39| Behavioral Interventions for Mild Cognitive Impairment – With Dr. Glenn Smith

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Speakers: Glenn Smith, John Bellone, Ryan Van Patten

Intro Music 00:00

John Bellone 00:17
Welcome, everyone, to Navigating Neuropsychology: A voyage into the depths of the brain and behavior. I'm John Bellone...

Ryan Van Patten 00:24

…and I'm Ryan Van Patten. Today we're speaking with Dr. Glenn Smith, professor of psychology at the University of Florida and also Past President of APA's Division 40 and ABCN. We speak with Glenn about multicomponent interventions for mild cognitive impairment, including his own interventions, HABIT and Peace of Mind. Today's episode dovetails well with our conversation with Beth Twamley from UCSD, this is episode number 15. The umbrella topic here is interventional neuropsychology, which we both find to be really interesting and helpful. We also want to give a special thanks to Leslie Gaynor for her help behind the scenes with this episode.

John Bellone 01:09

And now we give you our episode with Glenn.

Transition Music 01:11

John Bellone 01:20

Okay, we're here with Glenn. Thanks so much for coming on NavNeuro.

Glenn Smith 01:23

My pleasure. Thanks for inviting me.

John Bellone 01:25

We'll be talking about MCI, mild cognitive impairment, in the context of your interventions. But it might be helpful just first to get your take on the concept of MCI, the definition and how you conceptualize it.

Glenn Smith 01:39

Sure. I did have the good fortune of working closely with the whole group of Mayo collaborators that brought one version or vision of MCI to the literature. It seems to be a version or vision that took hold. But it was really just the fact that, as we were developing way back in the early ‘90s an Alzheimer's disease patient registry, we were trying to recruit from a community mental medicine practice, a person that looked like they had early Alzheimer's and then the very next age, gender, and sex matched person that came through the clinic as a control. But what we were routinely encountering was that they functionally looked pretty normal for their age, but then we'd give them our very sensitive cognitive tests and they would be

outside of our expectations. Now, of course, at the same time, I was working closely with Bob Ivnick and Jim Malick and others as we were developing the Mayo Older Americans Normative Studies. If we hadn't been doing that work, we certainly wouldn't have come to this notion of mild cognitive impairment. But it was quite simply just the situation where we had people that didn't meet criteria for dementia, but we didn't think [they] were testing in one or another way normally. And that's all MCI was.

In those early days, we decided to add the notion that there needed to be - the language we used was a “cognitive complaint”. Now, unfortunately, I think that got read somewhat too literally, because initially people thought we meant the person themselves had a cognitive complaint. What we're really reflecting on is that the people for whom there was some evidence of suboptimal neuropsych functioning, where there was also a concern by the primary provider, a knowledgeable informant, or the person themselves. Those were the people who were much more likely, as we're now pretty clearly aware, to progress further into worse cognitive and functional status. There was a sense early on that we were trying to capture the earliest signs of Alzheimer's disease because we were, it was an Alzheimer's disease study. But I don't know that it was ever our intention to say MCI is early Alzheimer's. That was something that got layered in by other people looking at our work. And that had some consequences that I think have subsequently been remedied. This may be looking through the retrospective scope a little bit and trying to clean up our process, but I don't think we ever meant at Mayo that it was anything other than a risk state.

John Bellone 04:51
And MCI says nothing about the underlying etiology, right? That’s what you are getting, right?

Glenn Smith 04:56
Yeah. I think that's been one of the really good points that we've progressed to. This separation between etiologies and syndromes. I think that's quite substantially improved the field and let us look at the complexity of neurodegenerative disease. We don't start with etiology first anymore. We tend to start with the syndrome and then say, “Well, what could explain it?” And that's been, I believe, good for the field.

Ryan Van Patten 05:28
Right. I like how you and Mark Bondi, in your 2013 AACN book, described MCI as a state of clinical uncertainty.

Glenn Smith 05:36
Yeah.

Ryan Van Patten 05:36
Which makes it so then if someone has MCI and then we find…

Glenn Smith 05:41
By the way, I want it to be known that that was me and not Bondi. [laughs]

Ryan Van Patten 05:44
[laughs]

John Bellone 05:44
[laughs] We will make sure he knows.

Ryan Van Patten 05:47
Give full credit where credit's due. [laughs]

Glenn Smith 05:50
I think Mark Bondi is smarter than me. So he rarely has uncertainty.

Ryan Van Patten 05:56
Got it. We're planning on talking to Mark later, so [we'll] make sure to pass that along to him. [laughs]

Glenn Smith 06:03
I was just in San Diego the other day and had a nice visit with him. It's been really, really my good fortune to be able to collaborate with him. We've been on a parallel course for much of our careers. Such a great contributor to the field.

Ryan Van Patten 06:19
Yeah, well, that the book that the two of you wrote together, I know I and many people I know have benefited from it greatly. It's a very helpful way to understand MCI. And the state of clinical uncertainty helps us explain and understand findings, such as people with MCI can "revert" to being healthy. So some people might be confused by that and think, “Well, if MCI is a stepping stone to dementia, how could you get better?” But that's really not how you were proposing thinking about it.

Glenn Smith 06:50

Right. Your frame, your population sample is so important to keep in mind in this regard. We weren't doing a door to door survey, but our early work was out of a community based sample. These were people that were, again, being flagged with some concern. So you can predict how likely people with MCI are to progress in part based on knowing - is this a general community survey? Are you going door to door? Are you, after the fact, identifying an MCI sample from a group that was recruited to be normal? Or are you dealing with people who are being dragged to a clinic and somebody is sufficiently worried about them such that they're getting clinical services? That dimension of where we're identifying people with MCI from is a really important part of base rates. It's a lot about base rates.

Ryan Van Patten 07:59

Yeah, well, we could grill you about MCI for hours. [laughs] We would like to spend the time we have with you today on interventions, the majority of it anyway. So we know there are several pharmacological interventions available for people with MCI and dementia. Aricept, cholinesterase inhibitor, and Namenda, the glutamate antagonist. Before we move into non-pharmacological interventions, I'm curious what advice you give to patients who are considering talking to their neurologist about these medications for memory?

Glenn Smith 08:29

I've been really influenced by behavioral neurologists and cognitive neurologists that I've worked with who really looked at the seminal Donepezil study in MCI that was led by Ron Petersen. [That] was 70 sites, 700 patients, the outcome of which was that [after] three years in terms of the primary outcome being progression to dementia, there is no difference between placebo or Aricept or high dose vitamin E. But in the middle there, at about 18 months, in post hoc analysis, they did show a separation of the curves that led everyone to say, "Well, maybe the medication works for some people for a while." Now subsequent research has suggested that maybe responder status is predicted by things like APOE status, for example. So there may well be this selective effect in the right populations where Donepezil is going to have a significant benefit. But I don't think anyone has yet shown that it changes disease trajectory, ultimately and fully, so people are still going to get worse.

When I talk to folks about this, what I say is that it seems the medication can be helpful for some people and that's between you and your prescriber. But understand that medications alone aren't all we have to offer. Some prescribers are

going to want to start them as early as possible and yet what I've seen more often is prescribers saying, “Let's keep your powder dry.” Almost like, “Let's wait till the person has a clinical dementia rating scale score on the cusp of 1 and that's where we'll try and sustain them for a longer period of time.” But, I mean, there's huge practice variability out there. What I struggle with more than that is the off label use where we give these medications to virtually anybody with a memory complaint, whether it's related to a vasculopathy, as if there's some broad memory benefit from the medication. I don't think it's ever truly been definitively shown to help declarative memory, per se. That's my take on it.

John Bellone 11:03

Do you think it's out of line for us if it does look like an Alzheimer's disease etiology, but it's clearly an MCI case, for us to put in the recommendations that the person, the patient could consider talking with their physician about adding an acetylcholinesterase inhibitor?

Glenn Smith 11:19

I think you absolutely should. Not trying to communicate that people shouldn't be given access to any and all potentially helpful prescriptions. In fact, we're going to get into a little bit in the non-pharmacologic interventions that's been from an early phase of my career where I was trying to say which behavioral intervention is better than which other one, I really had this shift to saying we should be trying to do everything we can, whatever might help a little bit. The risk of that is you don't want to be over promising or engaging in snake oil sales, for example. But just really think that it's ageist sometimes to think, “Well, what can we do? We shouldn't be wasting a lot of money on these kinds of interventions.” I often tell the story that when I was in the midst of thinking about this program we developed at Mayo called HABIT, I was at a point in time where my father had developed pancreatic cancer and came to Mayo to get his treatment. I was expecting to hear which range of interventions they were going to try. And, of course, what they said is, “We're going to try everything.” I thought to myself, “That's what we do in cancer. We treat cancer like a terminal illness. We don't treat Alzheimer's like a terminal illness, even though we know it is.” So it's important. It’s not necessarily a position one takes empirically, it's more a position one takes philosophically that we should be trying everything we can.

John Bellone 13:06

You definitely do that with your interventions. We'll get into the multi-prong approach. Before we talk about specific research, maybe we should orient our

listeners to a few core ideas. One of them is how the concepts of primary, secondary, and tertiary prevention apply to aging and neurodegenerative diseases. How do you think of these types of prevention?

Glenn Smith 13:27
I'm a simple minded epidemiologist. I have a simplistic understanding of these issues. But primary prevention is this idea of let's treat everybody or as much of everybody as we can to try and remedy a condition of interest. Of course, the classic example we point to is fluoride in the water. Look what's happened to the incidence of cavities and all of us. And vaccinations, right?

Secondary prevention is where you have a risk state. This is where MCI is a bit of a muddy concept, because is it the disease? Or is it a risk state for the disease? That's where increasingly it's important that we talk about the distinction between preventing Alzheimer's and preventing dementia. Because MCI is clearly a risk state for dementia, even if it actually in the majority of cases represents the presence of Alzheimer's. Because on the flip side, one of the most influential studies in my experience - I wasn't directly involved with but it was an analysis by David Knopman a behavioral neurologist at Mayo. Of the Mayo Clinic Study on Aging cohort, an early sample of about 15 or 20 people who've been followed longitudinally over 10 years in that study and died and they had brain autopsy. That

was actually far more than 20. Twenty was roughly the number of people who actually had full on Alzheimer's pathology in their brain. So it must have been more like 100. I don't particularly remember the details. The point is 12 to 15% of that cohort, who we knew to be, it wasn't just that we didn't pay attention to them, they had been followed annually and had cognitive evaluations and MRIs and they were deemed clinically normal at around the time of their death, and yet they had full on Alzheimer's pathology in their brain. So the pathology is not the condition, in that regard. It's possible, as we're learning quite well, to carry an awful lot of brain burden of disease and for one reason or another, remain functionally intact. So MCI is a risk state for the condition of interest, which is dementia. Can we intervene in a variety of ways to prevent or delay progression?

Of course, tertiary prevention is really just mitigating the morbidity of the disease. So in the case of dementia, it might be things like using modern telecommunications technologies to allow a dementia patient to remain in their own home longer. That would be a form, in my mind, of tertiary prevention as we apply it to neurodegenerative diseases. But that's a point, I think it's important to emphasize. It distinguishes in some ways, drug studies, which are targeting the reduction of some proton apathy in the brain and as a prevention strategy. Whereas

I think where we operate well, on the non-pharmacologic side, is focused on the syndromes, not the etiologies.

Ryan Van Patten 16:55
Yeah, I completely agree. That distinction is very important. We had an interesting discussion with Adam Brickman about Alzheimer's disease. Is it biological? Is it a syndrome? The differences there?

I'd like to now transition to really talking about interventions. And the first distinction I'd like you to make - I should say, non-pharmacological interventions. The first distinction I'd like you to make is your thoughts on the difference between restorative and compensatory cognitive training.

Glenn Smith 17:22
So I actually started my career at a rehabilitation center, doing stroke rehab, before I fortuitously got whisked away to Mayo Clinic to work with the Alzheimer's program. And that's where it got steeped in this idea. It's much clearer when you think about something like hemiparesis, right? When we watch people trying to recover from hemiparesis, say that it's a right handed person and they've got right sided hemiparesis, we watch the PT do a lot of things to try and recover muscle tone and coordinated movement in that hand. But, at the same time, they're probably teaching the person to eat left handed or to write left hand. So this is a very simple model that the effort to recover the function, that's restitution, but the effort to learn to do the same thing another way that's compensation, and that's rehab 101.

So having had that background, I went to Mayo. I spent some of my postdoc time at Mayo in the traumatic brain injury program, where you have a presumed trajectory that people are going to show some recovery following that insult. But you're engaged in the same philosophy in TBI - whenever the person may not be able to recover, how are we going to help them compensate for that? So as we started with this notion of mild cognitive impairment, we had those kinds of philosophies in the background. Again, it was serendipity that at about the time that this idea of MCI was gaining some traction, I went to, I think it was one of the first AACN meetings and a neuropsychologist from a place called Posit Science was presenting some preliminary data on a computerized brain training tool and asked me to come over and look at her poster and tell her what I thought. It was some data where they had given people some cognitive tasks and then had them undertake the intervention and then given them the same tasks again. It was uncontrolled study, etc, etc. And because I have very few social skills, I just said, "You know, you could have had

people stand on their head, you would have still seen this improvement on your cognitive tests. You've got to have an adequate control in your design here." I thought that was the end of it. I was not at all enamored with the computerized tests at the time. Then, to my amazement, they wrote to me and asked me to come out to San Francisco and help them run a trial. They had recruited Liz Zelinski from USC, who I greatly admired.

So we ran this initial trial of an intervention that's intended to stabilize or improve some aspects of cognitive function. We had that approach in our back pocket at the time. But also, at the same time, we were trying to apply the Sohlberg and Mateer memory notebook approach that both Melanie Chandler and I had learned while doing Mayo's traumatic brain injury model systems program and see how it could work in MCI. So our early studies really asked that question, “Should we be investing in compensation strategies to get better outcomes? Or should we be endeavoring to engage in restitution strategies?” And then at some point, as I alluded to, we said, “We don't have to choose. These people are so motivated, they'll do it all.” And that was where we started to develop our multicomponent intervention.

Ryan Van Patten 21:24
Yeah, that's a perfect segue. You had referenced HABIT, the Healthy Action to Benefit Independence and Thinking program. Tell us a little bit about what this program looks like.

Glenn Smith 21:34
So, in the end, we said, “What's everything for which there's at least a modicum of evidence to justify our using it?” So we had those two interventions, Melanie, at the time had an R01 where we were comparing them. I was also running support groups at the time for caregivers of people with mild dementia and starting to refer - "caregivers of people with MCI", it's probably better to call them partners because at that phase, there's very little care being given. But there is a lot of doubt and a lot of upset and a lot of emotional turmoil for those folks that we should attend to. So we had that support group component. We're also running a dementia education program there at Mayo as part of the ADRC. The only thing we really didn't have was the thing that probably had the strongest evidence base to it, and that was a physical exercise component. So we decided, “Let's just throw all these things together, figure out how to give people exposure to them, and see what happens.” So it's a whole group of people who deserve credit for HABIT, beyond just me, and

we were all in this environment of saying, "This feels like we've put the plane in the air and we're still trying to build it." But that's how we approached it.

And just tried to consistently collect data about it over time to see what works and what doesn't work. So, for example, we tried some early efforts at just doing walking as a physical exercise. We were stunned to find out how many people couldn't even walk through the underground hallways of the Mayo Clinic complex because they had balance issues or stamina issues or whatever. We ran the program once at a really nice senior living campus that had a beautiful gym. So we did resistance training in that setting. But ultimately, what we migrated to is we found that yoga was just so flexible in terms of engaging older adults because you can range from someone seated in the chair doing a pose to literally someone standing on their head doing a pose. So that was a really nice component. We began to really warm up to the meditative aspects of yoga as well.

So in the end, the five components of HABIT. We use the program BrainHQ as computerized cognitive training, in part because it's the latest generation of that original study that I did along with Liz Zelinski. We use this calendar training tool that was developed by Sohlberg and Mateer in the TBI literature. We do partner and participant support groups. We do a wellness education component and we do yoga. Those are the five components of the clinical program.

John Bellone 24:51

You had mentioned that you had adapted a lot of this from other studies and even with traumatic brain injury types of populations. Do you see any difference between the TBI versus MCI cases? I mean, there's a difference in that, obviously, the MCI could potentially be neurodegenerative diseases underlying them. Do you think they're similar?

Glenn Smith 25:13

No, you asked a great question about prevention. Let me give you a variation on prevention. That is that notion of compression of morbidity. We know that we can't, well, we're concerned that we may not be able to ultimately be disease modifying. But if we can compress the period of functional impairment - because what distinguishes dementia from MCI? It's not just the severity of cognitive change, but more importantly, it's the extent of functional impairment. So if we can delay functional impairment, even if cognition gets worse, we're delaying the point at which we say a person has dementia. If we do that, given that we're probably not modifying the disease, we're going to compress the period of dementia. That's a

form of prevention in its own right. So that's the argument we've long made to those people who say, "Well, they're going to get worse anyway." What we have to embrace when we think about that, and this actually reflects also on how we should talk about medications, is that anything you do to compress the period of morbidity is likely to speed the rate of ultimate decline. So, paradoxically, we often hear, “Don't take patients off of Donepezil because they might get worse faster.” Well, if you think about it, the best way to live this world is to have a one-day decline in functional status from being fully functional to being dead. So anything we do to steepen that curve, actually, I think, most people would embrace that as an appropriate set of outcomes for our interventions.

Ryan Van Patten 27:02

Yeah, I agree. I've thought about non-pharmacological interventions for AD, neurodegenerative disorders in that way for a long time. We want to ideally, sort of fall off the cliff, right? Not a slow, gradual decline with many years of functional incapacity, which has huge impacts on quality of life for you and your loved ones. So if we can keep people healthy and independent for as long as possible, and then when we can no longer keep them independent there's that quick drop, that's best for people's wellness and their experience.

Glenn Smith 27:36

Yeah.

Ryan Van Patten 27:37

Can you describe - just give us a broad overall take on the empirical evidence for HABIT?

Glenn Smith 27:43

This has been an interesting journey. The first thing I would say is, we've had to learn about when we say we want to have a positive outcome, which outcomes are we trying to influence? So that early work that Melanie Chandler and we did, comparing computerized brain training to the calendar training showed that, initially, the functional outcomes were better for the calendar training out to six months. But eventually that converged and we saw equivalent effects on a - well the ECOG measure for listeners that might be familiar with it, has been our favorite functional measure because it has some good scale or properties in MCI because it's measuring daily function that's dependent on memory. Both of those interventions did better than an active control arm or wellness education.

But, surprisingly, in our most recent study, which is a really challenging study to explain because it was conducted as a comparative effectiveness trial, which means everybody got some form of treatment in this recent publication that came out earlier this year. So what we did in the study, because it was through a comparative effectiveness mechanism, we had to design a study where instead of the base being nothing and then you add an intervention or two and see how that improves outcomes, we started from the frame of reference of what if the base was getting everything and what you did is subtract a component from that mix and see what it costs the person. So from that philosophy, we then said, "Okay, we're going to randomize people to get four of the five interventions." And actually to be quite explicit, we didn't randomize people. We randomized sessions. Because I should have explained about HABIT. It's always been a group based program where we ideally have between 8 and 12 couples or dyads going through the program together at a time. That's a really important detail because that group based intervention is powerful in its own right, no matter what you do, in the midst of it. So we randomized groups that, for a given session in this study, they would have one of the components withheld - maybe it'd be yoga for one session and the calendar training memory support system in another. And then we analyzed, okay, what happened? For a given outcome, which group had the greatest cost to the outcome? We were stunned to find that four outcomes that involved quality of life and self efficacy measures, actually the wellness education component, that not getting that cost people the most in comparison to the computerized brain training. And there's really no surprise that computerized brain training costs, not having that cost people virtually nothing in terms of their quality of life and their self efficacy. If you've done any of these Lumosity kinds of programs or BrainHQ, that doesn't surprise me, because they don't - I mean, they might help you with certain aspects of cognition, but they don't necessarily help you feel good about yourself or enhance your quality of life. But for the functional measure, if I'm remembering my data correctly, yoga was also a significant contributor to the functional outcomes.

We're about to publish on caregiver outcomes from that study. We're still analyzing the data. We used Cogstate as our primary cognitive outcome. But a funny story is that in most of our early publications on this topic, we didn't, as neuropsychologists, have any cognitive outcomes. We got so busy measuring functional measures and quality of life, that we ignored our own kind of fundamental discipline. So we added Cogstate into this big trial. We're waiting to see if that might not be the outcome that has the most cost if you didn't get the computerized brain training.

But I want to acknowledge one of the real challenges with this study, because it was a study done out to 18 months. So far, we've only published on our 12 month

outcomes, but even out to 12 months, adherence was a huge challenge for us. It was very uneven across groups. Some of that unevenness was because we had different levels of stringency for what we called “adherent”. Like if you were engaged in 150 minutes per week of any kind of physical activity, whether it was walking or pole vaulting, you would get credit for it. But you had to be, for example, using exactly our memory support calendar to get credit for the adherence in the calendar training component. If you had created your own calendar that was even better than ours, it still didn't count. So that was a little bit uneven. But, by and large, Melanie and I and some collaborators published a meta-analysis on this last year, too, you're getting effect sizes in the 0.25 to 0.35 range for most patient reported outcomes with these kinds of multi-component interventions. I think that roughly some people will be familiar with the FINGER trial in the Finnish Geriatric Intervention, which wasn't actually a study of MCI, it was a study of people at risk, however they defined it. But they saw comparable kinds of effect sizes in that study. In their study, the primary outcomes were cognitive in contrast to what our PCORI trial was. We chose non-cognitive outcomes as primary outcomes in that study, because we asked our clinical samples that had gone through HABIT to rank order the importance of outcomes and actual memory functioning finished like 6 out of 13 outcomes. That was, of course, quality of life, patient self efficacy, patient mood, and patient memory based daily functioning in that order were the top four. And then some caregiver outcomes got sprinkled in there too.

John Bellone 35:18

Comparing you to the Finnish study, do you think that HABIT could be used for older adults without MCI to maximize their cognitive abilities? Or conversely, for people with dementia or psychiatric issues?

Glenn Smith 35:32

I mean it's an exciting time to me because I'm hearing more and more about different variations of different trials. We have a loose collaboration, especially through my colleague, Dona Locke, who runs the Mayo HABIT program at Mayo, Arizona. She's been collaborating with Sarah Farias out of UC Davis, the original author of the ECog. Sarah has got a really interesting multi-component intervention that's targeted more to SCI, subjective cognitive complaint. That's a very reasonable target group. Lots of people are beginning to think about massive brain health initiatives. The CDC, of course, has a massive brain health initiative. It was a challenge of how do you scale this up. I also should have said this, but didn't - HABIT in our hands is a 50 hour intervention. You get one hour of each of those five interventions for 10 days, and just a quirk of history that we squish those 10 days

into two weeks originally. We're beginning to play around with other schedules that might spread that intervention out over time. But I think there's some trade here that culturally or economically or whatever, we're going to have this trade off between severity and intensity. So the more mild or more worried well, it may be harder to justify, certainly, intervention to that intensity. Then the other component of this is exactly the adherence conundrum, right?

John Bellone 37:23
That's the name of the game, adherence for any brain health types of interventions. Yeah.

Glenn Smith 37:27
Yeah.

Ryan Van Patten 37:28
So to summarize the data on the outcomes of HABIT. Does it work? Yes, it works. Effect sizes tend to be in a 0.3-ish range. The outcomes have included a broad range of areas of functioning - quality of life, wellness, psychiatric functioning, and some non-objective cognitive performance. Is that fair?

Glenn Smith 37:51
Yes. Succinctly put. Well done. Thank you.

John Bellone 37:55
[laughs] It's rare for Ryan to be cogent.

Glenn Smith 37:59
[laughs]

Ryan Van Patten 38:00
And accurate. Understandable. [laughs] Anyway. So now you have Peace of Mind. That's a program that you're currently running at University of Florida, correct? Can you talk about similarities and differences between HABIT and Peace of Mind?

Glenn Smith 38:16
Well, I've been a cynic myself as to whether these interventions could have a biomarker signature. As an aside, when I say that I mean a non-cognitive biomarker

signature because, I, amongst others, have long argued that neuropsychological measures are biomarkers according to the NIH definition of a biomarker and neuroimaging signal. But some other folks out there have shown that potentially, on say, default mode network connectivity measures or even in terms of brain volumes in terms of perfusion, proxies for cerebral perfusion, maybe that's how these different lifestyle modification and behavioral interventions assert their impact.

So we decided to try and undertake a shorter study than the PCORI study that was done of HABIT, so it's a six month trial. But this is the first collaborative study where we got neuroimaging pre- and post- the six months. And we've done a much tighter job in this study of following people and being right on top of their adherence because we figured if we were going to get a signal, we really needed to be sure we had optimum adherence. And in this study, we peeled it back further. We said, “We think, because they're the two most popular interventions, we should offer everybody support groups and calendar training.” So everybody got that. And we didn't, for theoretic reasons, think there's going to be much of a signal for either of those interventions in terms of neuroimaging measures. So what we randomized people to is yoga. So you get calendar training, support groups, and yoga, or BrainHQ, or our active control, which was our wellness education intervention. So it's still the five components of HABIT. But you get randomized to get one of the three choices of yoga, BrainHQ, or wellness. And of course, we launched that study before we'd seen the outcomes of the PCORI trial, which essentially shows that our active control in Peace of Mind was one of the more potent interventions.

John Bellone 40:56
Hate when that happens. [laughs]

Glenn Smith 40:57
That's the way research goes usually, [laughs]

Ryan Van Patten 41:03

So I'm sold on how HABIT and Peace of Mind work. The components to the original intervention are powerful. Where my mind goes next is the implementation science piece. Like within these RCTs while funded by the NIH, we can help people improve their well being, quality of life, and cognition. So then what does that mean for disseminating this to the masses, putting it in clinics?

Glenn Smith 41:33

So one paradox is that the trial I've discussed several times where people got randomized, the four out of five, was funded by the Patient Centered Outcomes Research Institute, the PCORI. PCORI also has a mechanism to fund dissemination and implementation research. Dr. Chandler had been diligently pursuing that funding so that we could launch at least five or six new sites of this intervention. Somewhat humorously, in the end, our very own funding agency decided they didn't want to fund the dissemination and implementation project.

I will share that we were doing those early comparative studies, which is better brain fitness or calendar training and then we decided to launch HABIT. We did it as a clinical program. Initially, we put it all backwards and started a clinical program before we'd fully shown the efficacy of it. As a clinical program, we could make it work financially. We could bill for a couple or three components of it and we could ask people to pay an out of pocket charge for the rest. Now, that has the downside, that perhaps some of the populations that could benefit for most might have some financial barriers to entry, but we were talking about a program with an out of pocket cost for a 10 day 50 hour intervention that was averaging like $700. So it was not a break the bank kind of intervention. The other components of it, since this is predominantly a Medicare population, were being paid for. One of the things that wasn't, of course, was yoga. But I've heard that yoga is starting to get paid for in cardiac rehab. And once Medicare starts paying for an intervention for one indication, it's hard for them to deny it to another indication. So I think other components of this will increasingly be paid for.

There is a way to stand this up as a program on clinical grounds. But the challenge often that places run into is just having the team because you need three or four people delivering the calendar training on a given day. Some of those people can also run the support groups, but you need yet another person to be running your computer lab for the BrainHQ stuff. So it takes three to four people to carry out this program if you run it the way we have historically. The other thing we often get questions about is why don't you just do this one at a time. I think you could bet again, as I think I said earlier, the power of group based intervention is substantial. If I had to choose between doing a group based program with fewer components or doing an individual program and giving all the components, I would choose the former over the latter.

John Bellone 44:51
Yeah, something about that group setting is just powerful.

Glenn Smith 44:54
Yeah.

Ryan Van Patten 44:55
It's more efficient to deliver an intervention to 10 people as opposed to two at a time. Most cost effective, obviously.

John Bellone 45:04
Do the participants remain in contact afterwards? I'd imagine maybe the caregivers?

Glenn Smith 45:10
It is an emotionally intense experience and you bond. Remember lots and lots of couples, and lots and lots - Just as an anecdote, it's just an N of 1, but one of the first 12 or so couples that went through the program - So it would have been in 2007-2008 time frame, the wife wrote me last year to let me know her husband had finally passed, and just talked about how the program had impacted them. That's having followed me from Minnesota to here in Florida, and hunted down my email, and just wanted me to know what that program had meant to them. So it really connects people to each other, and to their therapists in a lasting way. In fact, we've just launched a study built on the Peace of Mind platform where we're also going to get people back in for amyloid PET scans to answer the question, do outcomes differ based on whether you are amyloid positive or amyloid negative? We have no trouble getting people to agree to continue to interface with the research components of this because you build such a strong connection with them.

John Bellone 46:42
I'm curious, I practice in a group practice setting outpatient. For those of us neuropsychologists who don't have the infrastructure to have groups or these intensive interventions, is there anything that we can take away from your research that we can incorporate into our feedback recommendations? How can I implement this in my practice?

Glenn Smith 47:04
Yeah, well, one of the lessons from our early work, one of the things that we started cleverly, because we had to accumulate a cohort, we would encounter people and say, "We're going to run the program in January, but between now and then here's our calendar, here's a subscription, go do these things." And one of the humbling

lessons I tell my students all the time is, you need to consider that if you just write the recommendation in your report, but don't build a platform for people to engage, you're wasting the ink because it is so hard for people to initiate these kinds of health behavior changes on their own. When we retreat to our good training in psychology, we get that. Telling people to quit smoking is sort of ludicrous, right? So figuring out what are the platforms that help people engage in these activities is important. We should ask more of ourselves to go beyond just making the recommendation and walking away. Thinking about the Alzheimer's Association, what might they have? Are there OTs or speech therapists doing some form of this calendar training that we could partner with? We know that they understand what the challenges are here, and we're getting them lined up. I just really have started to push this notion that making the recommendations alone is not enough. How do we go one step more, even if we're not in the Mayo Clinic that has a big program running?

Ryan Van Patten 48:54

Yeah, as neuropsychologists, many of us think about ourselves as assessors and we do assessment very well and that's really important. There's no reason why we can't and shouldn't be interventionists as well. I think the future holds that for us to some extent that we will do more intervention. I know I want to do that. I want to do more than do an evaluation, tell someone what I found, give them a few recommendations and send them on their way. I'd love to help them improve whatever we found their weaknesses are.

John Bellone 49:27

Yeah, and even if we weren't [doing] intervention in the pure sense, we could in the feedback session, I like to incorporate some motivational interviewing techniques and build some of the platform that you were mentioning. I think the structure, because it's one thing to say, “Go exercise”, but it's another thing to talk through the specifics of when and where and for how long and what barriers would you anticipate encountering and setting up that structure I think is so necessary to behavior change.

Glenn Smith 49:57

Yeah. I think another thing we can do to be effective in talking especially to care partners is to help them understand, for the calendar training at least, the fundamental understanding of memory that matters that goes all the way back to HM. And that is that these folks who are having some significant problems with their declarative memory, still have perfectly intact procedural memory. When I'm talking

out in the community about this, I like to talk about a real lived experience that was part of the growth of this program. That was how, in addition to running HABIT, I would go out and consult in senior living settings and skilled care facilities about the little old grandma that was tearing up the place because of her dementia. I'd get into a senior living center, and often it was an assisted living center where the person was still pretty mild, go in to interview this person with early dementia and ask him, “How do you like living here?” And they would have no understanding. "Oh, I don't live here," because they couldn't encode that they'd moved. But then you'd say, “Well, okay, but let's go find your room" and they'd lead you right there. How is that possible? We know how it's possible to be able to wayfind without an understanding that you actually live there. That's what Sohlberg and Mateer's whole method is based on, is massive repetition until people start to automatically engage in this behavior of recording cues to help them compensate for their memory. So to just teach our caregivers that fundamental idea that if you really, really stridently engage in certain behavioral patterns, that build a habit, it's no accident, the program was called…

Ryan Van Patten 52:06
[laughs]

John Bellone 52:06
[laughs] I like that a lot.

Glenn Smith 52:08
If you build that habit, it's going to help. The habit of always having your phone on you, right? So that if you start to get really worse and wander, I can use the find me app to keep track of you or if you put your purse the same place every single day because you've been cued and mentored to do that until it so automatic that you're not losing your purse, those kinds of things is part of what HABIT is building.

The other thing I want to say about HABIT that's really important is to think about the psychology of all this. People who've just gotten a diagnosis of MCI, the person, their family, they're still muddled about what all of this means. They're muddled intellectually, but they're also muddled emotionally. I think one of the most powerful aspects of the HABIT journey is you watch people moving from confusion/denial to acceptance. They're able to make that move, in part, because you're giving them tools, which gives them hope. It's hard to reach acceptance unless you've got some capacity to have hope in spite of it. But that journey to acceptance is also the groundwork, as you're talking about motivational interviewing, that's also the

groundwork for getting people to do the hard work. Because if I disbelieve it or if I don't know exactly what it means, this MCI diagnosis, then I don't really have the foundation for why I want to work this hard. So that I think is a critical part of the process as well.

Ryan Van Patten 53:59
Yeah, well, thank you for talking through HABIT, what it looks like, the evidence for it, how it works, how we can implement it.

Glenn Smith 54:06
Thank you for asking about it.

Ryan Van Patten 54:07
It's very helpful. Yeah, for sure. In our remaining time, we'd like to shift gears and talk a little bit more about supervision, leadership, broadly in neuropsychology. I'm curious about your supervision style when you work with students. How do you approach that?

Glenn Smith 54:26
Well, I say this with a fair amount of sincerity.

Ryan Van Patten 54:32
Just a fair amount? [laughs]

Glenn Smith 54:33
Just a fair amount. I don't want to sound too kitschy, but I am so impressed with just the level of knowledge that our trainees bring to the field that I certainly didn't have at the same level of professional development. So some part of my supervision is from a sincere place of humility that these trainees in the field know so much more than I did back then and oftentimes so much more than I do now.

So I talk with the students a fair amount about a couple of things. One, you already alluded to, which is that I don't think in the long run, the profession of neuropsychology as an assessment only profession is viable. There's just going to be too many advances in technology and other areas, that’s going to at least shift the way in which we have to think about assessment. But adding intervention is an important part of professionally remaining viable in the long run. So I spend a fair amount of time talking with students about that. The other thing that's an obsession

right now is getting us all to think about access. It's interesting that I've been on this thing called the APA Clinical Practice Guideline Advisory Steering Committee. Somehow I did something wrong and got named to this APA committee. I say that, of course, tongue in cheek, because it's been a privilege and an honor. But on that committee, we're working with various groups that are issuing clinical practice guidelines on behalf of the APA. So I have a chance to interact with people like Jared Skillings, who's the head of the Practice Director at APA now. And when last I was in a meeting with him, he was talking about this problem of access. It really feels to me like we've won the war in that the health professions now really understand across psychology generally, including neuropsychology, what we have to offer. They understand that a lot of the problems left in health care are chronic problems, and lifestyle modification, behavioral management strategies are critical to a lot of the populations that are left. As a consequence, I don't know about you guys, but we're overwhelmed with demand for our clinical services. So you have to start to ask the question, if I'm seeing one patient today, and my neurology colleagues are seeing 16 a day, half of which need my services, that means we have a ratio here that's unsustainable. So thinking about how we offer high value services, in the most efficient way, is part of what I talk to my students about these days. I don't know if you guys - we're in an EMR system where it'll pull the medications and it'll pull the history, and yet I find the students enumerating the entire medication list and the entire history in their report and kind of go, “Why are you putting this here in the text when it's right there on the computer screen? One block above this? How is that efficient practice?” That's some of what I find myself talking with students about.

Ryan Van Patten 58:10

Yeah, we spoke with Jacobus Donders about shortening neuropsych reports and writing them in an efficient way. He had a lot of words of wisdom.

John Bellone 58:18

And then Bob Bilder about shortening the neuropsych batteries so that we can see more people.

Ryan Van Patten 58:24

You mentioned in an offline email exchange that we have a few moles in your department. I'm going to out them right now - this is Leslie Gaynor and Charles Moreno who help us with NavNeuro. They mentioned to us that something else that you talk to your trainees about is that you are a *clinical* neuropsychologist, not a clinical *neuro* psychologist.

Glenn Smith 58:48

A slight modification. What I say is I'm a clinical neuro *psychologist*. I believe that in our field, that's a important dimension that some people are fantastic clinical *neuro* psychologist, and some people are good clinical neuropsychologists. Difference being - I so admire, right around me on my faculty here, I have these people that are brilliant about functional neuroanatomy and far smarter than I'll ever be in those areas and really understand pathways in the brain and the syndromes that associate with them. That's a really important part of our profession and the advancement of our knowledge. On the other hand, as we've talked about for quite a bit in this hour, to think about quality of life and what are the dimensions of functioning that matter most to patients and how do we help people along this journey to acceptance. There's no necessary neuroanatomy invoked in those discussions and yet, it's an important part of who we are, as neuropsychologists, to know how to address those kinds of issues as well. So I just try and get my trainees to reflect on what's the balance between neuro in their skill set and psych in their skill set, to be sure that they are landing in a place that's going to benefit them most given what they want to do.

Ryan Van Patten 1:00:34

Right.

John Bellone 1:00:35

One other unique topic we wanted to talk to you about was that Leslie and Charles let us know you were recently a member of a department panel discussion on the concept of failure in professional lives. Failure is an especially hard topic to discuss in academic arenas where it might impede promotion and grant success. And none of us want to fail at anything.

Ryan Van Patten 1:00:59

We're perfectionists.

John Bellone 1:01:00

Right. Yeah, definitely. I mean, that's something that got us through our grad school and into our career. So why do you think it's important to discuss failure openly?

Glenn Smith 1:01:11

Yeah, it's funny because I now get tagged to do this talk around the University of Florida. I think someday people will know me as Dr. Failure or something like that.

Ryan Van Patten 1:01:23
[laughs] The failure guy.

Glenn Smith 1:01:24
Yes, failure guy.

John Bellone 1:01:26
That's what Ryan's already known for. So, you can take that. [laughs]

Glenn Smith 1:01:30
Failure and rejection. Another great opportunity I've had is, at Mayo, I got to be in charge of this program that was called the Clinical and Translational Science Center's KL2 program. It's a career development program that was developed out of NIH especially because they recognize that the MD researcher is becoming a very scarce commodity. They're trying to figure out how we get medically trained people to be better scientists. And lo and behold, it turns out that our good old scientist-practitioner model in psychology is something that medicine is beginning to realize the wisdom of and try and emulate. So I would be engaged with these medical students, residents all the way up to junior faculty. And I was just amazed at how little these people had ever experienced failure. How little anyone had ever said to them, “No, this isn't good enough. Rewrite it.” Or, “This idea seems silly if you think about it this way.” They just didn't have that experience. And then they started to try and do research, which is all about critiquing each other's ideas, right?

It's constant criticism. And so many of them would then say, “I don't need this. I'll just go see more patients.” And as a clinical discipline, we're also prone to having some people have that experience. So I think it's just really important that we reflect on that notion that it's part and parcel of being an academic, not only to experience criticism and rejection, but wise people actively seek it out. They say, “Tell me what's wrong with these ideas.” Because once they do, and once they can then defend or improve upon those ideas, they're going to have greater success. So I think you have to develop that thick skin to succeed and persist.

I like to tell this story about my myriad failures. I didn't get into graduate school the first time I tried. When I first applied to the postdoc at Mayo I didn't get it. It seems like I applied to internship at the University of Florida and was turned away. So the only thing I was good at doing was persisting, and ultimately that has paid some dividends. I just like trainees and students to reflect on that. Just persist. If you're good and just persist, eventually. I failed the board exam the first time I tried to take it and then went on to have the opportunity to lead the board exam process. So it's

important, I think, that people understand failure comes with being in this profession and especially in academics, and just embrace it. Actually seek it out and it'll be to your benefit.

John Bellone 1:04:50
Gosh, my anxiety just spiked because I took the board exam yesterday. [laughs]

Glenn Smith 1:04:55
[laughs]

John Bellone 1:05:01
I'm waiting to get my results back.

Ryan Van Patten 1:05:03
So, actually, Glenn, we really appreciate you sharing this, saying these things. I think the problem, part of the problem with failure and anxiety is that no one talks about it. Everyone has experienced that to some extent, but we don't hear other people talk about it. So we assume everyone else has been fully successful and has never failed the EPPP or the board exam or got into internship or grad school right away. Because we don't hear different, so "It must just be me. I am the fly in the ointment. I don't belong here."

Glenn Smith 1:05:37
Yeah, no. We put together this panel and we have three specialties here at the University of Florida, peds child, health, and neuropsych. And we got faculty from each area to sit on the panel. It's exactly as you say, almost everybody has their story. I think it's important that we share those and normalize it. If you do normalize it, I think a lot more people are going to hang in there and persist and realize that, in some ways, it's not just an uncomfortable experience, but it's a growth experience. And you get better from it.

Ryan Van Patten 1:06:22
Yeah, I couldn't agree more. That's great advice. So we've appreciated all the advice thus far. Before we finish today, we like to ask all of our guests a few bonus questions. So these are not specific to HABIT or MCI. These are about the field of neuropsychology broadly. If there's one thing you can improve about the field of neuropsych, what would you focus on?

Glenn Smith 1:06:46

Yeah, that's a great question. I think I would cycle back to that conversation we were having earlier about access and efficiency. Just really coming to recognize the healthy tension that exists between being truly comprehensive and thorough on the one hand, and the cost that that creates to the next patient in line having access to us. I think we've really got to grapple with that. We're part, through Russ Bauer, Bob Bilder's initiative in terms of the neuropsych testing, and how are we going to expedite that. Recognizing that we may - I've long been a bit of a skeptic about technology based approaches to assessment, but maybe we need to flip that on its head and really embrace those and figure out how that benefits us in terms of disseminating access to our skill sets even more. I think that's the key challenge for the next generation. Because, as I say, people really want what we have to offer now and because of that, there's just not enough of us right now. We need to make ourselves more available even as we endeavor to train even more of us. I think that's the real key.

John Bellone 1:08:10

Yeah. You answered our second bonus question already, which is some advice you would have for trainees - becoming more interventionalists, persisting, obviously. Was there anything else you wanted to add?

Glenn Smith 1:08:24

I think when you fed me the questions early, one thing that caught my attention was a question about something a mentor, a professor, said to me early in my career. So I just really wanted to say, explain to the trainees out there that when I finished my dissertation, it was a hot mess. It was just a piece of junk. And fortuitously, one of the members of my committee said to me, "Glenn, we don't expect your dissertation to be the best research you'll do in your career." And that really mattered to me. It made me recognize, "Yeah, this is my first real independent research, not my last one." I think I'd have been much more discouraged about my life as a researcher if he hadn't put it in that context. To really realize that if you're persistent and manage to find good collaborators and good settings and everything comes together, even if it doesn't come together perfectly, you'll still grow and develop. And hopefully, the best research you do in your career will be at the end of your career, not at the beginning of it. I just really take that to heart. If you're just starting out, again, don't hold yourself to a standard that's not really attainable for your level of professional development.

John Bellone 1:09:53
Yeah. Glad you said that. It's great advice.

Ryan Van Patten 1:09:56
Well, thank you so much, Glenn, for the time.

Glenn Smith 1:09:58
My pleasure. Thanks for inviting me.

Ryan Van Patten 1:10:00
Yeah. It's been great to have this conversation. We'll all benefit from it.

Glenn Smith 1:10:03
Good luck with the program. It's fantastic.

John Bellone 1:10:06
Appreciate it. All right. Take care.

Glenn Smith 1:10:08
Bye.

John Bellone 1:10:09
And that's it for today's episode. Thanks so much for listening, and join us next time as we continue to navigate the brain and behavior.

Exit Music 1:10:17

John Bellone 1:10:41

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Ryan Van Patten 1:10:52

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