I think if you again, if you kind of compare it to the cardiovascular world, right, there's all many of the clinical trials for PAP and those studies have been right. Basically negative, right? Mm hmm. But it's because a lot of different reasons. I mean, one of the big ones I think probably has to do with adherence.

Right. Right. Randomize people to PAP and then they don't really use it that much. And it's kind of like, okay, yeah. But you didn't see you didn't see an effect because people didn't use the treatment, right?

DR. KHOSLA: Well, that's right. 3.3 hours. It's like, you know, it's like taking your lisinopril every other night and expecting it to work.

DR. VARGA: Right? Right, exactly. Yeah.

DR. KHOSLA: Yeah. So I think you're so I think you've hit on something really important, right, that a lot of our data is based on sort of relooking at data that was from a study meant to look for something else, right? Like cardiovascular endpoints and those are the preliminary endpoints. And then we look at all these secondary endpoints to try to pull out sleep data.

DR. VARGA: Yeah. I mean, I think I think randomized clinical trials are useful, but I think, you know, relying on them as the sole source of data on which to A) make policy decisions or B) like guide your clinical practice is not a, not a great way to approach things, right? So you need like you need lots of approach. I will say I don't mean to like digress or very much, but you know, we're actually we've recently proposed to do a randomized clinical trial for the treatment of sleep apnea on memory and Alzheimer's disease biomarkers.

And part of the approach we're taking is to treat apnea kind of by any means. Right. That reduces the AHI. Right. So, yes, take people with newly diagnosed OSA and say instead of saying, we're going to randomize you to PAP or not say we're going to randomize you to OSA treatment or not, and we're going to try to maximize the treatment through a combination of both efficacy and and usage.

Right? So so we're trying to offer people, you know, oral appliances or positional therapy or some combination of those two in addition to PAP. And what we're proposing to do is to rapidly cycle people through each of these treatments with assessments, you know, very rapid rate within like a week or something. So to figure out, you know, a, whether the treatment that you're that the subject has selected works and whether they're really going to use it.

And then if that treatment meaningfully reduces their AHI, then you can say, okay, now I'm going to I'm going to keep you on that treatment and see what the outcomes are. And we're hoping that that approach, you know, really helps this adherence issue that's kind of plagued a lot of the other prior randomized clinical trials of the treatment of sleep apnea.

DR. KHOSLA: Well, and I think you've hit on something really important, right? Like when we talk about sleep apnea, the endgame isn't to get people into CPAP. The end game is to just treat the sleep apnea and it really doesn't, you know, however you want to treat it is fine. Right. So it's nice that you're you're willing to look at this and kind of get outside of CPAP, which I think means that it's going to be a little bit more challenging.

Right, because there's like this time involved in getting them an oral appliance or what have you. But I think it's meaningful because that's more real world experience, right? And that's more, you know, partnership and collaboration with our patients and doing something that I think makes sense to them and something really that we haven't hit on before, I don't think.

DR. VARGA: Yeah, I think you're absolutely right on both fronts. I mean, I think it will be more challenging. But but no, I think we have the infrastructure in place to really to really do it. And I think you're right. I think that in the end, it's it's something that I think mimics more real life, real world ways of approaching apnea. And if you can show that that approach, you know, has meaningful outcomes on, you know, whatever you're interested in, whether it's cardiovascular disease, sleepiness, you know, AB biomarkers. I mean, it's it's a potentially, you know, translatable approach for anybody who's interested in OSA treatment outcomes.

DR. KHOSLA: Wow a lot a lot has grown in neurology since like my one month rotation on neurology, my intern year, I'm glad to hear it. So any, any final thoughts?

DR. VARGA: I just I like I said, I appreciate the opportunity to talk about this work. And, you know, we are excited for many things that I talked about that we, you know, we're doing in our own lab currently at Mount Sinai in terms of looking at, you know, treatment, whether with PAP, whether with oral appliances and other things and, you know, encourage, you know, other sleep clinicians and scientists to consider, you know, brain outcomes, both in the memory domain and in the Alzheimer's domain as potential areas of interest.

DR. KHOSLA: No, I think you're right. And I and that's what I love about our field, is that, you know, you can come to our field with so many different backgrounds. Right. And I think that that only enhances us. You know, what we can offer, as, you know, this unified field of sleep medicine, because we're not all the same and we all, you know, come at it looking at something else. So I appreciate that.

DR. VARGA: Yeah, I think that's what so many people love about sleep medicine that get into it. Right. Is this just really sort of it bridges so many fields and it's great and you meet people and you collaborate and it's it's great. I love being in sleep medicine.

DR. KHOSLA: And you get to hang out with Sana in Finland. I mean, what could be better? Thank you so much for taking the time to talk to us today about your research and for continuing to explore the links between obstructive sleep apnea and cognition. And I really appreciate you highlighting the difference between recall memory and cognitive decline.

DR. VARGA: Absolutely. Thank you so much.

DR. KHOSLA: Thanks for listening to Talking Sleep, brought to you by the American Academy of Sleep Medicine. For more podcast episodes, please visit our website at aasm.org. You can also subscribe through your favorite podcast service. And if you enjoyed this episode, please take a moment to leave a rating or review. For more feedback or suggestions email us at podcast@aasm.org. I hope you'll join us again for more Talking Sleep. Until next time this is Seema Khosla, encouraging you to sleep well so you can live well.