

68| Obstructive Sleep Apnea and Neuropsychology – With Dr. Mark Aloia

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Speakers: Mark Aloia, Ryan Van Patten, John Bellone



Intro Music 00:00



Ryan Van Patten 00:17

Welcome, everyone, to Navigating Neuropsychology: A voyage into the depths of the brain and behavior, brought to you by INS. I'm Ryan Van Patten...



John Bellone 00:26

...and I'm John Bellone. One quick thing before we get into today's episode. Ryan and I are incredibly happy and proud to announce that our book "Becoming a

Neuropsychologist” was just published by Springer. In the book, we describe the field of neuropsychology and provide a step-by-step guide for how to become a neuropsychologist. You can learn more about it on our website at navneuro.com/book. Ryan and I are going to talk more about this in our next episode, set for release on April 15. So that's all we're going to say about it for now.

Today, we give you our conversation with Dr. Mark Aloia on obstructive sleep apnea, or OSA. Mark is a neuropsychologist and an Associate Professor of Medicine at National Jewish Health in Denver, Colorado. He also has a conflict of interest that he asked us to disclose. He's a paid employee and stockholder at Phillips Inc, a company that makes and sells sleep therapy devices. In our conversation with Mark, he talks about his dual roles in academia and industry, which is pretty unique for a neuropsychologist and interesting for us to talk about.

Ryan Van Patten 01:37

In case you're not familiar with obstructive sleep apnea, or OSA, it's a condition in which an obstruction in a person's upper airway leads to a disruption in breathing. This respiratory problem can cause both a reduction in oxygen delivered to the brain, or hypoxia, and interrupted sleep or sleep fragmentation, both of which can have significant negative effects on cognitive and emotional functioning. We talk more about all of this in our conversation with Mark.



Before we get to that, I wanted to say a few words about sleep more generally because I think this is an area where neuropsychologists potentially have a lot to offer. We know that sleep is incredibly important for cognitive and mental health. Everything from cerebrovascular functioning to mood and anxiety, Alzheimer's disease pathology, cancer, current cognitive functioning and more are all dependent on good sleep. And neuropsychologists are in a great position to assess for sleep disorders. Insomnia and sleep apnea are certainly at the top of that list, but parasomnias, such as REM sleep behavior disorder, restless leg syndrome, and sleep terrors, among others are relevant to us. We can't assume that our patients will be assessed by their PCPs or other physicians, so we have an opportunity to catch these conditions that may otherwise go undiagnosed and untreated. And, importantly, there are good interventions for many of the sleep disorders. We as neuropsychologists can certainly be a part of the treatment for insomnia with sleep hygiene and stimulus control, which can be delivered in our feedback sessions and/or as part of cognitive training. But even when we aren't directly treating the condition, like with OSA, if we identify it where it would have gone unnoticed, this can make a huge difference in our patient's cognitive and emotional trajectories. Unlike many of the degenerative diseases, for example, where rehab and recovery

can be quite limited, we have great treatments for OSA. So we, as experts in assessment and behavior change, can do a lot of good here.

John Bellone 03:53



One last thing before we get into the episode. We do want to apologize in advance that there are a few brief points in which Mark's audio is a bit muffled due to an issue with our remote connection. This is mostly [in] the beginning of the episode and it quickly goes back to normal the few times that it does happen. With that, we give you our conversation with Mark Aloia.



Transition Music 04:14



John Bellone 04:23

Mark, we wanted to make sure we're pronouncing your last name correctly.



Mark Aloia 04:26

It's Aloia.



John Bellone 04:27

Okay.



Mark Aloia 04:27

Like you were in Boston and you needed legal help.



Ryan Van Patten 04:31

[laughs]



John Bellone 04:31

[laughs] I like it.



Ryan Van Patten 04:35

Mark, thanks so much for making the time.



Mark Aloia 04:37

No problem. Thanks for having me.



Ryan Van Patten 04:39

Sure. Yeah. I attended INS 2015 in Denver, and you gave a talk on sleep that happened to be at 7:20 am. It was a CE workshop.



Mark Aloia 04:49

[laughs]



Ryan Van Patten 04:50

So, I was just wondering if all of your talks on sleep happen to be ungodly hours?

Mark Aloia 04:54



No, no. Actually, you know, it's funny. One of the grandfathers of sleep medicine, Bill Dement, who just passed in the past year, he used to get up - we'd have sleep conferences and it would be 10, 10:30, 11 o'clock at night, and he would just get up in the middle of a gala and just walk out to go to bed. [laughs]



Ryan Van Patten 05:18

[laughs]

Mark Aloia 05:18



I think you can get away with that at sleep [conferences], but I wasn't able to get away with that at the neuropsych conference. [laughs]



Ryan Van Patten 05:23

Yeah, I know. There were a lot of jokes around your 7:20 am talk. Everyone had coffee, of course. [laughs]

Mark Aloia 05:30



Right. Well, I appreciate you attending. It's good to see an interest among neuropsychologists in sleep because, as you'll see in our conversation today, there is quite a tie between sleep and cognition.

Ryan Van Patten 05:45



Yeah, for sure. So let's get into it. We will have already provided a basic definition of obstructive sleep apnea in the introduction to this episode. Is there anything that you want to say about what OSA is and how it differs from central sleep apnea?

Mark Aloia 06:02

We can talk a little bit about that. There are multiple ways to look at sleep apnea as a set of syndromes. And, by the way, I'm happy to talk about other sleep disorders like insomnia and other things that might affect cognitive function as well.



Sleep apnea is probably the third biggest sleep disorder. The first is just not getting enough sleep, just short sleep. That's self-restricted sleep, so it's volitional. These are people who just don't take enough time, they could get better sleep if they wanted to. That's probably the biggest sleep disorder. The second biggest sleep disorder, which is about probably a third of the population at any given point in time, is insomnia. And then the third biggest is sleep apnea. We really think of three types of sleep apnea. We think of obstructive, central, and mixed. And then there's this component of what we call complex sleep apnea. So I'll just talk briefly about them if they can.



Ryan Van Patten 06:54

Sure.



John Bellone 06:55

Please.

Mark Aloia 06:56

Obstruction is just what it sounds like - there's an obstruction in the airway. So someone's usually or often lying supine, and they stopped breathing because of obstruction in the airway. The chest wall continues to move up and down, there's continued effort, it can become more and more violent. They're still asleep, they don't see this. The spouse often sees this, which is often why the referral for treatment is driven by a partner and not by the patient. They're not breathing because of the obstruction. A message is sent to their brain, "You're not breathing", they kind of snore, gasp, catch their breath, and start breathing again, all unconsciously. That's usually an obstruction. We usually think of a small airway, but it's not just a small airway. As a matter of fact, that's probably a smaller amount of the cause of the obstruction.



Central sleep apnea is something - I'm sitting here in Boulder, Colorado, a mile high in the air - is something you often see at [high] altitude, but you see in patients at sea level as well. That is just the stopping of breathing, the complete cessation of breathing without an obstruction. So the airway is open, the chest wall is not moving and trying to breathe, you're not seeing that effort for breathing. They just

stopped breathing. [You] certainly see this in neurological conditions. You see this in older adults. But you also see at altitude. We see it in 20-year-olds who come to college at CU. So they'll have some central sleep apnea until they acclimate to the altitude, and that's different. That's more of a neurological thing.

Then you have this thing that's mixed. You can have a little bit of both, that's not uncommon, I'll say.

We have something called complex sleep apnea, which is relatively new that we've discovered over the past decade or so. It's a more obstructive sleep apnea picture. You use CPAP, and you start to see an increase in central sleep apneas with CPAP with treatment. What we found generally - all these are gross generalizations and any given individual can be different - but you see that over the course of about a month of treatment of sleep apnea, that central sleep apnea dissipates. We don't really know why that's happening, or I don't really know why that's happening. [laughs] I'm sure there are brighter people than me who have some hypotheses on that, but it's something to be aware of. If you see in a report from a physician "complex sleep apnea", that usually means there's an increase in apnea with treatment. And you should know that, in many cases, with continued treatment, that extra sleep apnea will dissipate.

John Bellone 09:27



Awesome. We're going to get into treatment, hopefully in depth, a little bit later in the conversation. And we will have already also covered typical symptoms of OSA in the intro. So, for now, maybe we could move straight to epidemiology. The prevalence of OSA increases pretty drastically with age as far as I'm aware. I've seen estimates of around 5 to 10% of the population for people under age 65, and then about 20 to 60%, pretty wide variability of people aged 65 and older. To your knowledge, what are the most up-to-date prevalence estimates?

Mark Aloia 10:02



So this is a bit of a moving target. It usually comes through large scale studies, which don't get funded continually. Most of them were funded in the past. And let me just start with a couple of points. One is sleep apnea is related to obesity. So when obesity rates change, the prevalence of sleep apnea changes. So we have to understand that. If we look at studies from Terry Young from 1996, those rates of obesity have changed. They're great studies, but now the epidemiology has changed. Another thing to recognize is how we define sleep apnea. So, if I may, I'll start with how we define sleep apnea and how we diagnose it.

We have something called the Apnea Hypopnea Index, which is most commonly seen in reports AHI. Apneas are complete cessation of breathing, we're not detecting airflow. Hypopneas are usually a reduction of airflow that's accompanied by either a 3 or 4% drop in blood oxygen level - that just depends on what definition you use. This is something that we observe in a polysomnography, in an overnight sleep study that can occur in a lab or at home. We observe this and we define, sort of arbitrarily. Historically, we've defined apnea as five events per hour of sleep for an adult under [age] 65. Older adults have a totally different definition. And, as you alluded, John, this increases with age. So all we did was change the definition, right? So now it's 10 if you're an older adult. We can talk about that, but what I want to make clear is that this definition was not based on any outcome. It's just based on observation and work through the normal distribution. So that becomes important when we start to talk about neuropsychology of OSA later because there seems to sometimes be a lack of connection between treatment and outcome. And that's important because treatment is defined by an arbitrary definition. So that's the AHI.

When we look at prevalence rates, we often see people parse this out because, in the field of sleep, we know that these definitions are somewhat arbitrary. So [for] an AHI of greater than or equal to five per hour, you'll see ranges from probably 6 to 38% of the population. If you look at an AHI of 15, you might see it drop and be up to 20-some percent. [If] you look at older adults, it's now up to 49%. So, prevalence is really hard to pin down, John. I think it's a fair question. It's not a great answer for you. But I think what we know is that the prevalence is higher than we ever expected. We used to say 2 to 4% of women and men, women were less than men. I think we're now seeing that women are less than men under the age of 65, but they catch up to men over the age of 65 and we're seeing rates much higher. My guess would be, if we just use a standard definition, we're probably seeing 10 to 15% of the population would meet this criteria.

John Bellone 11:36



Okay, that's really helpful. Of course, with any condition, the rates are going to depend on where you place that threshold, that bar. So it makes sense. And we'll talk a little bit more about the Apnea Hypopnea Index in a second because that's really helpful. I'm curious, do we know why OSA is so much more common in older adulthood? Is it just related to BMI?

Mark Aloia 13:56

No. So we think BMI drives OSA in many, many people, but you can be a thin, young person and have sleep apnea. And that could be due to how narrow your airway is. Definitely a narrow airway, which was early on the target of everything, "Oh, this person must have a narrow airway." And they would do things like - I'm trying to think, it's some sort of nasal surgery. I can't remember the specific word. Where they would sort of open up the nasal passages. They do uvulopalatopharyngoplasty, which is one of the UPPP - it's one of the most painful things you can have done, which takes out your uvula and opens up your throat. They would do that because the thought was, "Well, this is a small airway." And certainly some people have a small airway.



When you talk about aging, I think there are different things. I think you start to get a little bit more central sleep apnea. And this could be due to TIAs, to small vessel disease, those kinds of things. Cardiovascular disease, we know, is very prevalent among older adults. It could also be due to the laxity of the muscles in the neck. I mean, there are some studies, some really good studies, that show that people who - there was a didgeridoo study, actually, in Australia, that playing the didgeridoo decreased the rate of apnea. So when you're working those neck muscles, and you have tighter neck muscles, you have less laxity. You're lying supine and you're not getting that airway to close. We think that part of the reason for older adults that have more sleep apnea is laxity in muscles.



John Bellone 15:30

Interesting. Well, Ryan, you've got to take up didgeridoo. [laughs]



Ryan Van Patten 15:34

[laughs]



John Bellone 15:36

I wonder if that holds for bagpipe players and trumpeters. [laughs]

Mark Aloia 15:41



I really wanted to go to a city orchestra and look at wind instruments versus string instrument players. Because oftentimes it's easy to find people who are overweight or obese in any big population. And I wonder if they'd have less sleep apnea. We never got around to doing that study.



John Bellone 16:00

[laughs]



Ryan Van Patten 16:01

Yeah, very interesting. I'm concerned about risk factors and protective factors for OSA. Mark, you've mentioned several already - older age, obesity, male gender, narrow airway. Any other particular risk factors and any protective factors that you'd like to mention?

Mark Aloia 16:20

We know APOE is a risk factor for everything, right? So that's certainly been studied in the context of sleep apnea. People like Camus Furman (?) have done some great work in those areas. We absolutely see that as a risk factor for sleep apnea as well. I'm trying to think - you know, obesity is the big one that we think about. Snoring, although that's not necessarily a risk factor, it may be a symptom, but it is a hallmark sign in a lot of people. Those are the primary ones. I think you've listed the primary risk factors.



What's really interesting, though, is if I go back to that AHI conversation and we start to think deeper about outcomes, we don't know what the moderators are of good outcomes or bad outcomes. We do believe now that this definition is somewhat arbitrary. Arbitrary is probably too strong a word. It is not emblematic of outcomes. So we recognize [that] we need to [it] figure out because we're saying to insurance companies, "You got to take care of 20% of the population with an expensive treatment and expensive diagnosis and a lifelong treatment." That's untenable for our healthcare system. So what happens is insurers say, "Well, you know, we're not going to pay if people don't use their CPAP", which has already happened. There are limits. They will not reimburse DMEs if a person doesn't meet a certain adherence criteria, which is something you would never see happen with oxygen, for example. But you're already seeing it happen with CPAP for years now. They'll start to make guidelines on who they'll treat and who they'll diagnose. So we want to look at what are the moderators of good or bad outcome, regardless of whether you use the AHI criteria, because I can tell you there are people - I've tested hundreds of people with full neuropsychological batteries - and there are people who have moderate to severe sleep apnea who have no appreciative deficits and there are people with mild sleep apnea who look like they're suffering quite a bit. We need to figure out those moderators. There may be genetic factors that protect you; we don't know what those are yet. There may be genetic factors that predispose you to negative outcomes.



John Bellone 18:39

Yeah, excellent. Okay. So maybe it'll be helpful to break down the different categories of severity of sleep apnea for a second. So you had mentioned greater than five events per hour for someone under 65. And there's a difference between mild, moderate or severe, right?



Mark Aloia 18:57

Yeah. So when we think of the severity of sleep apnea, we have three general categories under the age of 65. Mild sleep apnea, which is five events or more per hour. Five to 15 is mild, 15 to 30 is moderate, and 30 or more is severe sleep apnea. And, by the way, these cessations of breathing, by definition, are 10 seconds or longer. So that's having a lapse of breathing 10 seconds or longer every other minute. So it's quite a bit. And we routinely see people with Apnea Hypopnea Indices in the 60s and so forth. So these are people who are having repeated - many, many, many repeated episodes. After the age of 65, the diagnostic criteria for treatment is over 10 events per hour.



John Bellone 19:48

Okay, and the different categories adjust accordingly I'm assuming?



Mark Aloia 19:52

We don't really think about mild, moderate, or severe so much with older adults. You still use the 30 or more for severe but it doesn't affect reimbursement for treatment or something.



John Bellone 20:03

I see. Okay. And since this is disrupting sleep, I'm assuming it's in the first couple stages of sleep. Can you talk through that?



Mark Aloia 20:13

So apnea is more prevalent in REM sleep, the second half of the night, than it is in deep slow wave sleep, which is the first half of the night, roughly. I'm oversimplifying that. It's certainly more prevalent in the supine position, when you're lying on your back, but it can occur in any position at any time of the night. We definitely see more of it in the second half of the night.

One of the interesting things I'll just mention about outcomes is that for quite a while we've been talking about the cardiovascular outcomes associated with sleep

apnea. And we think that one of the phenomena that we need to pay attention to is what we call “non-dippers”. So these are people whose heart rate and blood pressure are nice and high during REM sleep and then they're supposed to dip, right? So there's this crisis in the body when you stop breathing, and they don't dip. So you don't see this natural dip throughout the night - this cardiovascular signature of normal sleep. You see them sustaining high levels.



John Bellone 20:17

Of blood pressure?



Mark Aloia 21:22

Yeah. And that can actually cause additional - we think it's a hallmark of additional problems. So these are people who are having many, many episodes through the night. They don't get essentially a chance to rest, their heart doesn't.



John Bellone 21:36

Okay. So during the polysomnography, you're looking at not only apnea, but also blood pressure, I'm assuming.



Mark Aloia 21:42

You're looking at EEG; you're looking at EKG. In a lab, you look at a lot of leads. Now, about 80% of diagnoses are happening in the home, which means you'll have fewer leads. We can talk a little bit about that. I'm not a diagnostic expert, I don't do a lot of diagnoses. But we definitely do much more in the context of the patient's home these days. And it's fine to do so.



Ryan Van Patten 22:10

Speaking of diagnoses, there's a big problem in OSA with under-diagnosis that I've seen. I've seen estimates of around 5% of the overall general population in Western nations and over 80%, potentially, of people with moderate to severe symptoms of OSA are not diagnosed. So talk to us about this problem.



Mark Aloia 22:32

We do believe that about 70 to 80% of people, say, in the United States, are walking around with apnea and have no clue and are not diagnosed. Most of the time in my career, when I've done my best work, I've thought of myself more as a clinical psychologist than any specialist - just a good clinician. So when you think about that, you really have to put yourself in the shoes of the person out there. One,

they may not have symptoms. I've already talked about that. There're some people out there who have sleep apnea if we were to test them, but they don't have any symptoms. Two, they don't see themselves having sleep apnea. So this is not an alarm for them. People generally have a colloquial view of sleep that has morphed into the insomnia definition. So if you tell them, "You have a sleep problem", they say, "What do you mean? I can fall asleep whenever I want." Well, you're not supposed to be able to fall asleep in the middle of the day, right? So you're excessively sleepy. But they don't see it that way. The colloquial view of sleep apnea is not a common one. People aren't out there thinking about "Am I stopping breathing?" They're certainly rarely asking their spouse, "Hey, do you ever notice if I'm stopping breathing?" A third point is that we've had this issue around snoring - something that's an obvious disturbance to the bed partner. In that context, what we see typically happen is that a partner says, "Hey, you snore. You need to take care of that." Well, what do I do about that? Right? So you've just told me I have a problem I can't solve. So it ends up becoming either an argument or a joke about dad snoring, and we've just dissipated all of the sense of urgency around that. So that is not a hallmark sign seen in the context of the home as a hallmark sign. And then third, I think if you know someone who has apnea and is being treated, you don't really like what you've heard, right? This treatment is not something that's pleasant. Usually one of the first things patients ask is, "How long do I have to do this?" And if the answer is "The rest of your life", that's not a great answer. So I think there's not a hell of a lot of motivation out there to go out and get diagnosed, nor is there the context for an easy path to diagnosis. I do a lot of work in behavior change and changing behavior is hard. You have to have the right context and that's only part of it. I don't even really think we have the context. So yeah, there are a lot of people out there undiagnosed.

John Bellone 25:07



I also think people just don't understand the risks involved. They think, "Oh, you know, I wake up and I still perform my job." That it's not a problem. But they don't understand the long term health risks involved in OSA.

Mark Aloia 25:20



I mean, think about it this way, John. If we didn't screen for diabetes, would people be getting treated for diabetes? No. So, you're absolutely right. I think that is a component of it.



Ryan Van Patten 25:33

Yeah, it's more invisible to people than a broken leg or insomnia even. They [don't] experience [it] because they are unconscious when this is happening.



Mark Aloia 25:43

Absolutely.



John Bellone 25:44

Yeah, hopefully we'll save some time at the end to talk about what we as neuropsychologists can do to help that problem and we'll talk more about that.



Mark Aloia 25:52

Great.



Ryan Van Patten 26:04

Mark, you've mentioned polysomnography a few times. This is the gold standard diagnostic test for OSA, but there are validated self-report questionnaires, such as the Berlin Screening Questionnaire and the STOP-BANG questionnaire, which STOP-BANG is an acronym, 8 yes or no questions. So what can you tell us about the Berlin and the STOP-BANG questionnaires?



Mark Aloia 26:27

These are basic questionnaires. There was actually a study done at Harvard, I want to say [in] 92 or 96, that showed that you can ask a few simple questions, assess BMI and neck circumference, and accurately with like 90-some percent accuracy, determine if someone has sleep apnea. We've had these questions out for quite a long time. I think it's good for every clinician that's listening to this to become familiar with some of the basic questions. I think the STOP-BANG is a great one. They're validated questionnaires. Sure, they're not going to tell you exactly the severity that someone has, or even with 100% accuracy whether they have sleep apnea, but that's not your job. Your job is to sound the alarm, maybe raise a flag. We're all in healthcare, setting up the context for easier diagnosis. So, in that vein, ask some of those simple questions, put it in your report, put it as a potential diagnosis. Then it gets to the people whose job it is to send that person for a sleep study. So, I think that these are great questionnaires. I would say that most of your listeners, unless they have a deep interest in this, don't really need to learn a lot about polysomnography. They need to understand how to screen for something like this. Just like we did years ago - now it's over 20 or so years ago when I was at

Brown starting out there, there was this big push for depression screening, and it did quite a bit. People are now screening for depression in internal medicine, family practice. We need a little bit more of that in the context of sleep. It takes all of us to do our part.

Ryan Van Patten 28:18



And for listeners who are interested in STOP-BANG. STOP is loud snore, tired, observed apnea, and high blood pressure, P for pressure. BANG, is BMI, age, neck size, and gender. So the risk factors you've been talking about, Mark.

Mark Aloia 28:37



Yeah. Neck size is often funny because some people know their neck size and other people don't. But it's a big predictor. It's different for men and women. I can't remember the cutoff. I want to say it's 17 inch or so, or maybe it's 17 [inch] for women and 19 for men. Or 15 for women, 17 for men. Something like that.

John Bellone 28:55



Okay, excellent. Why don't we move to some of the cognitive and psychiatric effects now? To start off, what evidence do we have for a link between OSA and cognitive decline?

Mark Aloia 29:07



So you said cognitive decline, and I'm not going to make assumptions about the progress of cognitive dysfunction in the context of sleep apnea because I don't think we know enough about that [and] how it interacts with aging. We can talk a little bit about that, but this is kind of how I started out my career. It was interesting. I was at Brown and I was looking for an area that I could do research in. Kind of my niche [to] bring neuropsychology together with some other area and get grant funding - just like every ambitious young person is trying to do. [laughs] And so I thought, "Well, I'm going to study the neuropsychology of sleep apnea."

There are two primary factors that I think can contribute to cognitive dysfunction. Sleep fragmentation. Look, you're not getting good sleep throughout the night. I mean, if you're on EEG, and arousal is considered going from one stage of sleep to a lighter stage of sleep. And many times, that's an awakening. So if you have hundreds of these events per night, you might have many, many dozens of awakening, micro-awakenings. But it's sleep fragmentation nonetheless. So that could contribute to daytime function. The second certainly is hypoxemia with people who don't drop their blood oxygen level. We have people who dropped down into

the 70s in their blood oxygen level. Certainly that's got to affect cognitive function, right?

So we really tried in our lab early on to parse this stuff out. And it was not easy, you can imagine, because often these things coexist in the context of sleep apnea. So the first time we did this analysis, we had, I want to say, about 350 patients and we did full neuropsychological batteries. We took the upper tertile of hypoxemia and compared it to the lower tertile of hypoxemia and we matched these people on age, education, BMI, estimates of premorbid IQ, and on AHI. The only difference was hypoxemia. And we thought we were just doing the most amazing science. And we were dumbfounded with the results. What we found was that the groups were virtually the same on all cognitive areas with the exception of memory. The group with the low hypoxemia was a half a standard deviation below normal and the group with high hypoxemia was normal. It was just, you know, I was dumbfounded. I had to look at the data so many different times. We added more people to it, the results sustained themselves.

I called a friend and colleague of mine, Virend Somers, who's an amazing cardiovascular guy at Mayo Clinic in Rochester, and who does sleep and cardiovascular disease [research]. And I said "Virend, how can you help me understand these findings?" He said, "This makes total sense from the standpoint of what we see in the heart. If you have a little bit of sleep apnea, you can't accommodate to it. If you have a bit of hypoxemia, it affects you more than if you have a longer amount of hypoxemia." And I guess what he was getting at - and I don't know all the mechanisms, it's not my particular area - but that when we stop breathing, we release endothelial into the bloodstream, it's a vasodilator. It's a protective effect. And if you have enough hypoxemia, that cascade of things happens more readily. So, apparently, we see this at the level of the cell in the heart, too. These protective effects kick in, but if you have just a bit of it, not enough of it, you still have hypoxemia. The protective effects don't kick in. And so they may have more profound downstream effects. Now, we haven't validated [this] - you know, that's not been replicated, those findings. I don't think anyone else has ever really tried to do that. But that's a study, I think, published in Journal of Chest quite a number of years ago. But, ultimately, those are the two factors that we find contributing largely to cognitive [function].



John Bellone 33:01

That's helpful. And just to clarify, so you're looking at hypoxemia there because you control the AHI. You control for sleep apnea, basically.



Mark Aloia 33:08

We control for fragmentation, a loose measure of fragmentation. Correct.



John Bellone 33:13

Gotcha. So for our listeners, they shouldn't take away that there's no cognitive effects of sleep apnea, because you controlled for that.



Mark Aloia 33:19

Correct. Yeah, these were matched groups. I'm sure you've looked at the review articles, and we've written several ourselves - there are a whole host of things that are impaired in many people with sleep apnea.



Ryan Van Patten 33:33

Yeah, that's a great segue. The next logical question that I wanted to ask [is] we know that OSA does have deleterious cognitive effects. So we might ask what cognitive domains are affected? You mentioned [that] there [have] been a lot of reviews to the point where I found two meta-reviews. So reviews of reviews on cognition and OSA. Meta-reviews are not common [laughs] in my experience. So, clearly, there's a lot of literature. The 2013 meta-review was by Bucks and colleagues, and they report impairments in attention, delayed memory, visual spatial, visual constructional skills, executive functions. No changes in language and psychomotor skills. And mixed findings in terms of working memory and global cognition. But that paper is about eight years old now. How do you think about the cognitive profiles of people with OSA?



Mark Aloia 34:28

I'm a little biased in terms of the work that we've done. That kind of sticks with us a little bit more because I have experience with these patients. I agree with all of those with the exception of psychomotor. We would do grooved pegboard and we would find pretty profound deficits in grooved pegboard in people with sleep apnea. And this was a bit of a shocker for us because we had never really seen this. Now, I don't know - you can define psychomotor in a lot of different ways. Just fine motor coordination may be specific to that. But I don't know if many labs are using [the] grooved pegboard in that context or in the context of studying sleep apnea. And so, I'm a big fan of parsimony. So rather than list all the domains - I mean, they're all the domains you see in everything else, right? There's attention, executive function, memory, and all that.



John Bellone 35:20

Right. [laughs]

Mark Aloia 35:20

So rather than list, I'm trying to look at the big picture. I'm trying to look at the syndrome, right? And it was really the psychomotor effects that started pushing us toward looking at small vessel disease, and some of the depression and apathy that we were seeing in some of the folks, especially the older adults. I think that all of those domains are potential domains, but they're also potential domains for lots of other things. So, for your listeners, you need to be thinking about sleep apnea in addition to all the other things you think about when you see that cascade of deficits. If you have sleep apnea in that context, and you are testing something like fine motor coordination, think about those kinds of things as well. So that would be the only thing that I would say I might take a little bit of issue with.



We definitely didn't see language problems. It was a big differentiator for something like Alzheimer's disease. We definitely didn't see any language problems. But many domains could be affected. And, like I said, there are many people who had no appreciable cognitive deficits.



John Bellone 36:26

Yeah, it seems almost like a frontal subcortical profile overall.



Mark Aloia 36:30

That's kind of how we looked at it. Yeah.



John Bellone 36:32

Yeah.



Ryan Van Patten 36:33

As are so many things.



John Bellone 36:34

Right. [laughs] In terms of severity, you alluded earlier that there's variability here. Are we talking mild cognitive deficits? Are we talking that it could be pretty profound?

Mark Aloia 36:50



I think mild to moderate is what we generally see. We're not seeing profound things, but keep in mind, we've got people who are obese, we've got people who have high blood pressure, we've got people who have diabetes. I mean, honestly sleep apnea, it contributes. It's absolutely a significant contributor in many of these people. Is it the driving factor that led to the cardiovascular disease or [did] the cardiovascular disease feedback into the sleep apnea? We don't know.

Ryan Van Patten 37:21



Yeah, it's such a mess to try to disentangle so many risk factors in one person.

Mark Aloia 37:27



But I would say this guys, it may not be the job of your listeners to disentangle it, right? I think you're doing tremendous justice as a neuropsychologist by calling attention to it as a potential contributor, because we can treat diabetes, we can treat high blood pressure, we're not really treating small vessel disease that's already there, but if you've got something that's continually an insult, night after night, hour after hour of sleep, and you can treat that, then it is our job. It is our role to call attention to that.

John Bellone 38:03



Yeah. And it's really easy to do a pre-post assessment, where we have a baseline cognitive evaluation, they get treated, and then a year later we retest them. And if the problem goes away, there you go.

Mark Aloia 38:15



We've published studies on that. I don't know if you saw, we had a study on the normalization of memory impairment because we were trying to get at this issue of the correlation between AHI and memory. This was before, I think, we had come to the belief that this was a bit of an arbitrary diagnosis because there was no correlation. So then, as a neuropsychologist doing this research, I said to myself, "How would I categorize these patients if they came in at baseline?" So I just took the people who had memory impairment at baseline - they were mildly impaired on memory, at least one standard deviation below [the mean] - and we followed them for I think it was [a] three months study. I think this was published in Chest as well. We followed them using CPAP. And we looked because, I'm sure we're going to talk about CPAP, but adherence is not great. I made my career studying adherence. We use the reference group, in this logistical regression of two hours or less of use of CPAP over that three months, on average. The middle group was two to five hours,

and the optimal group was five or more hours of use of CPAP. And we found essentially, it wasn't a significant increase if you use two to five hours, but it was a three fold improvement in memory. You were eight times as likely to improve your memory if you use five or more hours a night compared to the reference group. So, that was a pretty compelling study suggesting that if you use CPAP all night, and you give them three months, they didn't look like they had memory impairment.

John Bellone 39:58



That's incredible. Often I get referrals from neurologists saying, "This person is complaining of memory problems, is this Alzheimer's disease?" And I'll do a screening and it's suggestive of potential sleep apnea. It's easy then if they get treated, and they come back next year, and they do better for me to say, "No, this doesn't look like Alzheimer's disease."

Mark Aloia 40:18



Yeah, just cite my paper. [laughs]

Ryan Van Patten 40:20



[laughs]

John Bellone 40:20



[laughs] I don't even have to do the email.

Mark Aloia 40:22



I don't think it was read enough. [laughs]

John Bellone 40:25



[laughs]

Mark Aloia 40:27



No, but, I mean, it was pretty compelling. We were pretty amazed to find that, and I thought it was the right way to look at it. Instead of just looking at all comers with sleep apnea, let's look at people who are really showing a deficit.

John Bellone 40:39



Yeah, I like that. Can you quickly tell us about the link between OSA and depression as well? You also mentioned that earlier.

Mark Aloia 40:45



Yeah. So we would see depressed mood, and there were some studies around depression and scores on depression inventories. We took this, again, one step a little further and we looked at the BDI and the psychosomatic versus the cognitive effects. When we started to look at that, what we found was a couple of interesting things. We found that, among women, the cognitive effects of depression were more related to obesity, BMI. And these are all people with sleep apnea. So we didn't find a relationship between AHI and depression in either cognitive or somatic complaints of depression in women. But we found a relationship between BMI and cognitive effects. So they felt badly about themselves in the context of their weight.

In men, we found the exact opposite. We found an association between AHI and more of the somatic aspects of depression. So these are probably people who are sleepy and apathetic and so forth. It was related more to AHI. So I think the take-home message from that is, it's not simple, just like everything else in sleep apnea. But that there may be some sex differences that we need to be attentive to.

Ryan Van Patten 40:45



Yeah. Another big picture takeaway is that OSA is a risk factor for depression. People with OSA are more likely to be depressed and have mood disturbance than those without. Correct?

Mark Aloia 42:13



Yeah. And, I'm going to just interject here a statement about insomnia because this now becomes really important in the context of insomnia. There are some great studies - boy, years and years ago, decades ago, by one of my mentors, Donna Giles, who found a couple things I want to mention. She found that - you know, we've all heard short run latency may be a signature for depression. That if you go into REM quickly, not narcolepsy quickly, but quicker than normal, that it may be a sign of depression. What she found is that if you were the first-degree relative of someone with a major depressive disorder, and you never had depression but you had a short REM latency, you were four times as likely to develop depression in the future. So this now becomes a physiological sign of susceptibility, or vulnerability. So sleep and depression we know are related. What we've also found is that there's a greater amount of depression in insomniacs. Certainly depression and insomnia can go together. Insomnia that we've always thought of as a symptom of depression. But further studies by a colleague of ours, both Donna and mine at Rochester when I was there, Michael Perlis, found that if you study someone who's in remission for depression, and their insomnia has gone away, and you follow

them long enough, you can see insomnia be a hallmark sign for the recurrence of another depressive episode. So when you see people with insomnia, you start asking questions about insomnia. And that's usually, just to go in a little more deeply on the definition - it's usually: takes you 30 minutes or longer to fall asleep, or you're up 30 minutes or longer in the middle of the night. And the "middle of the night" can be early morning awakenings that you can't fall back to sleep - you intended to get up at seven and you woke up at six. That's still considered. They call that terminal insomnia, not because it kills you but it happens at the end of the night. So if you start to see that, and you see depressed mood or you have a history of depression, you can start to think about possibly the onslaught of a new depressive episode.



John Bellone 44:20

That's helpful.



Ryan Van Patten 44:21

Yeah. You've mentioned REM sleep a number of times already and part of OSA is the sleep fragmentation that tends to happen in the second half of the night when we're getting REM. And REM is so incredibly important for mood regulation. So that seems to be one way in which OSA can lead to or make depression more likely - by disrupting REM, which is when we are sort of anchoring, recovering. If we don't get REM sleep, we tend to be irritable and dysregulated. Is that how you think about it?



Mark Aloia 44:52

Yeah, I think that's a great point, Ryan. I hadn't really thought about it in the context of REM and mood, but that's just because I hadn't thought about it. I think you're absolutely right. I think we have to remember that sleep is a relatively new field. I told you Bill Demette just passed away and we're starting to see the pioneers of the field of sleep just now dying. So it's a relatively new field. I mean, we know the people who discovered REM, right? [laughs] So this is a relatively new field. And we're just figuring out what these different stages of sleep and the architecture with which we go in and out of these stages, what they mean to us. We certainly know the tie between REM and memory. If you teach someone a whole list of words, and you deprive them of REM, they're not going to remember those words in the morning. If you let them have REM, they're going to remember them much better. So, we know some of the functions of different stages. Slow wave sleep is a big one now that we're focusing on, which occurs in the first half of the night, which we think has immune function associates. It has memory associations, we think it may have executive function associations. So there's a whole list of things.

I'll just mention that, for your listeners who are looking for a field to go into and study, sleep is not a bad one. Because what's happening is that the sleep experts, and they're great scientists, are studying the cognitive effects of different stages of sleep, but they're not necessarily coming at it with a clinical eye for cognition. So I'll give you a good example. Years ago, we would talk about sleep and cognitive functioning and we meant the PVT, psychomotor vigilance task, it's a reaction time test. Pioneers in the field, great scientists, looking at PVT and calling it cognitive function. As we looked at this, and as I kept hearing this, I eventually went up to them and I said, "You know, this is a sensitive measure but it's not specific to anything." And, ultimately, they agreed. One of the one of the real things that we've ignored so far in the conversation is the biggest addiction in the world, which is caffeine, right? It's a great bandaid, and it absolutely can affect the psychomotor vigilance test. So if you feel sleepy at all, you're just dosing up on caffeine and then you go take these tests. It takes a real clinical eye to start to parse out the real, clinically relevant cognitive functions associated with these different sleep stages and disorders.



John Bellone 47:31

That caffeine might help with the vigilance in the moment, but doesn't help your memory for what you learned the day before or many other cognitive abilities.



Mark Aloia 47:39

Yeah, exactly. I don't want to make it sound like the scientists aren't aware of all of this. They absolutely are. And they're testing people without caffeine and all this kind of stuff. But I'm just saying, I think that one of the things that we do bring to the table is this understanding of how cognitive function manifests itself variably in a normal state versus an abnormal state. It's that perspective that absolutely brings value to the field of sleep, and they're welcoming it.



Ryan Van Patten 48:10

Yeah, this is great stuff, I think. I find the topic of sleep broadly to be fascinating. I recently read Matthew Walker's book, "Why We Sleep", which I found to be very good. I recommend it to people more broadly. And if we had five hours with you, Mark, we would ask you every question about sleep that we could. [laughs]



Mark Aloia 48:29

[laughs] I'm not as smart as Matt Walker. So, yeah, you can't lump me into that bucket.



Ryan Van Patten 48:34

Well, you don't have his accent, but I'm not saying you're not as smart. [laughs]



Mark Aloia 48:40

Yeah, he's a great guy. It's a good book.

Ryan Van Patten 48:42

Yeah. But sticking to OSA, you've briefly mentioned some of the neural mechanisms that link OSA to neuropsychiatric symptoms and cognitive decline, which we've been discussing. I'll list a few of them, there are many. OSA has been linked to hypertension, as you mentioned, small vessel supravascular disease, amyloid and tau, blood brain barrier hyperpermeability, depleted nitric oxide, oxidative stress, and neuroinflammation among others. So, of course, there are very complex interactions going on here. We can't just draw a straight line from one to another. And you've sort of simplified it for us thus far and pointed to two proximate causes of the symptoms - the hypoxia on one hand and sleep fragmentation on the other. I'm wondering if you can sort of boil down the mechanistic picture and talk to us about what's going on with all of the cerebrovascular and other mechanisms underneath OSA.



Mark Aloia 49:39

So the answer is "No".



Ryan Van Patten 49:43

[laughs] Fair.



Mark Aloia 49:43

Look, I will tell you a little bit of how this manifested in our own research. So, you know, again, I told you I was friends with Virend Somers, who's a cardiologist and I was listening to a lot of his work on endothelial and endothelial function in the context of sleep apnea. We were testing these patients [and] we saw this pattern as something that was akin to small vessel disease. So, as good neuropsychologists, we said, "Well, let's start to look at this a little bit." And so we looked at some of our folks, and we got a small pilot grant. I think we looked at 12 individuals, people with mild sleep apnea and severe sleep apnea. We got a grant to put them in the scanner [and] we looked for small vessel disease. And sure enough, we saw in the people with severe sleep apnea, rimming capping around the ventricles. We saw small vessel disease, we saw it in basal ganglia. And so we took that as - and then



this was published in a discussion section of one of our papers. We took that as some evidence that maybe this endothelial dysfunction, whether it was happening in everyone or not, was happening in many people and was leading to this neuropsychiatric presentation as well as this cognitive presentation. So we got a grant to look at this large Sleep Heart Health Study.

I'll take a minute just to say how genius this Sleep Heart Health Study was. Some sleep scientists said, "Hey, look, they're all these large epidemiological cardiovascular disease studies and none of them are really measuring sleep. So let's get a grant to do sleep studies in each of these other studies" - the Framingham Study, the Cardiovascular Health Study, you know, there was one other I can't recall. So they got this massive grant to do sleep studies in all these other studies. So all the data were already collected except for sleep. So we got a grant to look at the relationship in the cardiovascular health study between the sleep studies and the MRIs. We thought it was a brilliant idea, and it didn't turn out real well. In part because you had to be over the age of 65 to get into the Cardiovascular Health Study to begin with. You only got your first sleep study on average five years after because that epidemiological study came after the first step of the epidemiological study. So there's this delayed effect. So what we found was by the time you were 70 years old, you had white matter disease for a whole host of other reasons. So trying to parse out the effects of sleep apnea was not very useful.

I think we had to go through that process to figure it out. But I have since been fortunate enough for many reasons to connect with some researchers in Milan, in Italy. We published three papers in a series of the same patients. They did, maybe more than three papers at this point, but we did neuropsych assessments, we did VBM, voxel based morphometry, we did DTI, and we did functional imaging in all of these people. We did it at baseline and we did it over the course of a year. And we found really impressive findings.

We did this in Italy for a couple of reasons. One, it was cheaper because we don't have to pay salaries in Italy. The second was that adherence to CPAP was much higher. In Italy, when you're going to get diagnosed for sleep apnea, you're put in the hospital and you have an overnight sleep study. Then the whole family comes in, right? "Oh my God. Pop is in the hospital." You know, they bring food and all that kind of stuff. And, "Yes, you have sleep apnea." And then the next night you're given a full night of CPAP. Then you're in for one more night. So three nights in the hospital. So the sense of urgency is quite high and people use CPAP more. So in the course of this study, what we found was, first, reduction of gray matter volume in the hippocampus and in a few other areas. The hippocampal reduction of gray

matter volume correlated with memory. We saw that reversed, believe it or not, in three months using CPAP, which was phenomenal to us. We definitely saw the fMRI stuff, which was over recruitment when you weren't treated and less recruitment over time. So you were more efficient. Then we saw DTI changes over the course of a year. So it took longer to see those DTI changes. So all of this together, I think, still doesn't refute and possibly supports this small vessel disease picture. I'll just end by saying that, of course, this is in the areas that are innovated by small vessels. This is watershed areas, this is basal ganglia, subcortical areas, and all the white matter hyperintensities that you see on imaging.



Ryan Van Patten 54:37

The reversal you mentioned, does that include the hippocampal atrophy? The brain based changes?



Mark Aloia 54:43

Yeah, and that was pretty amazing to me. These are really top notch scientists. These are people who know what they're doing. And we made them look at that quite a number of times because this is not something you typically see and, quite frankly, the picture sounds clearer than it should. So all this kind of stuff needs to be replicated, but at least it gives us some indication that there's something going on here along lines of what we thought was happening.



John Bellone 55:19

Mark, I'm curious if we have any idea about the correlation with Alzheimer's disease separate from the cerebrovascular component because we know that CBD is a risk factor for Alzheimer's disease as well. We talked to Adam Brickman a little while ago about that in depth, but specifically increased amyloid and tau burden. Can we know if that's a direct correlate of the OSA?



Mark Aloia 55:42

Yeah, I don't think we can know that, John. I think that these are all candidates that we need to look at more deeply. There were some and there still are some good studies going on in the context of Alzheimer's disease and sleep apnea. We certainly see a high prevalence of sleep apnea in Alzheimer's patients. We see a high prevalence of sleep apnea in cardiovascular patients. Huge prevalence post stroke, whether it's TIA or large vessel stroke, we see huge prevalence of sleep apnea. We often see central sleep apnea with brainstem involvement. I mean, you know, so it's such a messy picture. Not to mention the fact that when you get into studies of Alzheimer's disease and sleep, so many other factors play in. So Sonia

Ancoli-Israel, she's now retired, but when she was at UCSD did tremendous work on circadian rhythms in the context of Alzheimer's disease. To the point where she found that if you were in a nursing home in sunny San Diego, you would see something like two hours of sunlight [inaudible]. So people would seek out dark corners and sleep. When you eliminate the circadian phase - and we haven't even really talked about the potential effect of the circadian phase on testing - but that certainly becomes more relevant when you have a potential circadian disorder. So [if] someone's not getting good light, they don't have a regular sleep rhythm. How does that affect cognitive functioning? We know that happens broadly in the context of sleep apnea. When I was working on the inpatient unit at Butler Hospital at Brown as an intern, we talked about sundowning all the time as a behavioral disorder, but it's probably a sleep disorder. So it's emblematic of a circadian rhythm problem.



John Bellone 57:37

Fascinating.



Ryan Van Patten 57:37

Along the lines of mechanisms, we made the link between OSA and depression through disrupted REM sleep, but something else I've seen in the literature is cardiovascular, cerebrovascular changes due to OSA being a major potential mechanism that leads to depression. What do you think about that?



Mark Aloia 57:57

Yeah, I think, Ryan, that was our take. Look, you can't study everything. But that was the path that we took. That this was largely contributed to by small vessel brain disease. And maybe this is some of the reasons we don't see negative outcomes associated with AHI in some people because they're not building up cerebrovascular disease or they haven't reached a threshold of that cerebrovascular disease. I mean, we know that not everyone develops cerebrovascular disease in the same way, even with the same contextual elements over life. That was the hypothesis that we've pursued for quite a while. Now [for] the past 10, 15 years, most of my research has been on treatment adherence. So it's kind of left behind a lot of the mechanisms of cognitive dysfunction. But I still believe that that is one of the biggest drivers, and that we need to be looking more carefully for that.



Ryan Van Patten 58:58

Yeah. So this seems like a great time to transition into CPAP in more depth. You've mentioned it several times, Mark. So before we get into some of the most interesting stuff, describe the rationale behind how a continuous positive airway pressure device or CPAP works.

Mark Aloia 59:19



We should probably think of them as PAP devices, positive airway pressure devices, because they used to be continuous positive airway. So what happens in the context of CPAP - CPAP is essentially a blower that you strap to your face, right? [laughs] A pneumatic splint in the upper airway by covering your nose and mouth, or sometimes your nose if you keep your mouth closed. It pushes air into that, opening up that airway, creating a pneumatic splint in that airway so that you don't have a collapse. That doesn't work for central sleep apnea very well. It works for the obstructive version, which is the most prevalent version. So it opens up that airway all throughout the night so that if you have this tendency to collapse, you're not going to collapse because you have a patent airway that's open. It used to be that you would ramp up. So [it] used to be, you'd have a full night of polysomnography and the full night of CPAP, then we went to this barbaric method of waking people up in the middle of the night and putting a blower on their face and trying to see. And this was all for reimbursement purposes because insurance companies didn't want to reimburse for two nights in the hospital. So if they had enough sleep apnea, you would put a blower on their face and you'd ramp it up. There'd be a technician back there who would be ramping up to try to get the right pressure for you to keep your airway open. So that was where you then left it at that pressure - say it was 10 centimeters of water, you left it at that pressure, that was continuous positive airway pressure. Then we started to develop mechanisms of delivering positive airway pressure because, of course, if you're breathing in, 10 centimeters of water is different shooting against it. We all breathe in and out during sleep. So we developed mechanisms of delivering the airway pressure so that it's not steady at one pressure, but it can detect when you're starting to exhale and drop the pressure, so it's easier to breathe. And then inhale, it ramps up that pressure. So that was a flexible pressure delivery. At first, it was a boxed wave where there was upper pressure and a lower pressure, that's called BiPAP. Then they had flexible pressure that was called C-Flex, or some flexible pressure delivery. Some of these are trademarked. I worked for one of the companies. So I don't want to, you know, mislead anyone, but they're all flexible pressure deliveries. Now we have this system - and it's been around for many, many years - which, if I had sleep apnea, I would want. It's what we call an Auto PAP. So the Auto PAP, depending on the company - in our company, the Auto PAP is always trying to

reduce the pressure to see when apneas bleed through. So it wants to pump at the lowest possible pressure for you. You can still have auto flex where it goes down when you're breathing out and all that kind of stuff. But it's always looking for the lowest possible pressure to eliminate your apneas. So it's a smart system that's detecting your breathing and detecting your apneas, just through the PAP device. So we should refer to them as PAP devices. And what you'll often see are these Auto PAP devices. I'll just say the reason I think this is beneficial is, a) we don't get 10 nights of sleep study to know the variability in your sleep apnea. We just get one, one snapshot. We all know, as scientists, that variability is the key to a lot of things, right? We know that if you drink alcohol, it's a respiratory depressant, and you're going to end up having more apneas. We know that if you gain weight, your apnea may get worse. If you lose weight, your apnea may get better. So really, in terms of longitudinally, I'd rather be on an Auto PAP that's monitoring me on any given moment.



John Bellone 1:02:58

Do you know if this is widely reimbursed in the US through insurance?



Mark Aloia 1:03:03

It was used more with cardiovascular disease patients. There was a study that suggested that, in this particular large scale study, people were at greater risk on an Auto PAP. That people were dying from cardiovascular problems on an Auto PAP. It was since found that those were a particular subset of patients and it was specific to that algorithm on that Auto PAP, we think. So now the studies we've seen are quite favorable toward APAP. It costs more and so insurance companies sometimes weren't reimbursing it. It's far more common in Europe than it is in the United States, in part cost related, I think. So I think we're going to see more and more of it. It totally just makes sense as technology improves. But, yeah, I'd say they're relatively common, but certainly not as common as something like a flexible delivery.



Ryan Van Patten 1:03:57

If patients aren't using it, if adherence is low, you said earlier that sometimes insurance won't pay in the US, right? So there's some adherence threshold that the patient has to reach in order to get reimbursed for it.



Mark Aloia 1:04:09

And it's a government definition, so it's going to sound like one. So it is over the first 90 days, you have to have a 30 day consecutive period where 70% of those days you use four hours or more. So, yeah, think about it for a while.



John Bellone 1:04:25

[laughs]



Ryan Van Patten 1:04:25

[laughs]



Mark Aloia 1:04:27

You know, it's really an interesting sort of sociological conversation [that] we don't need to get into but I enjoy. Really the only reason I got into studying sleep was because we had the best monitor of health behavior in the world. We knew every minute when someone was using the CPAP or not. We've known this for 25 plus years. If you had the device on and the mask was on your nightstand, we could tell because it would register a large leak. So we would know you weren't using the CPAP. At the time, this was before any wearable devices, this was the best wearable device. It was great data. I got into it because it was great data. But in some ways, we put a target on our back. Because at the same time, we're looking at the prevalence and we're saying, "Oh, you know what? It's not 2%. It's 5%. Oh, it's 7%. It's 10%. It's 15%. And, by the way, it costs this much for diagnosis and it costs this much for a CPAP." So now the insurance companies say, "Hey, look, this is an untenable situation." We published oodles of papers saying the average CPAP use was four hours a night. And so they essentially said, "We're not going to pay if they're not using it four hours a night." So, I think that's how that happened. That's this sort of sociological thing that happened.



John Bellone 1:05:48

So that could be harm done by people actually not using it. By prescribing it, giving it to somebody.



Mark Aloia 1:05:54

We did publish a paper, I think it was in 2010. [I'm] trying to remember who the first author was, it might have been Chris Kanapky (?), who was in my lab at the time. But we published a paper that was looking at these definitions because we had already followed people for a year. So we went back and said, "Okay, look, let's

take a look at our people who would have qualified to keep it versus those who wouldn't have qualified to keep it at 90 days, at three months." And we saw differences in cognitive change between those people. But then we asked a critical question, "What if you were to allow the people who you now are going to take it away from to keep it for a while? Do they continue to make gains cognitively?" And they did. They continued to make gains on executive function.



Ryan Van Patten 1:06:38

Even with incomplete adherence?

Mark Aloia 1:06:41



Even with incomplete adherence. And that started the whole series of questions of how much CPAP do you need to see a change in cognitive function. My response was always, "What cognitive function?" It's dependent on the dependent variable for method reasons because some of these things change more easily than others. Also, for mechanistic reasons. So we tried to address that issue and essentially found that how much sleep we needed a night to change, say, attention in a meaningful way was far different than might be what you needed for memory. I told you what we needed for memory to make dramatic effects but you could see attentional changes before that.



John Bellone 1:07:25

The bottom line for patients, though, is this is the same recommendation that we get for exercise. The more adherent you are to these guidelines, the more you use your CPAP while you're sleeping, the more gains you could potentially have across different cognitive abilities.



Mark Aloia 1:07:41

Exactly. There was one paper that was published that I was a reviewer on, and that was their take-home. That this was a linear relationship. I gave them a bunch of crap for that, because I felt like you know, we weren't saying use [it] 18 hours.



John Bellone 1:07:56

Right. [laughs] There's no ceiling to it, you just have it on all day.



Mark Aloia 1:08:01

But essentially, maybe even if [it's] really a linear relationship, the slope of the line differs depending on the outcome measure.



John Bellone 1:08:08

Right. Sure. Okay. And this is regardless of the severity of apnea as well? Does anyone on the spectrum get benefit?



Mark Aloia 1:08:17

That's a good question. I don't know that we know the answer to that. I think we looked at it really more from the severity of the baseline deficit, which isn't always correlated to the severity of the apnea.



Ryan Van Patten 1:08:29

In the topic of non-adherence or incomplete adherence to the PAP devices, you mentioned earlier that you are a clinical psychologist and you've worked a lot with behavior change. So you're a part of a randomized clinical trial examining the effectiveness of motivational enhancement techniques and improving PAP or CPAP adherence. Can MI help with adherence?



Mark Aloia 1:08:51

Yeah, so MI is really how I made my career and how our lab developed. I'll just take a minute to talk about that because I was trained as a staunch behaviorist. I wasn't really trained deeply in MI at the time that I had gone to internship. I was doing this study that was my own study, looking at giving feedback. I would do neuropsych assessments in older adults with sleep apnea and give them feedback on their neurocognitive function. Then I'd watch their adherence, and the other group didn't get the feedback. So the idea was because the provision of feedback on cognitive function [is] a threat essentially associated with sleep apnea in the context of aging, did that change adherence to CPAP? And it dramatically changed adherence CPAP in the small pilot study. So, of course, being at Brown with some amazing scientists, many behavior change experts, I'm talking to some colleagues and friends and they're like, "You kind of did motivational interviewing." And I was like, "Well maybe I should do that." So I got a group of people to support me on that and to teach me a lot about motivational interviewing. And that's really how I built my career.

We developed the Motivational Enhancement for CPAP Protocol. We published it. We've studied it in several randomized clinical trials. It's been called out in Cochrane Reviews as the one of the main things that works in the context of improving CPAP adherence. And it's not surprising, right? We didn't develop MI. MI has been used across multiple chronic disease states and addictions and so forth, and it works relatively well. So I always sort of remind people to not forget their roots as clinical psychologists.



John Bellone 1:10:39

I think we have a lot to offer here. I mean, OSA is pretty unique in the world of aging and cognitive decline because it's an identifiable risk factor. We have a good effective treatment. There are many other risk factors like age or APOE status that you can't control. I want to talk a little bit more about the importance of psychologists in treatment. I'm curious about your feedback sessions, the MI focused feedback. I'm a big fan, and I think Ryan is too, of MI techniques. Any pearls of wisdom for the neuropsychologists out there as they're approaching a feedback session with a patient who they're not sure is going to be adherent?



Mark Aloia 1:11:19

I think one of the things I would say is, we just have to go back to our roots of being good listeners. I think it's all about really understanding their perspective. I always see that. And I work for a large company now, Phillips out of Amsterdam. It's a healthcare company. We're all talking about telehealth and digital medicine. I'm not a fan of trying to digitize a broken process. I think that, in many ways, our process of medicine is great. In many ways it's broken. Think of your interaction with your physicians. Oftentimes, our physicians, not always, but oftentimes they talk to us from their value system. "You need to do this because it could reduce your risk for cardiovascular disease." Right? Talk to me about my value system. Understand me. Listen to what I'm coming to the table with. I think that's the place to start, John. I mean, I really think it's about hearing patients. Hearing their context, understanding their context, eliciting. I mean, motivational interviewing is all about eliciting critical thought in the patient about what's going to motivate her to stick with it when it becomes problematic. We don't ever have a problem talking to patients who get it. Who know it's important and they feel confident they can do it. The patients that are struggling are the ones that struggle with confidence. We talk about being good listeners, we talk about eliciting that critical thought and feeding it back to them. We talk about reframing when someone - we have great videos of training in MI and one of the patients says, "You know, I just don't know that I can keep doing this. It's a struggle. Take it off every night. It drives me crazy." And the therapist has a great reframing response. He says, "You're really struggling with this, but yet you keep trying every night. Making this change must be important to you." That's a great reframe and perfect motivational interviewing because she's exhibiting a behavior that is emblematic of how important it is. She's struggling with her competence, right? Reminding people past successes, all of those kinds of things are terribly relevant. In MI, we're kind of planting seeds for them to get over those humps themselves.

I'll mention one other thing that becomes really important, and that is normalizing ambivalence. So what happens as humans, and maybe even more as Americans, when we get uncomfortable, we just kind of go, "This is uncomfortable, we're going to go back to our old ways." I tried to tell my patients that. I don't see many anymore, but I tried to tell patients when I talk to them that that discomfort is a sign of progress. If you felt comfortable, you'd be doing the old stuff, right? The goal is to move forward and that's going to bring discomfort. So normalizing the ambivalence sometimes is enough to get someone through that hump. "Oh, this is normal. This is what I'm supposed to feel and it's going to go away" is beneficial. So you can see that all of that is just psychology.

John Bellone 1:14:29



Yeah. That's why we are psychologists first and neuropsychologists second. We talked with Dr. Karen Postal about feedback and giving feedback. It's my hope that every neuropsychologist will get at least some training in MI. She had mentioned, specific to OSA to PAP devices, that she sometimes recommends that patients get "friendly" with their device. You know, when they first get it, they wear it while they're watching TV, not try it first at night. I don't know if you have any recommendations for this.

Mark Aloia 1:14:30



Yeah, so there was a graded exposure study done by Jack Edinger and Melanie Means out of Duke several years ago with some veterans. First of all, it's absolutely the right way to get used to something like CPAP. We don't do that. I talked about how barbaric the diagnostic [exam] is. And then you go to a DME, and they tell you everything in whatever - 15, 20, 30 minutes - and you go home and you lay it out all on your bed and you're like, "What happened?" So acclimating is a good way, especially if someone has an anxiety response to it. Graded exposure is great for anxiety. When I tried it on at 10 centimeters of water, I remember I had a flashback to when I went snorkeling the first time. I could hear my heart beating and I had an anxiety response. I did diaphragmatic breathing, and I was okay. But most people don't come to the table with those skills, so acclimating is a good way to do it. You don't find a lot of clinicians advocating that - a lot of say, pulmonologists or sleep docs. In part because they don't want to delay treatment, which makes sense on one hand. On the other hand, these people have probably been walking around with sleep apnea for 10 years, five years.



John Bellone 1:15:36

Right. What's another couple days, right?



Mark Aloia 1:16:16

Yeah. But now they're under my care, right?



John Bellone 1:16:18

Yeah, sure.



Mark Aloia 1:16:18

So, we do that. But the other thing we do is, I think, a really nice motivational interviewing tool, which is the scaling tool. So we say "On a scale of 1 to 10, how motivated are you to do this? Probably not a 1 or you wouldn't be here. Probably not a 10 or you wouldn't need me, right? So let's talk about what it really is." So they might say it's a 6. So why isn't it a 7 or an 8? So that elicits all the barriers, which is what everyone wants to solve. As healthcare providers, we want to eliminate all the barriers, but we know that new barriers will arise. So what we do with that is we express empathy, we reflect that back. "Okay, you've identified some things that might get in your way. It's good that you know that that could be hard. Let's keep an eye on that." We ask a critical question, "Why isn't your number like a 4 or 5?"



John Bellone 1:17:08

Yeah.



Mark Aloia 1:17:08

That's really them eliciting that critical thought. Now we've done this, we built a mobile application that does this where you can type it all in. When we see someone dip in their CPAP use, we feed them back their own words. We first express empathy. "We realize you've been struggling. Making a change like this can be hard. Here's why you said it was important to you. Do you still feel that way?" They have the opportunity to change their words, but feeding back their own words reflects back to them their value system. And we find that that works tremendously well. I'll say that, when we built this mobile application - it's not the only piece of MI in the mobile application - but when we built [it], this was with the company Philips, we saw a 22% improvement in adherence. A huge improvement in adherence. And I didn't believe it. That was when we looked at the first 15,000 people. We now have over two and a half million people on this mobile application. Then we looked at 172,000 people and we still saw that level of improvement in adherence. Then someone at Walter Reed did a randomized control trial, without even us knowing about it, and saw an 18% improvement in adherence in their military population. So we know that these techniques can work.



John Bellone 1:18:18

Is that mobile app commercially available?



Mark Aloia 1:18:20

Yeah, it's called DreamMapper. It's commercially available, but it only syncs with the Philips device.



John Bellone 1:18:27

I see.



Mark Aloia 1:18:27

Because we don't have access to other people's data.



Ryan Van Patten 1:18:31

So to all of our listeners, read your Miller and Rollnick "Motivational Interviewing" and become friends with that book. [laughs] So you can help your patients become friends with their CPAP.



Mark Aloia 1:18:42

I think it's Pip, Butler, and Mason, maybe not in that order. It's a really good small paperback. Its "Health Behavior Change for Healthcare Practitioners"*. Very easy read. Great book.

*Transcriber's Note: "Health Behavior Change: A Guide for Practitioners" by Stephen Rollnick, Pip Mason, and Chris Butler.



John Bellone 1:18:57

Excellent. We'll try to link to these in the show notes for listeners to go right there if they want.



Mark Aloia 1:19:01

Great.



Ryan Van Patten 1:19:13

I think you spoke to this earlier, Mark, but I want to highlight it. We know that these PAP devices are effective in improving airflow, reducing apnea, hypopnea. But you've also mentioned that a lot of these patients suffer from OSA for months or years before being diagnosed and treated. So, to be clear, can a good PAP device

that's used regularly reverse long term cognitive and emotional effects that are accumulated from years of sleep fragmentation and hypoxia?

Mark Aloia 1:19:42



So the answer is, "It can." We've seen that they can in the context of memory. I told you [about] that paper that we published. Again, that's not been replicated, but it's been out for many years and [unintelligible]. I would say, "Yeah, they can." Will they? That's a whole different question. I believe that in order to sustain this field, we need to figure out who is susceptible to their apnea and who's not. We can't cast a wide net anymore. We need to get more astute about who's going to suffer deleterious effects of their apnea. Then we'll be able to see the true effects of CPAP. What we've had is after CPAP - look, you find out someone's eating, you have a treatment for it, you don't need a whole hell of a lot of clinical trials to tell you that you should be doing something. So we had 20 years of CPAP before we did our first real clinical trials. Randomized controlled trials with sham devices and that was a whole mess, right? Because now we're not going to treat for six months someone who has these breathing cessations. So running into these trials, there were a couple of them, we eliminated people who had near misses in motor vehicles, who had car accidents, so we now get this sampling bias - we tried not to, but that's what we had to do for ethical reasons. I wasn't a part of the study, by the way, I say "we" as the global "we". Then we did neuropsych assessments, we did all this kind of stuff and we essentially showed that CPAP didn't really do much. But adherence was poor, and it was a sampling bias. I think what happens is when you take everyone, some people don't need CPAP. We've seen that in our own studies. Just like the memory thing - there's no correlation between AHI and memory, but when you start to look at people who have a memory problem, CPAP is absolutely what you want to give them.



John Bellone 1:21:47

There's no correlation between AHI and memory? Or that hypoxemia?



Mark Aloia 1:21:50

Broadly, either. Broadly. Because there are some people who have hypoxemia or have sleep fragmentation and they're not having memory problems.



Ryan Van Patten 1:22:02

So it washes out an effect. If we look at a subgroup of people who are having impairments, they are normalized, most of them, many of them are normalized.

Mark Aloia 1:22:12



Right. And we just don't know, Ryan, how to define that group yet. But we have to. In clinical medicine, we have to figure that out. Or else we're going to be - it's just going to be a commodity. Everyone's going to be getting sleep studies and everyone's gonna be getting CPAP, which is, again, untenable. Or insurance companies are going to say, "Hey, look, we can't keep doing this. We've got to figure something out." So I think we are trying to move into a better discovery of what predicts negative outcomes. Now, the problem with that is, which negative outcomes? I may be able to tell you about cognitive function. But that doesn't necessarily mean I'm telling you about the cardiovascular problems, right? I'm sure it's all a Venn diagram where they overlap. But, you know, it's very complex.

John Bellone 1:22:59



Mark, you were part of a qualitative research study with OSA patients and their partners, as well as a couples-oriented intervention for adherence. Can you briefly kind of tell us about your work and the benefits of including the patient's partner in this treatment?

Mark Aloia 1:23:14



Yeah. So when I was working for Philips - I've been working for them for 14 years, I've been NIH funded for 20 years, I have an academic role, and I have an industry role. So I kind of have a foot in both camps. But when I finally started to convince people at a company that behavior change was a relevant topic to invest in and to think about and they saw what we did with the mobile application, they asked me, as only industry can do, "Can you put on one slide what you do for behavior change?" [laughs]



John Bellone 1:23:48
[laughs]

Mark Aloia 1:23:48



And I thought to myself, like, "I've been doing this for 25 years." It was a great exercise. So, ultimately, I came down to five pillars that affect behavior change. I won't go into detail, [but] personalization, creating a sense of urgency, building competence - that's the self efficacy one - social support, and supporting autonomy. Social support is really where I think we have a tremendous opportunity in the context of the family or partners. Oftentimes, partners have great intentions of supporting their partner in their medical treatment but they don't really know how to do so. And [there's] a long history of, say, arguing over whether or not I snore, it

becomes difficult, right? "You're not using your CPAP" or "How come you're not using your CPAP?" or "Put your CPAP on" or "You took your CPAP off in the middle of the night" is not the proper way to approach it. So what we try to do is engage couples in the context of some tricks in motivational interviewing. We try to get them to become better listeners. We try to get them to do reflective listening. We try to maybe get them to do some content reflections, or even some reframing, or highlighting past successes. You know, "I know you can do this." I mean, one of our best studies - many, many, many people in the field published that four hours a night was the average use of CPAP. And for years, we thought about CPAP adherence as a 0 or a 1, you're either non-adherent or you were adherent. And in our lab, we said, "This is kind of crazy. This is a behavior." So we did a time series data analysis, where we looked at 85 individuals and we graphed their use over 365 days. We put like images together and we found you could very easily - there was a not insignificant number of people who were averaging four hours a night, but using eight hours on some nights and not using any another night. So those are people, as a psychologist, I'm going to speak to differently than the person who's taking it off in the middle of the night. So understanding and helping the spouse with expressing her view or his views on why this is important to them, either for their own sleep or for the benefit of their partner or both - often it's both. By helping them, almost in couples therapy, you can have a more positive effect on the patient. So really sort of dyadic conversations, and really understanding how to build those conversations in a meaningful way.



John Bellone 1:23:48

Yeah. We know that behavior change is always better if we have accountability. We have a partner who's going through it with us. And so this is...



Mark Aloia 1:26:26

Accountability and support, right?



John Bellone 1:26:31

Support as well. Yeah. True. Before we leave the realm of treatment and start to wrap up the interview, I want to talk a little bit about other treatments like positional.

You mentioned [the] supine position apnea is usually worse. Some people wear backpacks with tennis balls on them or different ways to prevent them from rolling onto their back. There are surgeries. I recently found out about this Inspire treatment where there's a stimulator that's implanted to keep the airway open. Can you talk a little bit about these? There's a nasal kind of - I forget what it's called.

Mark Aloia 1:27:08



The Prova. Right. Yeah, that creates negative pressure. So there have been many efforts to put CPAP out of business, and rightfully so. Even in our CPAP company, right? Everyone understands the problems associated with CPAP and, quite frankly, we just want options. We want options for patients. So this is where that diagnosis of mild to moderate comes in. Because if your clinician feels a little bit more comfortable, if you're mild and you don't want CPAP, trying something else. There are mandibular advancement devices - if you just try to make a snore [sound], I'm going to be gross here...



John Bellone 1:27:48
[laughs]



Mark Aloia 1:27:48

But like, [makes a snore sound]. Right, you make a snore. But if you move your jaw forward, it's harder to do that. It's harder to have that airway closed. So there are many mandibular advancement devices.



John Bellone 1:28:00

Like a piece that you put in your mouth? A mouth piece?



Mark Aloia 1:28:02

A piece that you put in your mouth. They actually have surgery sometimes where they really advance your mandible. There are oral appliances that can be titrated to do some of that. You mentioned a lot of other techniques. So those are generally used in the mild to moderate folks. The UPPP I don't hear as much [about] anymore. This was surgery to remove the uvula and the upper palate. And, in part, because it was very painful and what we found is that maybe it was 50% effective, and then over 10 years scar tissue grew and you had apnea again.



John Bellone 1:28:41

I think Mike Piazza had it, or somebody prominent had a lot of complications.



Mark Aloia 1:28:49

I mean, I'm not trying to throw any surgeons under the bus, but it's not the best treatment. It's not something I would opt for. I'll just say that. If you have positional apnea and if you get a good sleep study, certainly in the lab, you'll know. A lot of times you'll know. We have a device now, you can just snap it around your

midsection, put on a nasal cannula, sleep with it, and we can tell you if you have apnea. We can tell if it's positional because of accelerometers and so forth. If you have positional apnea, we just need to get you off your back. So years ago there was, I think it was a letter to Dear Abby, I think I have a copy of this somewhere. This patient said "Yeah, my wife just gave me one of her bras. I put it on backwards and put two tennis balls in the cups and when I roll on my back I move back over." And it stopped his snoring. Well, we actually have a device now that's a positional device that can tell when you lie supine, gives you gentle vibration, you're wearing it around your chest, your midsection, gives you a gentle vibration that moves you now to your side, and stops you snoring. It's designed for snoring. That's a consumer device. And by the way it learns you overtime. So it doesn't arouse you but it turns you over to your side. We have a device called Night Balance that's for positional apnea. That's a scripted device that then communicates with your doctor, and so forth. So there are devices for positional apnea. There are pills that people are working on to see if it can change the patency of the upper airway. There's also multiple ways in which you can develop apnea. There's something far more complicated than I can get into right now, in pulmonary medicine called laking (?) that may be a cause for sleep apnea and medications may be able to change that. So, many, many people are looking at different avenues other than CPAP. But I'll say that they've been doing that for decades, and there's really not been anything that works to the degree that CPAP works. I should just say CPAP works for all of these causes. But there may be other alternatives for certain causes. You first have to identify the cause and the treatment. And then you have to have a diagnostic mechanism by which you can say, "John, your cause is this. You have these options. Ryan, your cause is this. You have these options."

John Bellone 1:31:13



So, just to summarize, there's a lot of options for more mild, maybe mild to moderate. But really, for moderate to severe, the PAP devices are the gold standard and we should point people in that direction.

Mark Aloia 1:31:26



At this point. Many people make a reasonable argument to say, "Hey, look, if my patient's not going to use CPAP, why not just put them on an oral appliance?" Now, as a psychologist, I believe, and I don't have any data to support this, that this is - see, I think one of the biggest problems we make in medicine is thinking that the behavior is associated with the treatment. I think the behavior is more associated with the person. So if I have a non-adherent CPAP user, I'm not going to put money

on the fact that if I put her on an oral appliance, she's all of a sudden going to be terribly adherent.



John Bellone 1:31:59

Yeah, that's a good point.



Ryan Van Patten 1:32:00

Some people wear night guards, which is very low burden but they're not actually adherent to them because it's too much change. So even a lower bar might be too much.



Mark Aloia 1:32:10

I mean, I'll tell you what I think. There's evidence in the literature that half of the people don't take their medication the way they're supposed to. So. And that's a pill.



John Bellone 1:32:22

Or even exercising. Well, yeah, it's a higher bar than taking a pill. Yeah, sure.



Mark Aloia 1:32:26

Right. You know, it's important to think about how onerous the behavior is that you're asking them to change. But it's not just how onerous the behavior is.



John Bellone 1:32:37

So, Mark, we've covered a lot of the clinical neuropsychology pieces, but we have a couple other questions for you. We talked about the MI and what we should do in the feedback session, which I think is great. In terms of how we, as neuropsychologists, should be screening for sleep apnea, do you have any ideas? Like, should we be using these self-report questionnaires like the Berlin or the STOP-BANG? Or can we just ask about snoring or apneic events?



Mark Aloia 1:33:06

Yeah, I think you can do either. When we did intakes for our sleep patients, and oftentimes, this was in an insomnia clinic, but we were screening for apneas as well. We did an hour and a half interview. We looked at all the different sleep behaviors. We looked at sleep scheduling, we looked at apnea. And we would ask questions about "Do you wake up with a dry mouth or morning headache? Do you snore? Do you ever snort or gasp to catch your breath, either as you're falling asleep or in the middle of the night? Has anyone ever told you that you stopped

breathing at night?" You know, those are the primary questions. "Do you feel sleepy during the day?" But I should tell you that only 40 to 50% of people with moderate to severe sleep apnea report feeling sleepy during the day. Maybe that's because you asked them after they're loaded up on caffeine, who knows.



John Bellone 1:33:50

[laughs]



Ryan Van Patten 1:33:50

[laughs]

Mark Aloia 1:33:51

So I think these are - and then you ask about blood pressure and diabetes. When you see the picture of high blood pressure, diabetes, overweight or obesity, and snoring, look, you got some pretty good evidence, right? And then take a look at their neck. I mean, you have some pretty good evidence that this person might have sleep apnea. And, quite frankly, it might not be a problem just to ask them "Has anyone ever told you you have sleep apnea?" Because I said it's not prevalent, like depression in terms of screening, but it's far more prevalent and there's far more awareness around it than there ever was. Oftentimes patients know someone else who has sleep apnea. I can't tell you how many times I've heard people say, "Yeah, my buddies won't sleep in the same room with me when we go hunting or fishing together." So it's those situations that they start to hear more about it.



John Bellone 1:34:43

Right. That brings up the traveling PAP device because you have to get a different device if you're going to use it.



Mark Aloia 1:34:51

You don't have to. There are travel PAP devices that are smaller battery packs, stuff like that, that can help you. If you're going camping, you can use your CPAP.

There's really no excuse not to use CPAP anymore. But they do cost money, and those travel PAPs aren't paid for, usually, by insurance. I think I've [seen] one somewhere in the \$700 range or so, maybe a little more or a little less depending on where you find them. You can find these travel PAP devices. There's about, I'd say, 15% of people who just love their CPAP because they feel better than they ever felt before. Those are people going out there buying travel PAPs, and they



never leave without them. But you see people walking with CPAP in the airport too. Full on regular sized CPAPs.

John Bellone 1:35:36



Yeah, sometimes I've had patients tell me that they didn't really notice the benefits of it until they spent a night without their PAP device. And then they really notice a big change, a big decline the next day.

Mark Aloia 1:35:51



That is a great point, John. I mean, oftentimes, when we're making changes like that and we're struggling through the difficulty of it, it's hard to appreciate the value right? Then once the change is made, and you take a hiatus or a vacation from it, you see that.

John Bellone 1:36:07



So it sounds like the threshold, if we do have a patient with hyperlipidemia, hypertension, obesity, etc., and they report snoring, we should really be including a recommendation, as neuropsychologists, for the referring physician to consider referral for a sleep study. Or how do you usually incorporate that into the neuropsych recommendations?

Mark Aloia 1:36:30



You raise an interesting point that you probably didn't intend to raise. Maybe it's not just snoring, but snoring in and of itself may confer some negative effects, right? So there's more and more literature now that suggests snoring, even outside of the context of sleep apnea, can confer some negative effects potentially even on cardiovascular disease. So, yes, that's a yellow flag. And you start to see the constellation of things like you mentioned, that becomes more of a red flag, orange flag, whatever. You know, they have a big neck and they're overweight, then this is a red flag.

So, then, in the context of the report, it's not just like you're going to write your regular report and say, "Oh, by the way, I noticed this person endorsed these things, maybe they should have a sleep study." I think what the smart thing to do - and we all do this, our reports are way too long and too complex and most people don't read them, right? - is in the recommendation section, you have a bullet point that says either, "Rule out sleep apnea as a contributing factor to the cognitive problem" or "Sleep apnea may contribute, although he hasn't been diagnosed". So you absolutely have to call one's attention to that. I do it in the context of medical

history as a potential. I do it in the context of case conceptualization and recommendation.



John Bellone 1:37:50

Yeah. Excellent.

Ryan Van Patten 1:37:52

Well, this has been a great conversation, Mark. I think a lot of people will benefit from learning more about OSA. I think it's a unique syndrome compared to [something] like Alzheimer's disease, for example, which OSA is a problem. But a big part of the problem is behavior change, which psychologists are the people to come to, clinical psychologists, to do that, right? Whereas, obviously, [for] AD we're waiting on the pharmaceuticals and we can't prevent all TBIs, but here it's a place where we are perfectly trained to help. So thanks for talking about all these issues with us.



Before we let you go, we have two bonus questions for you. These are about the field of neuropsychology more broadly, and don't necessarily have to apply to sleep or OSA but they can. The first one is: if you can improve one thing about the field of neuropsychology, what would that be?

Mark Aloia 1:38:47

Oh, gosh. You know, I've been out of clinical practice in neuropsychology for quite a while. I am married to a neuropsychologist [laughs], so I've experienced this through her. So, I guess I would say we need to remember that we're clinical psychologists first. I mentioned the long reports. I think it's important that we understand who our audience is and what our audience is getting out of those reports. What my wife will tell me, and she's absolutely right, is that in many cases, and she does pediatric neuropsychology, it's the first time people have pulled all this information together for the patient and it's terribly meaningful. And I get that. But especially working sometimes with older adults and so forth, I wonder how often our reports are read. So, as clinical psychologists, we need to think about what the best way to get our information across is. It's not just up to us to conceptualize the case. I'm far more effective if I can change the course of treatment than just conceptualize the case. So that involves all of our skills as psychologists. I think that's really where a lot of the work comes in. So, I think I would say, in our training, we have to embrace the clinical psychologist as well as the neuropsychologist.





John Bellone 1:40:12

Excellent. And, to wrap up, what is one bit of advice you wish someone had told you when you were training, or that someone maybe did tell you that really made a difference? Just an actionable step that trainees can take.



Mark Aloia 1:40:23

I had so much good advice. I went to a small Catholic college to get my bachelor's in psychology and there was one clinical psychologist and she was a nun, but she was not your typical nun. I mean, she would be going to a union seminar from Indianapolis to Chicago and reading while driving and got pulled over and I think lost her license at some point. But she gave me some great advice that said, "If you want to be a clinical psychologist, experience as much as you can so that you can take perspective from your patients." I thought that was really good advice. In neuropsychology and as, I'd say, as an academician, I always had heard, "Do what you love and it'll all work out." And I hate to say it, but I think that's only part of it. [laughs] So, for me, I had a fire in my belly for science. So, you know, I started a grant writing seminar. I've run a couple different grant writing seminars, one in bench science. I love that. So if you can embrace the process of science, then it's a little easier to find what's going to be fundable. I never thought I'd be in the field of sleep. For years, I went to conferences and I would start conversations by saying, "Well, I'm not a sleep scientist." And at some point after, like, my second grant someone's like, "You're a sleep scientist. Just stop saying that".



John Bellone 1:41:47

[laughs]



Mark Aloia 1:41:48

Right. So, I don't know if that's advice, but I guess those are things that have happened to me that have shaped my future.



John Bellone 1:41:59

Awesome.



Ryan Van Patten 1:41:59

Great advice.



Mark Aloia 1:42:01

Thanks, guys, for having me. I really appreciate [it] and I have to say I appreciate you calling the attention of other neuropsychologists. It's something that I feel is really critical and important.



Ryan Van Patten 1:42:11

Yeah. Yeah.



John Bellone 1:42:12

We couldn't agree more.



Ryan Van Patten 1:42:13

Yeah. Thank you for making the time today.



Mark Aloia 1:42:15

No problem. All right. Take care guys.



Transition Music 1:42:17



Ryan Van Patten 1:42:21

Well, that does it for our conversation with Mark. Be on the lookout for upcoming episodes on transverse myelitis, adult ADHD, cultural neuropsychology, aerospace neuropsychology and more. And, as always, thanks for listening, and join us next time as we continue to navigate the brain and behavior.



Exit Music 1:42:40



John Bellone 1:43:04

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Ryan Van Patten 1:43:15

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