50| Non-CNS Cancer and Cognition – With Dr. Mike Parson

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NAVIGATING NEUROPSYCHOLOGY

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Speakers: Mike Parsons, 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, brought to you by INS. I'm John Bellone...

Ryan Van Patten 00:25
...and I'm Ryan Van Patten. Today we bring you our conversation with Dr. Michael Parsons on non-CNS cancer and cognition. Mike is a board certified clinical

neuropsychologist at Harvard and Massachusetts General Hospital, and he has over 10 years of research and clinical experience in cancer and cognition. Neuropsychologists often spend their time thinking about neurological and psychiatric conditions, and appropriately so, but systemic and non-central nervous system diseases such as cancer can have major impacts on thinking and mood. So we have a lot to offer in this corner of the medical world as well.

John Bellone 01:04
Two quick notes before we get started. First, several more NavNeuro episodes were recently made available for CE credits through our partners at INS. So we encourage you to check out those options. Just go to navneuro.com/ins.

And second, we recorded this episode back in December of 2019. So you'll hear a reference to the upcoming 2020 INS and ICCTF meeting, which has obviously already happened, so keep that in mind. The ICCTF is the International Cognition and Cancer Task Force, which we discussed with Mike. If you liked this episode, we'd encourage you to check out their website at ICCTF.com.

And now we give you our conversation with Mike.

Transition Music 01:52

John Bellone 02:01
So, Mike, welcome to NavNeuro. We're really excited to have you.

Mike Parsons 02:04
Thank you guys for having me. It's a pleasure to get to have a conversation about this stuff.

John Bellone 02:08


Sure. Yeah, it's gonna be fun. We've only really been aware of the potential for cognitive changes from cancer-related treatments for a couple decades now, right? That's my understanding. Can you briefly tell us about the history of scientific investigation into cognition and cancer?

Mike Parsons 02:26

Sure. I think it's probably fair to say the past couple of decades, that's reasonably accurate. The question of whether or not cancer and cancer-related treatments had affected cognition really was first brought up in some more case-based studies as early as the 1980s or 1990 or so. But it was really in the 1990s that neuropsychology and neurology started to gain traction with their belief that cognitive symptoms were a common consequence of cancer therapy, and sometimes even cancer itself. The main drivers behind that movement really have to be credited to the group of neuropsychologists at MD Anderson Cancer Center. Christina Meyers was the leader of that program when they first really developed routine methods of evaluating cognition in the context of cancer, and primarily that took place in patients with brain tumors. But as their research gained momentum and acceptance within the oncology world, the studies branched out to really delve into non-brain cancers. Most of the early studies were done in patients with breast cancer, typically younger women often in a phase of life where high levels of cognitive functioning made a critical difference in their day to day lives - work and raising family and so forth. The complaints and concerns from the point of view of the patients became more and more prominent. There were some early studies in the early 2000s that were the first to really demonstrate, with pretty rigorous methodological approaches, that cognitive symptoms and changes were occurring in these women with breast cancer. Those early studies, including some from Christina Meyers and then Jeff Wefle, who took over management of that program, were the ones that really set the stage for neuropsychology being an important player in the care of patients with cancer.

Ryan Van Patten 04:55

Really interesting. I want to get into more about the topic of breast cancer and why that may be a model for studying cognition in cancer. But before we get there, I wanted to touch on the term “chemo brain” because I've heard it so many times. [laughs] My understanding is that it has fallen out of favor because many cancer patients receive multi-modality treatment and each treatment type as well as the disease itself might impact cognition. So with that in mind, a broader term that is sometimes used is “cancer and cancer treatment-associated cognitive change”.

John Bellone 05:31

A mouthful. [laughs]

Mike Parsons 05:32

Yeah.

Ryan Van Patten 05:33
Yeah. What terminology do you prefer?

Mike Parsons 05:38
There's two sides of the coin to the term chemo brain. On the one side, as you pointed out, the term implies that all cognitive symptoms in cancer emanate from chemotherapy, which we now know it's not entirely true. So it's somewhat inaccurate. That's where the term cancer-related cognitive impairment really came from, and that is somewhat more accurate. It has the limitation perhaps of being not as catchy and easy to use in a sentence, but may be more scientifically accurate. So, many people favor using that term.

On the other side of the coin is the argument that chemo brain is a problem that was brought to light by patients. Patients confronting their doctors and pointing out over and over again, oftentimes in the face of some ridicule or at least dismissal, that they were having this problem. The term is meaningful to patients. It was developed by patients, and it's understandable to patients. We, as the scientific community, should not necessarily hijack the terminology that patients developed to try to talk about things more accurately. Among those of us who work in this area, we have this conversation periodically. My general feeling is I don't have a problem with the term chemo brain and use it interchangeably with something like cancer-related cognitive impairment. When I write a paper, I'll use the ladder term. But I'm not going to get too up in arms about the terminology and try to alter it within the conversations that I have with patients and their families, just out of respect for their experience and recognizing what they're trying to deal with.

Ryan Van Patten 07:35

But when you're using it clinically with patients, you're understanding and communicating that - you're saying chemo brain, but it may be more than just the chemo that is causing the cognitive changes, correct?

Mike Parsons 07:49

That is true. That is true. Though, I would say that, at least based on the sort of effect size that we can see at this point, to the extent that cancer itself affects cognition, for the most part, it tends to be a smaller and much subtler effect than the chemotherapy effects themselves.

Ryan Van Patten 08:13
Interesting.

Mike Parsons 08:14

I did have one patient recently who came here to see me for an evaluation because she had read somewhere that even though she didn't have chemotherapy for her cancer, she had surgery only, she had read that cancer itself can cause cognitive problems. And, you know, I had to try to explain to her that the size of the cognitive changes we've been able to measure as a side effect of cancer itself are quite small in general. If that average effect size were taking place in an individual, the likelihood is they'd be hard pressed to notice it and we'd be hard pressed to measure it with standard neuropsychological evaluation. So it's still, I think, a matter of some debate and a lot of questions about why the size of the cognitive effect in individual experiences varies greatly from one person to another. In other words, some people who are having chemotherapy-related side effects in cognition may have them to be quite significant, whereas others may have absolutely no changes whatsoever. That individual variability is not well understood at all.

Ryan Van Patten 09:25

Okay, this is all great. We're going to dive into more detail about mechanisms and what are the specific cognitive contributors comparing chemo, radiation, cancer itself, etc. Before we get there, you mentioned breast cancer and I've come across breast cancer as the primary model of non-CNS cancer in the cognitive literature. Can you talk about why it is that we use breast cancer as a model to understand cognition in cancer more broadly?

Mike Parsons 09:59

I think there are a combination of reasons. One of them has to do more with the availability factor, which I alluded to earlier. That is, many of the patients with breast cancer tend to be younger women who are in a phase of life where cognitive changes are really having a significant impact on their ability to function. There also tend to be, within the breast cancer world, over the past 10 to 20 years, a lot larger number of people have become good advocates for their own health. So, we have a disease that affects indiscriminately - people have a large range of education, health literacy, and so forth. They were not afraid to raise questions with their doctors and challenge their doctors, which brought this into the clinic. They're also a group of people, by and large, that are willing to volunteer for research projects and participate in ongoing research in a longitudinal way. So they've been a sample of convenience to some extent. It's also a very common disease within the world of cancer. So there's large numbers of these people dealing with these symptoms. So it made them a very easy to study group who were motivated and being affected by this problem.

Number two, there's been a huge range of treatments that have been applied to breast cancer depending on the specifics of the tumor type and the various molecular features of cancer. It has allowed a large volume of research to be conducted on a variety of different treatment models some of which include different chemotherapy agents, some of which include multiple chemotherapy agents, some of which include no chemotherapy. So you have the ability to have built-in control groups, for example, where you have some patients who are getting chemotherapy, some who are not, some are getting biopsy only, some are getting extensive surgery, some who are getting multi-agent treatment and so forth. So the volume of patients, the nature of the cognitive complaints, and their availability and willingness to participate in research has led them to be the largest, most frequently studied groups in the area.

Ryan Van Patten 12:22

This reminds me a little bit of sport concussion as a model to understand TBI more generally. They tend to be young and healthy and available, and we can study them more easily. It makes sense. My next question would be, to what extent do you think the research in breast cancer generalizes to all the other types of non-CNS cancer? Do we have any evidence one way or the other on that?

Mike Parsons 12:48

Well, I think that, in general, the effects of chemotherapy, a variety of different agents, seem to be pretty similar across cancer types and even across chemotherapy agents. So, for example, there may be different agents that are used to treat triple negative breast cancer from, say, non-small cell lung cancer, but they seem to operate very similarly in terms of their neurotoxic effects. And that's true not just in the way they affect cognition in people, but the way they affect neuronal cells in vitro or animal models. Basically, that literature has shown that most of these traditional chemotherapy agents have a pretty broad range of neurotoxic effects. They tend to be pretty similar from one to another. So in terms of the role that chemotherapy plays in causing cognitive problems, yes, the effects are pretty generalizable. There are features about the breast cancer population that are unique. Again, they're young, many of them tend to otherwise be pretty healthy. They're female, almost exclusively. So there are some limitations in terms of the way that information generalizes to different populations, say, the lung cancer population of older smokers who have a variety of other vascular risk factors, age-related factors, potential differences in socioeconomic status, and other demographic factors, as well as obviously different gender distribution. So the

effects of cancer therapy seem to be pretty uniform or similar, but the sort of characteristics of the soil, if you will, the individual on whom the seed is acting, are maybe a little bit different.

John Bellone 14:46

Do we have a sense of how common these cancer-related cognitive impairments are, both during treatment and also after treatment? My understanding is it's quite variable. I've seen anywhere from 15 to 70%. I'm also curious about this subset of people who do have cognitive impairment. Is there anything different about them?

Mike Parsons 15:08

I think you raise a good point that's a problem for the field. There's a huge range of variability in how frequent the incidents that we think cancer-related cognitive impairment occurs with. And most of that has to do with how you measure it, just like anything in mental health. Many of the studies where you'll see really high estimates of frequency use a method that basically asks people to rate their own cognition with a series of questionnaires. Sometimes they'll draw, say, two questions out of a larger quality of life questionnaire, two questions that have to do with cognition, and then rate the frequency of cognitive impairment within a population based on saying, "Well, 70% of people rated themselves as having cognitive problems on these two items on a questionnaire." That's very different than the more careful studies that use what we might think of as performance-based cognitive testing or objective neuropsychological measures. In general, when we use neuropsych based metrics to decide the proportion of people that are having cognitive impairment, we'll see ranges anywhere from 20 to 60% of people, depending on where you set your cut offs. So if you say, "Okay, well, I gave a battery of 10 tests. Anybody who scores one and a half standard deviations below the norm on any one of those tests, we're going to count that person as having a cognitive impairment." Then, just by statistics alone, you're going to have a pretty high rate of cognitive impairment, right? Most of the best studies which measure longitudinally do come up with a rate of somewhere around 15 to 25% of people experiencing cognitive symptoms at some point in their treatment. And a significant percentage of those seem to recover and improve after treatment is completed.

John Bellone 17:15

Okay. That was my next question, whether it's transient or more chronic. So some percentage of those, let's say 25% at the highest, those cognitive problems are going to go away entirely. But for the other subset, is it pretty persistent? Or is that also transient? After a year, let's say, post treatment?

Mike Parsons 17:35

Well, there's some of both. So, again, this literature is still struggling, I think, with a heterogeneity problem. I'll come back to that. But to answer your question, there's a proportion of people for whom these cognitive symptoms seem to abate and get better, I would say the majority. There's a proportion of people, the majority of the remainders for whom this problem seems to be persistent a year, two years, three years, even five years after treatment. Then there's a small percentage in whom there seems to be a worsening of cognitive function over time that we really don't understand. The issue of the heterogeneity problem is that, again, we're defining a neuropsychological problem by a symptom. That is probably akin to the post-concussive syndrome problem. Which is to say that when you ask people about the symptom, you're filtering your data through the lens of introspection. And we all know how good we are at that, right? Not very. So, I think that if you define your group at the start as based on people who have this complaint or concern, you're going to have a very heterogeneous group. Some of those people are undoubtedly experiencing the neurotoxicity of cancer therapy and are probably the ones we want to study. Others of those we know are having more of a psychological syndrome that might be related to the traumatic effects of dealing with cancer and the impact that has on their own view of their cognition. And there are some who are absolutely experiencing the same kind of thing we see in persistent post-concussive syndrome, in my opinion. Then others probably have something else going on. For instance, is there some interaction between chemotherapy agents and risk for dementia or other neurologic risk factors that we really don't understand very well yet?

John Bellone 19:49

I think the analogy to the post-concussive symptoms - in that population, we see a lot of poor sleep and fatigue and stress. Definitely people who are dealing with cancer have all that.

Mike Parsons 20:01

Absolutely, absolutely. I don't want to get us off track, but if you want to talk about some of the biological mechanisms that we do know play a role in the relationship between chemotherapy and cognition, I can give you a couple of examples of models that are being worked on now that probably will eventually subdivide this heterogeneous population into more disease-based or biologically-defined problems. But, right now, we're kind of all mixed together in the same big bag.

John Bellone 20:40
Are there sociodemographic - race, sex, education - differences in prevalence of cognitive impairment in cancer survivors?

Mike Parsons 20:49
I don't think we have good answers to that. It does overlap a little bit with the different disease models, as I was saying. I think it cuts two ways and the primary issues are education and cognitive reserve that come to mind for me, which is to say that people with a high level of education and high cognitive reserve tend to be more sensitive to subtle changes in their cognition. But at the same time, they also have that cognitive reserve to potentially overcome those issues. So I think it's both a risk factor and a protective factor for chemo brain, if you will. I'm not aware of any research looking at racial differences in the prevalence of this problem, but that is not to say that such research does not exist. It's not something that's on my radar, though.

Ryan Van Patten 21:50
So you've mentioned that this population of people with non-CNS cancer who undergo chemo and/or other treatments are heterogeneous, and there's a lot of work to be done. With that in mind, what can we say about the neurocognitive profiles, if anything, of people with cancer? Are there any patterns? Is it subcortical, as are most other medical conditions? Is there anything unique about the profile?

Mike Parsons 22:21
For the most part, most of the studies have shown that the deficits or changes that we see in cognitive function both during and after chemotherapy tend to be on tests of recent memory, attention, executive function, and processing speed. It's very much a diffuse, nonspecific pattern that feels subcortical, if you would. But it's not subcortical in the same way you would think of a small vessel dementia. Not dominated by slowed information processing speed, more dominated by executive and memory types of deficits. The pattern, I think, links to and has driven some of the thoughts about mechanism, which I suspect is where we're going next. So maybe I'll let you ask the next question. [laughs]

John Bellone 23:17
[laughs] Yep, you're right with us here. So let's talk about all the different mechanisms in more detail. We touched upon chemotherapy, there's also radiation, surgery, endocrine therapies, and the cancer itself. So maybe it's most helpful to start with chemotherapy in more depth. My initial understanding, and I'm interested

in your thoughts on this, obviously, is that most agents don't cross the blood brain barrier and so aren't necessarily going to cause direct effects to the brain but there are exceptions to that, right? There's intrathecal administration, like methotrexate is often administered intrathecally, which means it's going directly into the cerebral spinal fluid and gets direct access to the brain. Is that your understanding? Maybe we start there with what actually crosses the blood brain barrier and what are some of the specific mechanisms by which chemotherapy can cause some toxicity?

Mike Parsons 24:13
Yeah, absolutely. There are a few leading candidate mechanisms. And again, odds are that we'll ultimately determine that either different people are having different reactions that subdivide this group, or that potentially multiple factors are combining to cause the effects that we're seeing. One of the primary candidate mechanisms falls under the category of what we would call a cytokine hypothesis or, essentially, immune activation hypothesis. Where we know that many of the chemotherapy

agents increase blood concentrations of a variety of cytokines that we know to have cognitive and neural effects, things like TNF alpha, interleukin 6, and other similar cytokines that have been implicated in a variety of diseases. The mechanisms by which those cytokines influence cognition are pretty complex and probably require a semester's worth of a neuroscience course to really unpack them. But suffice to say that there are a number of ways in which these immune markers and immune chemicals interact with the central nervous system to influence the function of that system at multiple levels, including at the neural level itself interacting with neurotransmitters and at the level of demyelinating toxicities and so forth.

John Bellone 25:53
This is even for agents that don't cross the blood brain barrier?

Mike Parsons 25:56
Right. That is very relevant for chemotherapy agents that don't cross the blood brain barrier. It's very possible that the way these things are influencing the brain is not necessarily a direct toxicity, as you said, but rather mediated through these immune modulations that are caused by chemotherapy.

Now, a completely different hypothesis has come from a line of research that started in the petri dish and progressed through animal models and has now been demonstrated in humans as well, which is that many chemotherapy agents destroy what are known as oligodendrocyte precursor cells. These are essentially part of the neural stem cell population that tends to exist in a couple of key areas of the

brain, including the subventricular zone, in some of the periventricular areas of the white matter, the dentate gyrus. Those cells, in the past 10 to 15 years, have been demonstrated to play a key role in neuroplasticity, including in adults. When I went to graduate school, approximately 1000 years ago, we were taught that the adult human nervous system has no capacity for neural regeneration. You've got what you're got by your 20s and then it's just a straight downhill slide in terms of number of neurons after that. And although that's probably true for me, many other people seem to be able to generate neurons in a meaningful way throughout their adult life. And very elegant studies have now demonstrated that not only do those neurons develop, but they migrate and integrate into functional neural networks throughout adulthood - maybe play a role in learning, maybe play a role in recovery of function, and so forth. Chemotherapy agents devastate that population of cells. In some of the studies, 95% of those cells in animals seem to be destroyed by various chemotherapy agents. And, again, in very elegant translational research ways, it's been shown that those animals then have deficits in their ability to learn after this kind of intervention, and that not only does that cognitive problem persist, but in some animals it actually progresses. So that model is one that maybe lays a mechanism out for how cognitive symptoms might persist or even progress after treatment. Now you've undermined the brain's mechanism for plasticity, which just goes on to have accelerating effects as aging takes its toll.

John Bellone 28:48
That makes sense in terms of impacting memory, primarily because of the dentate gyrus. For listeners that don't know, that's part of the hippocampus and so very intricately involved in memory consolidation and new learning.

Mike Parsons 29:02
Exactly.

Ryan Van Patten 29:03
I have a quick follow up question on that, Mike. This idea that you just presented about how neurogenesis is potentially really impacted. A way to think about that: Chemotherapy tends to target rapidly dividing cells, right? That's what we're looking for, to target tumors that are rapidly dividing. Other types of cells are caught in the crossfire, hence, we lose our hair and the lining of the stomach causing nausea, vomiting, those types of side effects. Is that a similar mechanism here? Is it, like, because there's neurogenesis and there's actually new neurons being produced in the brain, there's this cellular target for chemotherapy that's meant for brain tumors

that are rapidly dividing, but it also hits neurons that are being produced. Is that why we think that's happening specifically to neurogenesis?

Mike Parsons 29:56

I think that's right on target. Although, again, that's a relatively new idea. We have neural cells dividing in the adult brain, you're exactly right. It's basically an off target effect of the therapy.

Ryan Van Patten 30:15

Okay.

John Bellone 30:16

And for agents that are introduced intrathecally, I would imagine that problem may be more prominent?

Mike Parsons 30:22

Intrathecal administration of methotrexate, as you mentioned, is probably the most commonly intrathecal used agent. It's a little bit of a mixed bag. So when you administer the agent intrathecally, it's usually done into the ventricle itself or into the cerebrospinal fluid through a lumbar access, like you would do with a lumbar puncture or a lumbar catheter. That agent does not penetrate very deeply into the nervous tissue around there. But it does induce some very focal injuries, which you can sometimes see on an MRI scan around, say, an intraventricular catheter. It seems to combine with other treatments, particularly brain irradiation, to accelerate some of the negative side effects of brain irradiation. That's usually taking place in people either who have a central nervous system brain tumor or who have a disease that is known to essentially be a very high risk to spread to the central nervous system where you would treat ahead of time, mostly lymphoma. But it's a little bit of a mixed bag with methotrexate, other than to say that high dose methotrexate does certainly carry significant risk of cognitive toxicity.

John Bellone 31:46

I see. I've heard that it's a similar mechanism to what Ryan brought up with radiation. That it also adversely targets the rapidly dividing cells more than other other types.

Mike Parsons 31:56
Absolutely. Basically, the goal of those treatments is to destroy DNA. And so anytime you have a cell dividing, where it's dependent on DNA replication to divide accurately, those are going to be the cells that are most severely affected.

John Bellone 32:13
I see. Okay.

Ryan Van Patten 32:15
Going back to chemotherapy, briefly, you've talked about it for several minutes. I'm wondering if we know anything about differential impacts on cognition of different chemotherapeutic agents. Are some worse than others in terms of cognitive functioning?

Mike Parsons 32:32
That's a common question. I think that it is so complex to keep up with the different chemotherapy agents. There was a nice demonstration in animal models and single cell preparations that demonstrated that almost all of the commonly used chemotherapy agents, this was in about 2009, had significant neurotoxicity. Since that time, there has been an explosion of different approaches to cancer therapy, many of which are the so-called targeted treatments - you know, very specific agents that are targeting a particular molecular pathway. And, ywe really don't know at this point the extent to which some of those agents may have less risk than the more traditional alkylating chemotherapy agents. That is, those agents that are designed to destroy DNA, we think they all do affect to some extent. The newer agents we're really just catching up with. Some of those [have] really specific and fascinating effects. Others are hopefully going to turn out to be much less toxic.

John Bellone 33:49
There's a dose response relationship, right? I've seen higher doses more adversely impact cognition.

Mike Parsons 33:59
Generally speaking, that's the case. I think that the caveat to that is, again, it seems to interact with individual differences in risk. We really don't understand why some individuals might be much more prone to develop problems than others. So that's an ongoing question.

John Bellone 34:22

Just to go back to radiation treatment really quick. For listeners who aren't aware, usually it's delivered in a fractionated dose rather than getting one giant dose of radiation. We give smaller doses over the course of days and weeks. My understanding is that this is meant to give healthy cells a chance to repair themselves. But, like you mentioned, radiation has some neurotoxicity as well, both during treatment and also late effects. Could you talk us through a little bit about the radiation effects?

Mike Parsons 34:52

Sure. I think it's important when you talk about radiation to divide the effects by the target of treatment. Many times, in cancer in the body, radiation will be delivered and targeted at the part of the body where the cancer is. So in breast cancer, lung cancer, that's going to be the chest area, etc. When it comes to cognitive side effects of radiation not delivered to the brain - radiation that's delivered to the body - there is the possibility of some subtle negative effects that probably act through the same kind of oxidative stress cytokine types of mechanisms I was talking about earlier.

On the other hand, when you deliver radiation to the brain itself, you're in a whole different ballpark of toxicity. So I think it's fair to say that radiation is much more damaging to the central nervous system than chemotherapy, if you just held them up against each other. When you deliver radiation to the brain, you run a higher risk of having cognitive toxicity than you do from having chemotherapy. Oftentimes, almost all the time, they're going to be combined, so you're getting both and the effects in some situations may be additive.

When it comes to the effects of radiation on the brain then, as you said, the delivery method tends to be this fractionated method where small doses are delivered, day after day after day to get to a total dose that the radiation oncologist know is effective at killing the cancer cells and trying to do the minimal damage to healthy cells. There are also other methods of trying to reduce radiation toxicity, such as targeting the radiation even within the brain. So when you're delivering it to a brain tumor or brain metastasis, you can try to shape the radiation field so as not to expose the whole brain.

John Bellone 37:02

This is better with proton types of deliveries or gamma knife, right? Where it's more concentrated.

Mike Parsons 37:08
That's correct. Right. So those methods are less generally toxic to the brain. But with radiation to the brain, there's a much greater likelihood of a long term and progressive effect on brain and cognition than there is with chemotherapy. So that is something you always have to be looking out for after brain radiation. Not everybody gets it, but most people will suffer some cognitive consequences eventually.

One of the more interesting advances in radiation was just presented at a conference I was at last week or two weeks ago, which is the use of what is called hippocampal avoidance radiation. So that's a method for delivering radiation to the whole brain, with the exception of the hippocampal region. They essentially create treatment cold areas, or holes, around the hippocampi bilaterally, primarily out of respect for both the role of the hippocampus in memory, and also those dividing cells that we just talked about, to try to minimize damage to the cells. And in large scale studies that were, again, coordinated through our colleagues at MD Anderson, it's been shown that there is a beneficial effect of hippocampal avoiding whole brain radiation, as compared with regular whole brain radiation, on tests like Hopkins Verbal Learning Test, for example, Trail Making, and so forth - shows fewer deficits. There's many questions there. But there are a lot of people putting their minds [together] to trying to come up with safer ways. Ultimately, coming up with better treatments for cancer that do not involve radiating the brain is going to be our best bet.

Ryan Van Patten 38:59
Right. So in this new technique, you have a seahorse shaped shadow, basically, that the radiation is not penetrating.

Mike Parsons 39:11
They're more like two big holes, one on either side. So I don't fully respect the hippocamp himself.

John Bellone 39:18
[laughs]

Ryan Van Patten 39:21
We mentioned early on that a lot of the literature we are using to inform this conversation reflects studies in breast cancer. I want to touch on other types of cancer and what we may know about differential cognitive effects in people who

have pancreatic, liver, kidney cancer. People are getting the same chemotherapy agents and/or non- brain radiation, we might see similar cognitive effects. Do we know of any differences in terms of the severity or persistence of cognitive impairment in different non-CNS types of cancer?

Mike Parsons 40:02

The main driving force behind cognitive symptoms in the range of non-CNS cancers has to do with two factors. Number one, the likelihood that non-CNS cancer will send metastases to the brain, which really tends to override the cancer related cognitive impairments. And number two, the degree of illness that people suffer in the context of that cancer. Again, for the cancer and cognition literature to keep up with the changes in cancer, we're a little bit behind because things change so quickly and it takes a long time to do our studies. We just don't know how outcomes are going to be yet for people with these various cancer types and newer treatments. In general, for those other cancer types, such as pancreatic or sarcomas or liver cancer, we know that cognitive symptoms can and do occur, and the rates seem to be generally similar to what we see in breast cancer. But that's also because most of the studies that have been done in those groups have been done using similar agents. In many of those cancers, things are really changing in the treatments that are being used. Only time will tell whether we can start to separate out the effects of the cancer itself from the cancer therapy. But I think, as a general rule, if you think of, say, liver cancer patients as being much much sicker and having a variety of other blood metabolic related issues to deal with that breast cancer patients often don't, they're likely to have more cognitive symptoms as a consequence of those other illness related factors.

John Bellone 41:54

You mentioned metastases just a second ago, maybe we can talk quickly about this. So the idea is that the tumor can originate in the liver or another organ and metastasize or spread to the brain. This is more common with certain types of cancers. I've read that breast and colon and lung and skin are the four main primary tumors that result in brain metastases. And I read that about a third of people with non-CNS cancer end up having some brain metastases. Can you talk a little bit about this? I think it's a pretty fascinating area.

Mike Parsons 42:29

Yeah, you're on target there with the types of cancer that most commonly spread to the brain - small cell lung cancer is the most common, breast and melanoma after that, and then some of the others do with smaller degrees of frequency. But in lung

cancers, there are subtypes of lung cancer that have about a 50% likelihood of developing brain metastases - very high frequency. In those patients, it used to be the case that the oncologist would deliver what was called prophylactic cranial radiation, where they would essentially irradiate the brain and could reduce the frequency of brain metastases in that subtype of lung cancer from 50 or 60% down to about 10 to 12%. The consequence, though, is that now you have whole brain radiation. Over time, the severity of long term effects from that has been determined to outweigh the risk of waiting to see if the metastases do develop and then treating them with a more focal type of radiation. So they really don't do prophylactic cranial radiation anymore. In breast cancer, again, the rate depends a lot on the specific molecular subtype of the cancer, but rates anywhere from 10 to 20% depending on those subtypes. In metastatic melanoma, I think about 10 to 15% of people with melanoma will develop brain metastases during the course of their illness. So, when you put all of those different subtypes together, and factor in the fact that those cancers - breast cancer, lung cancer, melanoma - are much more common than, say, primary brain tumors. The reality is that the majority of people with brain tumors have them of metastatic origin, as opposed to primary brain tumors like glioma, glioblastoma, meningioma. So there are more people with brain metastases from systemic cancer than primary brain tumors.

John Bellone 44:35
Right. And we're talking about adults, right?

Ryan Van Patten 44:36
Yeah, it differs in children. Primary brain tumors are common, right?

John Bellone 44:40
Yeah.

Mike Parsons 44:41
That is correct.

John Bellone 44:42

Maybe we can also talk about another potential problem, which is paraneoplastic syndrome, which, in my understanding, is pretty rare, like less than 5% of patients. But this is potentially more severe, right?

Mike Parsons 44:55

Yeah. So paraneoplastic syndrome really falls under the umbrella of the autoimmune encephalopathies. Essentially, what's happening in paraneoplastic syndrome is that the immune system has detected the cancer, which is its own category of issues - the relationship between immunity and cancer. The immune cells that are attacking cancer are also having off-target effects on structures within the brain, usually in the hippocampus or cerebellum. People who develop paraneoplastic syndrome will often develop a pretty acute encephalopathy type of picture, even very profound anterograde amnesia and so forth. The goal in those cases is to identify what the abnormal immune cell is, identify the target that's triggering that antibody, and then remove the target. Once the target, i.e. the tumor, is gone usually the immune system will ramp itself down and stop attacking the brain. In other conditions where you can't find the target then you need to administer immunosuppressant drugs, which will suppress the reaction and prevent or slow the impact of that autoimmune encephalopathy on the brain. Sometimes the treatment strategy is, "Okay, we'll suppress the immune system because the immune system has effectively reduced the tumor to a size where we can't find it." So you do immunosuppression, the tumor grows, then you remove the tumor. And then hopefully, if you're able to do that effectively, you can prevent the paraneoplastic syndrome.

John Bellone 46:39

Pretty complicated, it sounds like.

Ryan Van Patten 46:41

Yeah, that's really, really interesting. So, so far, we've been talking mostly about the impact of cancer and cancer treatments on cognition. So that's been the directionality of the questions we've been asking you. Another potential way that we can arrive at people who have both cancer and cognition is through shared mechanisms, right? I've read a little bit about the potential for poor DNA repair mechanisms as being a potential shared factor or cause of both risk for cancer and poor cognitive outcomes. Can you speak to what we know about this?

Mike Parsons 47:24

I think that is a really evolving, new topic in the area. I think that right now it's more at the point of speculation than a great deal of data on that as a mechanism. But the understanding of molecular and genetic factors in tumor development has just exploded over the past 5 to 10 years. In neuroscience, we're really just beginning to tap into the degree of complexity that's involved in those various subtypes and

molecular factors in cognition. So I think that's an evolving area that hopefully over the next several years we'll understand more about. But at this point, I'm not sure that we have much data to speak of other than some driving theories.

Ryan Van Patten 48:19

Well, in the meantime, it's something interesting for us to think about. It's always easy to take cognition and disease X and see an association. And then we think, "Oh, disease X causes poor cognition," right? I try to think deeper and think about other options. Like, could there be a third variable that's causing both? Is [there] a more complex pathway? So I'll be interested to see what the data say in the future moving forward.

Mike Parsons 48:50

Those kinds of genetic studies are so complicated to do because you need such huge numbers of people in order to really - say, a full GWAS type of study, if that's what you're talking about, where you can basically sift through all the possible genetic polymorphisms and identify patterns. That kind of work has obviously led us to understand some things better about, say, the relationship of epilepsy and cognition. Those kinds of studies are ongoing and I think we will see some relationships there, but I'm not sure what those are going to be at this point.

Ryan Van Patten 49:31

In a moment, we're going to move into more clinical neuropsychology of cancer and cognition. I have one more question about mechanisms and different types of cancer first. This is pretty selective. We haven't talked about prostate cancer yet, but I read a little bit about anti-androgen deprivation therapy and cognition in patients who have prostate cancer. Can you speak to this topic?

Mike Parsons 49:56

This is an interesting topic. It's, I think, stillone that's gotten some play, but there's a lot to it and I'm not necessarily sure that we have a good sense of the answers yet. But, basically, the early studies looking at this androgen deprivation therapy used [it] as a mechanism to control prostate cancer in older men [and] found some relationships between the administration of the androgen deprivation therapy and changes in tests of visuospatial function or spatial memory. And given that one of the few or maybe the only way in which males have ever tested superior to females has been in spatial skills, there was a sense of synchronicity there. That you're suppressing male hormones, maybe that has a driving role in this slight visuospatial cognitive advantage that males have over females, and so forth. And I think that

there are some reasons to believe that that could be the case. But the studies that have been done so far have been relatively small and a little speculative. There are a number of studies that are getting geared up that will have a truly multicenter - hundreds and hundreds of patients followed over time - looking at the interaction between androgen deprivation therapy, specific cognitive function, and more interestingly I think, dementia risk in these men. The interaction of androgens with other dementia risk factors. And we'll know in probably the next 5 to 10 years whether those early signals that we saw in these smaller studies really pan out to be the case once we have more population representative data.

John Bellone 52:06
Just to clarify this is different from brachytherapy, which is more common?

Mike Parsons 52:11
Yes. So the brachytherapy will be using radiation containing seeds, which are left in the prostate region to deliver a small dose of radiation over a long period of time and damage the tumor cells. Androgen deprivation therapy is using a hormone to reduce androgen levels throughout the bloodstream and also undermine one of the mechanisms by which prostate cancer grows.

John Bellone 52:38
Okay. Well, I think we've thoroughly vetted the mechanism. [laughs]

Ryan Van Patten 52:42
For a couple of psychologists. [laughs]

Mike Parsons 52:45
Yeah, we're probably way out on a limb.

John Bellone 52:48
So let's talk about the clinical neuropsych piece a little bit. Let's start with what type of referral questions do you usually get? What types of patients do you usually see in a clinical setting?

Ryan Van Patten 52:59
In these non-CNS cancers...

John Bellone 53:00
Non-CNS specifically, right.

Mike Parsons 53:02
Sure. Most of the patients that I see for clinical neuropsych evals come through two routes. One, either referred directly from their oncologist, usually after they've completed some sequence of treatment for their cancer, usually involving chemotherapy. When the patient has mentioned cognitive problems to the oncologist enough times, after the treatment is over, that the oncologist says, "Well, we probably better look into this." By now, many of the oncologists are aware of and receptive, acknowledging the notion that cognitive problems occur during cancer therapy. But they also see in their clinical practice that most people who experience those get better afterwards and stop complaining of it - to their oncologists, at least. So they let that period usually pass and when a patient keeps complaining of it, then they send them to me.

The other place the referrals come to for me is through our group here at MGH, which is a program that is specifically dedicated to neurotoxicity of cancer therapy, which is headed up by a neurologist in the neuro-oncology department. And he is really looking for specific patterns and tendencies that look much more suspicious from a neurological point of view. The story here is one of somebody who got through their cancer therapy and then had some pretty negative outcome that either progressively worsened or persisted in a way that really seems neurologically abnormal. So those patients tend to be neurologically more complicated and potentially more specific in that heterogeneity problem we talked about earlier.

Ryan Van Patten 54:54
When you receive referrals from oncologists, obviously they're not asking you for a differential diagnosis so much. I'm assuming they're asking you for characterizing cognitive strengths and weaknesses, providing recommendations for vocational outcomes, other things like that. Is that right? Anything I'm missing?

Mike Parsons 55:12
Those are all important parts of it. I would say, though, there is a way in which they're still sort of asking for the differential diagnosis because I think, as we were discussing before, the psychological effects of cancer and the interaction between depression, anxiety, trauma, or other psychological factors, broadly speaking, and cognition is playing a role. That's an open question for the oncologist. They want to know, does this look really suspicious, neurological worrisome? Or does this look

like someone who is struggling with an adjustment-related issue in one way or another? And which avenue should we go down here, treatment wise?

Ryan Van Patten 55:55
I see.

Mike Parsons 55:56
So that is definitely a part of the evaluation. But then, in general, if I evaluate someone and try to participate in their care, it does have a lot to do with suggestions for management of the cognitive or other symptoms that can help improve their quality of life.

John Bellone 56:16
Do you feel the need to parse out the effects of chemotherapy from radiation from the cancer itself? I mean, not that we can do that.

Ryan Van Patten 56:23
Can you?

John Bellone 56:24
But sometimes I feel like the oncologist - because I also get some of these referrals - is somewhat expecting... Or, I don't know, sometimes they feel it would be helpful.

Mike Parsons 56:33
I think, as a general rule, when we're talking about a cancer that has not affected the CNS directly, it is really difficult to do that kind of teasing out. I think the thing that is more commonly something I can get a handle on is the relationship between the chemotherapy treatment or the cancer and chemotherapy combined with age. Where sometimes, because cancers are more common in older people, what we're seeing is an interaction between age-related changes, or maybe even pathological conditions associated with aging, such as vascular dementia, Alzheimer's disease, whatever, and the cancer and its treatment. So those things I feel more comfortable teasing apart, but I try not to get into, you know, what percentage of this is cancer, what percentage is chemotherapy, and so forth.

Ryan Van Patten 57:30
Sure.

John Bellone 57:30
You just list them in the etiology section? I usually say there could be a contribution of chemotherapy or radiation. Is that how you usually write the report?

Mike Parsons 57:41
I lost you there. Your question broke up a bit. Sorry.

John Bellone 57:45
Oh, yeah. In the etiology section, do usually just mention the possibilities? Like that, you know, there could be a contribution from chemotherapy and radiation and the location of the cancer?

Mike Parsons 57:57
Yeah. I mean, usually what I'll do is lump that together under the heading of neurotoxicity of cancer and cancer therapy. That, yes, this looks to be a pattern that is very typical of cognitive side effects of cancer and cancer therapy. And, you know, not try to unpack it any more than that because I just don't believe our clinical tests have the specificity to do that.

John Bellone 58:23
Right. And then you'll separately, I'm assuming, have a section about sleep and fatigue and maybe depression or stress?

Mike Parsons 58:31
Absolutely. I mean, those are often factors. And,again, I think there is a subset of individuals who are in this situation that are dealing very much with a syndrome that we can analogize to post-concussive syndrome. In the sense that they've had a traumatic experience, they go into it with now an expectation of cognitive symptoms as a real possibility and then there are expectancy effects and the difficulty we all have in comparing our current cognitive function to how we used to function and all that's entailed in that leads them to have a negative view of their own cognition when that may not be warranted.

John Bellone 59:19
I was thinking about the "good old days" phenomenon, right, where you think you did so much better before.

Mike Parsons 59:24
Right, right.

Ryan Van Patten 59:25
The analogy to PCS is really helpful. I like drawing that. To back up a little bit in terms of a clinical neuropsych eval, how do you approach gathering information on cancer from records review and clinical interview with a patient and their family?

Mike Parsons 59:42
I'm in an advantageous position. Most of my patients come from within the hospital system I work in, so I usually have the cancer related information including the treatment available to me in the medical record. It makes life a lot easier because the regimens are incredibly complex. Most patients, normal human beings, would not be able to tell you reliably what agents they had, when, and how many cycles and all that stuff. Not that that necessarily has a direct implication on their performance anyway, but it is helpful to have a sense of how extensive and prolonged their chemotherapy treatment was. So I gather that from the medical record. And then, obviously, just like any neuropsychological evaluation, balancing both the perspective of the individual who's experiencing the problems with observations from collateral sources is extremely important in getting a feel for what the nature of these changes and symptoms might be.

Ryan Van Patten 1:00:47
And then moving forward, what are some considerations regarding the neuropsych test battery? Is there anything specific to cancer? Or does your test battery look very similar to a battery you might use in another neuro-medical condition?

Mike Parsons 1:01:02
I think it's pretty broad and similar in many senses to what you would use for any relatively subtle and diffused kinds of cognitive problem. So, obviously, it's going to be heavy on executive function, memory, and processing speed. It's going to be tailored to the individual's expected level of functioning. And it's going to be broad enough to detect anything that might be more focal or lateralized. Even though you wouldn't necessarily expect that as a side effect of chemotherapy, you're obviously looking for other things as well, just in case. So it tends to be pretty broad. I flex it slightly based on things like the patient's age and education level, whether I'm going to use, say, something like the CVLT for a memory list versus the HVLT, you know, might depend on some of those factors. But, in general, you're using a pretty standard battery. There is one resource that might be of interest. There is a battery

that has been recommended for research in non-CNS cancer. There's a group called the International Cancer and Cognition Task Force, which has published two guidelines papers. One about the cognitive assessment that should be used in cancer and cognition research, and the other about the brain imaging sequences that should be used in that research. Both of those papers are freely available. If you just search for International Cancer and Cognition Task Force recommendations, you'll find them.

John Bellone 1:02:48
We'll link to them in the show notes as well so listeners can go to them directly.

Mike Parsons 1:02:52
That'd be great. Their battery includes all of the usual suspects. They define a core battery that they will want you to use in any research study of this. And that gives you a sense of like, "Okay, well, what do I need to include in my clinical battery at a minimum to make sure I'm being sensitive to the kind of issues we're concerned about?"

John Bellone 1:03:11
In terms of the neuropsych report and feedback process, is there anything unique in this population?

Mike Parsons 1:03:17
I think that it's always helpful in this population to connect with the concept of cancer survivorship. So I think a unique factor about cancer patients, not completely unique, but different from other general neuropsych evals, perhaps, is that the experience for many people of having, being treated for, and surviving cancer is a life changing experience. It may really define someone's identity or change their identity as a part of going through that. As a neuropsychologist, developing an understanding of the kind of landscape of cancer survivorship resources and the driving thought processes behind adapting to life changes after cancer is a useful rubric to fit the neuropsychology evaluation into. So in other words, when you're doing feedback with a patient who's dealing with cancer and cognitive problems in the context of their cancer survivorship, knowing what resources they have already available to them, using some of the language that cancer survivorship includes, and then acknowledging the traumatic experience that they've been through becomes part of that process. Otherwise, I think interpreting and giving feedback on your neuropsych eval is pretty much like it would be for any other condition. You're going to interpret the patterns. You're going

to talk about their performance relative to norms, relative to your expectations for them. And [provide] feedback about how that fits into their daily experience of symptoms. But doing all that within the framework of cancer survivorship is, I think, the thing that's an added skill set. If you see a lot of cancer patients, it's worth putting in some time and continuing education to really get a feel for what that world is all about.

John Bellone 1:05:18
I completely agree. There's so many resources available and we'll list some of those in the show notes as well. The support groups that are available for cancer survivors is great to see. Do you have any specific recommendations on how to mitigate some of the effects of cancer treatment on cognition? Like during the feedback session, does that come up?

Mike Parsons 1:05:40
It comes up maybe not so much during treatment as much as afterwards because, again, most of the people that I see, I'm seeing after treatment for this kind of problem. The number one thing that comes through in that literature is really physical exercise, as well as potentially cognitive stimulation, much like other literature that I think most neuropsychologists are very familiar with now. But really the impact of exercise on outcome and cancer, not just cognition and cancer, but in cancer in general is pretty impressive and wide ranging. So when it comes to the kinds of things you as a human can do while you have to take this toxic therapy and feel like absolute hell and lose your hair and lose your muscle tone and gain weight and not be able to work and feel terrible, all that stuff. Figuring out how you can then get back on the horse in terms of physical activity and exercise is probably the number one thing.

John Bellone 1:06:43
Is there anything that exercise doesn't help with? [laughs]

Ryan Van Patten 1:06:48
[laughs]

Mike Parsons 1:06:48
Maybe knee pain. I don't know. [laughs]

Ryan Van Patten 1:06:53
[laughs]

John Bellone 1:06:53
[laughs] That's true. But, no, it's such a panacea. I wish people would take that to heart.

Ryan Van Patten 1:06:57
And ride their bikes everywhere. Like you aspire to.

John Bellone 1:07:00
Yeah. [laughs]

Ryan Van Patten 1:07:02
Mike, a minute ago, you mentioned the International Cognitive and Cancer Taskforce. I'm wondering if you could tell us a little bit more about it. Like, for example, I know that they have a conference right before INS in February in Denver. Can you briefly describe this organization to us and what they're doing?

Mike Parsons 1:07:22

Absolutely. Yeah, thank you for asking, honestly, because I think it's a fantastic organization for anybody who's interested in this topic. The conference itself, which they have every two years, is a really interesting meeting. It's basically held all in one room for two days. The leaders in this field, the people who are really doing the cutting edge research, will present and lead small group discussions on topics like neuroimaging and mechanisms and therapies and all kinds of stuff. It's really a great blend of science and clinical care in a way that I think you can only get when you focus on a particular disease area. I highly encourage anyone who's interested in this topic to just go. Add a couple of days on to their INS week and go. You'll learn a ton about cancer and cognition. It will help really give you some perspective on it and fit together pieces that we're only beginning to understand. The organization itself is really dedicated to optimizing research efforts to understand this problem by doing things like their guidelines papers and holding the conference to bring the leaders in the field together. I think they've done a fantastic [job] - it's really a grassroots organization. There is no organization. There's a steering committee of basically four people who just make this happen every couple of years. It's a tremendous amount of work and a great meeting if you can make it happen.

John Bellone 1:09:06
Well, Mike, this has been really incredible. We've covered so much today. We have a couple of bonus questions before we let you go. These don't have to be specific to cancer, they can be general neuropsych related. The first one is if you can improve one thing about the field of neuropsychology, what would it be?

Mike Parsons 1:09:27
Well, I think probably the biggest impediment to offering services in the way that I would like to be able to do is oftentimes the hurdle of insurance authorization and the integration of cognitive care in cancer. So it's a battle that's been fought for a while, particularly because we didn't necessarily have the belief that this was a real problem. In other words, insurance organizations would not pay for neuropsychological evaluations if the indication was breast cancer. So being able to evaluate, track, and manage cognitive problems without necessarily having to spend a lot of time justifying the reason you're doing it, I think, would allow us to provide a lot better care for our patients. I don't think it needs to always be a very high intensity, expensive process. We can monitor cognitive function with sensitive tests without taking a ton of time. We can direct people to the right resources that will lead to better outcomes for these patients without necessarily spending a ton of healthcare money on it. But it is just this constant battle that we're facing.

Ryan Van Patten 1:10:49
Moving on, Mike, what is one bit of advice you wish someone told you while you're training, or someone did tell you that really made a difference? So we're looking for an actionable step that trainees can take that they may not have thought of that could improve their training performance going forward?

Mike Parsons 1:11:06
Yeah, that's a great question. I think probably the most useful advice or nugget that I got came from Tom Hammeke who was one of my mentors. When I was finishing postdoc, he told me that "I learned more in my first five years of professional practice than I did in all of my training combined." Which, of course, at the time, I thought was complete BS because I already knew everything.

Ryan Van Patten 1:11:36
[laughs]

Mike Parsons 1:11:36

So it was impossible to learn more. But as is often the case, Tom was right. And I think setting your expectations for what the first stage of your professional career is going to be about is a critically important step for becoming a successful and competent neuropsychologist. That the learning is not done when you finish your postdoc. That's really when it's beginning. And it's when you're signing on the bottom line that the rubber hits the road and all of a sudden that commitment to learning has to be redoubled because you just realize how much you don't know. So stick with it. Don't be afraid. You will get off of that horse after five-ish years. But the learning curve continues. I'm 20-some years into it now and I'm happy to say the learning curve is still going.

Ryan Van Patten 1:12:34

Yeah, we are truly lifelong learners and I look forward to that.

John Bellone 1:12:37

That's one of the reasons that got us into the field to begin with.

Ryan Van Patten 1:12:40

So that's a good segue into our very last question, we promise. [laughs]

Mike Parsons 1:12:44

[laughs] Thank you for promising.

John Bellone 1:12:45

You've been a good sport. So now that I've asked you about advice for trainees, we want to finish up by asking for specific advice for early career professionals. So the context of this question is the changing healthcare landscape, as you referenced. As neuropsychologists we want to remain relevant and useful. I'm wondering what steps we can take to ensure that we're providing cutting edge scientific and clinical services for the next several decades?

Mike Parsons 1:13:15

Well, I think that the movement that is taking place within groups like the American Academy of Clinical Neuropsychology and others to modernize the field and move our tools from the 19th and 20th century into the 21st century is probably the most important practical step that we need to be pushing. You know, Bob Bilder and others who have written about this, I think, have it right in that we are, as

neuropsychologists, optimally positioned to have an impact on healthcare in the next century. Many of the diseases that are going to be faced are going to have a cognitive component. Many of the diseases, like cancer, which have a cognitive component, are going to turn into chronic conditions that people are going to have to live with. And finding a way to move our field from an individual intensive assessment on a very small number of people to being able to provide useful management of populations is the way in which neuropsychology can really stay relevant and be of benefit to more people going forward. That's a huge challenge for all of us. Even [for] young people like you guys, as opposed to old people like me who are stuck in our ways. It's finding a new way to do what we do. And it links to the issue I was mentioning before about reimbursement and insurance authorization and so forth, the current model of healthcare financing. In other words, where each individual is paying an insurance plan and each individual provider is getting paid by that individual's insurance plan is completely upside down from the system that we're going to need to manage populations. The models of healthcare finance that are coming down the pike that involve population management and that will recognize the role that cognitive outcomes can play in quality of care, I think, will be set up to support this new way of doing business as neuropsychologists. But it's going to challenge us to move from looking at that one individual in depth, which I don't think we'll ever stop doing, but we need to also develop our ability to recognize patterns in populations. Provide screening and a useful and inexpensive way that tracks people into the level of care they need and so forth. That's where we're headed. And I hope smart people will make that happen.

Ryan Van Patten 1:16:03

A lot of what you're saying bears directly into the problem of health care disparities, right? And reducing those by - if we are less expensive, we don't only offer four hour intensive batteries, we can get our services out there to more people who need us, who can't afford us, and or just don't know about us, or have access to us, which is really important.

Mike Parsons 1:16:26

And using tools that can do a reasonable job of screening cognition on a broad based level that can then identify patterns, identify problem areas, and screen out areas where there are not problems. I think that's coming. And we want to have a hand in developing those tools, as neuropsychologists. We don't want Lumosity to do that for us.

John Bellone 1:16:52
[laughs] Absolutely.

Ryan Van Patten 1:16:53
[laughs] Yeah.

John Bellone 1:16:54
Yeah. We could not agree more. And when we release this episode with you we'll have already released our episodes with Bob Bilder. We spoke with him for a couple hours and we had a commentary on it. So listeners should go check that out because we completely agree. It's going to need new technology, new kinds of innovation to do that.

Mike Parsons 1:17:12
Yeah.

Ryan Van Patten 1:17:12
Mike, thank you so much for your time and being on the hot seat for over an hour and a half now. We really appreciate this conversation.

Mike Parsons 1:17:20
Absolutely. I appreciate you guys' interest in this topic and thinking of me as someone who might try to represent part of it for our field.

Ryan Van Patten 1:17:30
Yeah.

John Bellone 1:17:30
Great.

Ryan Van Patten 1:17:31
Yeah. Well, thanks.

John Bellone 1:17:32
Thanks again.

Ryan Van Patten 1:17:32
Take care.

Transition Music 1:17:32

John Bellone 1:17:37
That's all for our conversation with Mike. Remember that we now offer CE credit for listening to select episodes. So check out navneuro.com/ins or tell your colleagues or supervisors about it. Thanks for listening and join us next time as we continue to navigate the brain and behavior.

Exit Music 1:17:54

John Bellone 1:18:18
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Ryan Van Patten 1:18:29
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