27| Pediatric Traumatic Brain Injury – With Dr. Keith Yeates

September 1, 2019

This is an audio transcription of an episode on the Navigating Neuropsychology podcast. Visit www.NavNeuro.com for the show notes or to listen to the audio. It is also available on the following platforms:

Listen on Apple Podcasts | Listen on Google Podcasts | LISTEN ON STITCHER | Listen on Spotify

Speakers: Keith Yeates, Ryan Van Patten, John Bellone

Intro Music 00:00

Ryan Van Patten 00:17

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

John Bellone 00:23
And I'm John Bellone. Before we get into content, we would like to point out that today is a very special day. Today is the day that NavNeuro turns 1 year old. It was on September 1, 2018 that we released our very first podcast content. Ryan, how do you feel about that?

Ryan Van Patten 00:39
You know, I feel very warm and fuzzy, John.

John Bellone 00:41
[laughs]

Ryan Van Patten 00:41
You know, the first few weeks and months are always the hardest. I know we've both experienced the sleep deprivation, the pressure, the stress, the crying and wailing at all hours of the day and night, being forced to give up our hobbies and free time - it can be really taxing on any two people. But watching your little one grow up, makes everything so very worth it. [laughs]

John Bellone 01:02
[laughs] Well, I'm sure all the parents out there have tons of empathy for us [and] for what we've been through this past year. It's definitely comparable to raising a human.

Ryan Van Patten 01:10
Exactly, exactly.

John Bellone 01:12
[laughs]

Ryan Van Patten 01:12
But in all seriousness, the past year has really been a blast. I know we're both thrilled with all the support and the interest that people have taken in the podcast. John, I recall telling you that I would have been happy if 20 to 30 people downloaded each episode because that's way more people than are usually interested in anything I have to say.

John Bellone 01:30
That's still the case, I'm pretty sure. [laughs]

Ryan Van Patten 01:32
Yikes. Harsh. Way to bring me down a few notches.

John Bellone 01:36
[laughs]

Ryan Van Patten 01:36
In any case, John, why don't you summarize the current state of NavNeuro for our listeners.

John Bellone 01:43
So we released 25 episodes in our first year. Many of the episodes have several thousand downloads. We have about 100 ratings in the US-based iTunes with a 5-star average, and we have a sizable international listenership. We also have received really helpful suggestions and feedback from a lot of people both in person and via email. We are more than thrilled with the reception and growth of the podcast. This has been so much more successful than we could have imagined. And we have lots of great content planned for the next year, and several side projects. We're working on some partnerships. So be on the lookout for updates in the near future. We are both really excited to see where this takes us.

Ryan Van Patten 02:26
For sure. We also want to send out a big thanks to all of our guests for graciously volunteering their time and energy to speak with us. In addition, we want to thank our advisory board, Drs. Steve Correia, Tanya Nguyen, and Beth Slomine. We really appreciate the guidance and suggestions that you gave us. And a big thanks to our co-production coordinators, Leslie Gaynor and Charles Moreno. They've both put in a huge amount of time and effort on the podcast and they've made our lives much easier. And, of course, we want to thank all of our listeners. We're really honored that you offer your time and attention to listen to each of the episodes. And I agree, I'm thrilled to see what the future holds for NavNeuro. But for now let's turn our attention to today's topic.

Today you'll hear from Dr. Keith Yates on the topic of pediatric traumatic brain injury. We spoke to Keith at INS back in February of this year. That was Episode 16 and it

covered professional development. Today's episode represents a follow up phone call we had where we explored Keith's content area and received excellent education and conversation.

John Bellone 03:36

A lot of parents worry about their children getting head injuries and I can understand why. We want to protect those developing brains as much as we can. Before we transition into our discussion with Keith, though, I'll briefly review his background for our listeners. Keith is the head of the department of psychology and adjunct professor of pediatrics and clinical neurosciences at the University of Calgary in Alberta, Canada. He's a board certified neuropsychologist. He has a 30 year track record of funded research and is incredibly prolific. According to Scopus, he has been the most highly published investigator of pediatric traumatic brain injury in the world over the past 10 years. We're so fortunate to have him here today.

Ryan Van Patten 04:17

So, John, are you ready to start off year 2 with a bang?

John Bellone 04:22

[laughs] Yes, I am. And, with that, we'll give you Keith Yeates.

Transition Music 04:25

Ryan Van Patten 04:34

Great. Well, we are back once again with Keith Yeates. Keith, thanks so much for coming back to NavNeuro again. Although, unfortunately, we're not all together in the same room in New York City, we still appreciate you talking to us remotely.

Keith Yeates 04:47

Well, you could have flown me in of course. Just joking. Yeah, no, happy to be here.

Ryan Van Patten 04:52

We've had several guests request that we fly them out to San Diego.

John Bellone 04:55
Yeah. Although today is a rainy day in San Diego. [laughs]

Keith Yeates 04:58
Yeah, well we got 5 inches of snow on Saturday night. So I'll take a little bit of rain.

John Bellone 05:03
Oh, no. Geez.

Ryan Van Patten 05:05
Alright, so we're going to jump into talking about pediatric TBI. A trend that we have in NavNeuro [is] we like to begin most of our episodes by defining some basic terminology. So, for the sake of our listeners, can you delineate childhood mild, moderate, and severe traumatic brain injury, as well as the concept of concussion? Talk about the overlap and differences between those terms.

Keith Yeates 05:30
Sure. You know, traditionally, the severity of traumatic brain injury has been characterized based on the Glasgow Coma Scale. And as many people know, in this area, the scores on the scale vary from 3 to 15, with 3 to 8 generally being regarded as being in coma and hence having a severe traumatic brain injury. Scores of 9 to 12 being regarded as a moderate TBI. And 13 to 15 being regarded as a mild TBI. There have been a lot of criticisms of the use of this Glasgow Coma Scale for the purposes of severity because it's uni-dimensional, because it is really a marker of level of consciousness not necessarily of the underlying injury. And because we know that, within those categories there's tremendous heterogeneity, both in the underlying pathophysiology as well as in the resulting outcomes. But the Glasgow has served a tremendous purpose in terms of being able to begin to stratify severity and we've learned a lot using it, but it probably is time to try to move beyond that.

Now, concussion is interesting because the world of concussion sort of came out of a different direction than traumatic brain injury in some sense. In the sense that concussion was often focused on sport in its more modern incarnations, and there wasn't necessarily a lot of thought put into whether or not mild TBI and concussion are one in the same thing or not. There's been a lot more consideration of that question as research on concussion has moved well beyond sport now and into populations where the overlap or distinctiveness, or non-distinctiveness, for mild traumatic brain injury is in question. I think there's not a universally accepted

resolution to that. I think almost all people think that concussion is a mild TBI. But many of us, including me, don't think that all mild TBI are concussion. That there are some mild TBI, particularly those that are sometimes characterized as complicated, that may be associated with visible lesions on imaging meeting the criteria for mild that would be ruled out by most people's definitions of concussion. But there are those out there who would make an argument of concussion to be distinguished as being on the very mild end and mild TBI shouldn't include concussion. And there are some that will use the terms largely interchangeably. I don't think we really have a discipline-wide agreement on how those two terms should be used.

Ryan Van Patten 08:11

Yeah, that's a great point. Largely, I've seen people use them interchangeably. But it's confusing especially for people outside the field when they might be the same or they might be different. We're defining them differently. I wanted to back up for a moment. Complicated mild TBI, as I understand it, meets the criteria for mTBI. Whether we're using Glasgow Coma Scale or post-traumatic amnesia - loss of consciousness meets mTBI criteria. But then, like you said, there's also neuroimaging findings. Right?

Keith Yeates 08:43

Right.

Ryan Van Patten 08:43

So that it, in some ways, behaves more like moderate TBI because of the imaging abnormalities.

Keith Yeates 08:50

Yeah, there's research to suggest the outcomes can be similar between what's regarded typically as moderate TBI and complicated mild TBI. It's a distinction that Harvey Levin and his group really first drew based on CT scans, and has been now extended to include MR and other imaging modalities. But the problem is that as we get more and more sophisticated with imaging and better and better at detecting subtle lesions, the definition or who it encompasses changes. That's problematic because certainly the underlying injury is the same, we're just getting better at finding lesions and saying, "Oh, it's not a concussion." Well, clinically, it certainly appeared as if it was in the past. So I think we probably need to get away a little bit from defining severity, differentiation between complicated and uncomplicated, based strictly on imaging because we're just going to get better and better at finding

abnormalities and particularly as we start moving into more subtle ways of detecting differences in brain function that may be a consequence of the injury.

One thing you mentioned that I should say - I mean, most conventional definitions of mild TBI and moderate and severe TBI do tend to take into account other clinical characteristics like post-traumatic amnesia or duration of unconsciousness, often defined as how long it is before you're back to a normal motor score on the Glasgow. So there are multiple characteristics that tend to get taken into account, But nobody really ever tries to deal with the fact when they're inconsistent. Even issues like which Glasgow Coma Scale score to use. Do you use the score when somebody is intubated and sedated? There's some technical issues at a research level, but they actually have clinical implications as well. So it's still a messy issue in terms of the classification of TBI. Whether it's done based on pathophysiology and presenting clinical characteristics is still up for debate.

Ryan Van Patten 10:49

Yeah, it's challenging, like you say, when those acute severity indicators - GCS, loss of consciousness, and post traumatic amnesia - if they don't agree. Then, you know, which one do we use? I guess what I'm most interested in, and if you could speak to this, Keith, is the extent to which each predicts later outcomes. That's what we're interested in. I've done much more reading in the adult TBI literature.

Keith Yeates 11:14

I don't think there - there haven't been a lot of studies that really looked at that in depth in kids. Linda Ewing-Cobbs, just one paper I can think of off top of my head. Certainly the variables that tell you more about rate of recovery are probably better predictors than static measures. So if you take duration of unconsciousness, or duration of PTA, typically those are somewhat better predictors of neuropsychological outcomes than a single time measure, like a particular GCS score or just a measure of whether or not there was a loss of consciousness. But I don't think there's tended to be a lot of work done really trying to compare and contrast those different indicators. Part of the challenge is most of those indicators in actuality aren't routinely collected on any ongoing basis. Of course, measuring post-traumatic amnesia is usually done very impressionistically rather than with any sort of systematic tool like the GOAT or the COAT. The same [for] duration of unconsciousness - what marker you're using to measure that? Whether it's a motor score on a Glasgow or not, all those sorts of issues of measurement come in there as well. So I don't think we have a great literature that really tells us which of those markers is better. The Glasgow gets used as a default, in part because it does tend

to be routinely available in emergency settings and neurosurgical settings, whereas PTA, duration of unconsciousness, may not be because you need to use GCS, let's say, at least daily to get a sense of duration of unconsciousness or duration of coma. So it's tricky. When you rely on clinical data, you have to often base [it] on what's actually available on someone's record.

Ryan Van Patten 13:02

Yeah. In the adult TBI literature, Mike McCrae, is a big name [who] has done a lot of work. He talks a lot about the differences between mTBI, mild TBI, and then moderate to severe TBI. He will even call mTBI a different animal. So that's how I've really thought about it. That there's mTBI in one camp and then in another camp is a continuum of moderate to severe TBI. And that the main difference between them is if someone has a mild TBI, they tend to recover back to baseline. But if they have a moderate to severe TBI, then they don't recover back to their baseline. The more severe the TBI, the more impairment they end up having. Again, all of this that I've just laid out is based on the adult literature. I'm curious if that applies to children, [or] if you have a different conceptualization of those things.

Keith Yeates 13:52

I think those generalizations might be true and underlying it is a hell of a lot of heterogeneity. In fact, one of the things we remarked when I went to Berlin for the sport concussion meeting for the first time, I was really struck by the fact how many people that work in concussion have never seen a moderate to severe TBI. Even folks who do mild TBI sometimes haven't done anything with more severe TBI. To me, I really do actually think of them as a continuum. I don't think of them as that clearly demarcated from one another. The mechanism is the same. It's a trauma to the head in most cases, although it may be a transmission of force. The question is what it produces. So, from my perspective, the distinction between mild, moderate, and severe is more one of convenience than any obvious way in which nature cleaves at those joints. Particularly given that we really base that whole distinction, at least initially, on a scale that was devised basically for emergency first responders or emergency personnel to make a quick assessment of consciousness. So we shouldn't be too surprised that those labels break down at times. There are folks who have severe TBI who do very well, surprisingly well. And there are, as we all know, folks with mild TBI who do surprisingly badly. The injury, at least the features we currently use to make those characterizations, don't capture a lot of the variance in outcomes. So I think we have a long way to go in terms of better capturing what we mean by severity.

I think the medical profession would like us to move to a way of characterizing severity that's largely based on pathophysiology broadly construed, whether it's imaging or underlying inflammation or what have you. But the danger with that, to me, is you then forget what's happening clinically with the patient. It may be helpful from a medical perspective to think about it that way as long as we don't lose sight of whether or not that sort of multi-dimensional approach to classifying pathophysiology actually, as you say, gives us meaningful information in terms of outcomes. So I think there's still a long way to go in trying to figure out how we're going to differentiate different aspects of TBI. I was really struck by a paper that Erin Bigler led out of some data that we had that looked at just the heterogeneity of lesions in kids all with moderate to severe TBI and there's hardly any overlap from one child to the next. Even when we're dealing with a group of people that have severe TBI, at least as usually clinically diagnosed, you wind up with terrific variation in outcome. Terrific variation actually in underlying abnormalities on imaging. So I think there's still a lot of work to be done in that area.

John Bellone 16:36

Yeah. Just for our listeners who might not be as familiar, when we talk about post-traumatic amnesia, or PTA, we're referring to a lapse in memory, usually after the events, but also sometimes before the event where someone might not remember, let's say, an hour before the traumatic brain injury. They might not remember anything about what caused it and then they might not remember the next hour after. Their memory might pick up in the hospital and they might remember something about the hospital but not about the ambulance ride, for example. So, just for people who might not be as familiar with that.

But we're talking about childhood TBI specifically, and TBI is one of the most common causes of childhood morbidity. Can you give us a sense of the overall prevalence? The numbers that I've seen have suggested maybe 1 in 6 kids under age 10 are going to sustain a TBI and that the rates are maybe higher for adolescents and young adults. Is that accurate?

Keith Yeates 17:29

It depends on, again, going back to the severity question. It probably depends on who we include. We have better data at hospitals than we do outside of hospitals. Clearly, there's an age-related gradient in terms of prevalence. When you look at hospital cases, and actually it's a bit bimodal in that under age 2 is actually probably the most common presentation for TBI broadly, even though many of them are mild. Then it decreases and slowly increases over childhood. But it shows a significant

bump in adolescence, just as a function of kids driving is largely where that comes from. Then it tails off again in young and middle adulthood before it springs back up in older adults. You know, 1 in 6, 1 in 10, you hear lots of different numbers and it depends on the age ranges you're looking at. Then if you begin to include concussion, where so much of it happens outside of medical attention, or at least outside of the hospital, you're looking at a pretty substantial prevalence rate. I don't think that we actually have all that good data for the injuries that don't come to medical attention, almost by definition. Even those that come into medical attention outside of the hospital are not easily tracked. There are no good national or even state level surveillance systems in place to capture the milder end of the spectrum, which is where we know probably 90 to 95% of the injuries happen. So I don't know that we actually - I'm always a little nervous about quoting prevalence numbers because I don't think we actually have a good grasp of it outside of hospital-based samples.

John Bellone 19:12

Yeah. It's hard to pin down. Now when you said that under age 2 is one of the age groups that has the highest rates, we're talking about babies that were shaken, or falls, or...?

Keith Yeates 19:24

It's a combination. Yeah. I mean, you have the inflicted injuries or the intentional injuries which certainly are a portion of that sample, but falls are clearly also a very major cause of those sorts of injuries. Anybody who's had kids knows how often they fall over or fall off things and bonk their head. So it's falls, it's intentional injury. Younger kids are sometimes involved in motor vehicle accidents as well. So it's a variety. But I'd say falls and inflicted injury, unfortunately, are two of the more common causes in that age range.

Ryan Van Patten 19:59

Do current day car seats tend to protect children's heads pretty well?

Keith Yeates 20:05

Yeah. In fact, we've seen, since the days when I started doing research in this area almost 30 years ago, there's been a dramatic decline in the number of more severe traumatic brain injuries in kids and adolescents. In the younger age range, a lot of that has to do with the combination of much better car seats and, more importantly, probably better use of car seats, more universal use of car seats combined with better cars. Just generally, our cars are a lot safer than they used to be because of

crumple zones and airbags and the like. If a car seat is used properly in the rear, seat rear facing for the kids below a certain age, it's not totally foolproof but it really does provide a lot of protection. So I think we've actually - that's one of the better public health successes, I think, that we can point here in terms of brain injuries, both car seats and seatbelts, both depending on their age and becoming much more universal in the context of safer cars and safer roads.

Ryan Van Patten 21:10
Right.

John Bellone 21:11

Can we talk a little bit about the symptoms involved? Like, if a parent has a child who bumped their head, like you mentioned happens all the time, when would a parent get worried? When would they go to the hospital?

Keith Yeates 21:21
Well, when we talk about concussion, it's pretty clear if you've got a kid who's out and had a really severe injury, obviously, you get medical care right away or emergency care transportation. But in the concussion area, mild TBI area, which is rarely this, where this question comes up the most often, the decision that we tell people to make is based on whether or not the kids present with certain red flags, as they're called in the Concussion Recognition Tool that came out of the International Consensus Group. So, if a child actually does have a loss of consciousness, or reports a lot of neck pain, or has what appears to be a convulsive event, a seizure, there are others, vomiting. Anything ever suggests a more severe injury, those are the kids that should be transported right away either

by emergency transport personnel or by a parent if they're able to do it. Where it's not as emergent is where they show some of the more subtle signs of concussion, whether they be headache, a little bit of mental fogginess, some dizziness. We actually nowadays don't encourage parents to rush their kids off to the emergency department when they have injuries like that partly because there's not much an emergency department is going to do. We don't image hardly at all anymore kids with these injuries because we have a pretty good idea that the vast majority of them will have negative findings and we are able to predict pretty well who's at risk of having a finding. So if you have a high velocity injury, you have loss of consciousness, you have a skull fracture, we know the factors that increase the risk, and the vast majority of kids don't have any of those and don't need to be imaged. So I think that the first determination is whether a kid has any of the red flags or not. If they do, then you cart the kid off to emergency care. But otherwise, if

there's a question of whether or not they had a concussion, we usually recommend that they seek out their pediatrician or their family physician on a reasonably rapid basis, presumably, or urgent care if such a thing exists in their community and get evaluated that way.

John Bellone 23:34

You mentioned how heterogeneous this population is in symptoms, and even the medical history, the clinical presentation. In one of your very recent articles, the Journal of Neurotrauma just this year, you talked about how clinical phenotypes might help parse some of that out. Can you unpack that a little bit? Tell us the kind of take home message from that work?

Keith Yeates 23:55

I've always been interested in trying to take a more clinical perspective in data analysis. Traditionally, most of our data analyses are very variable centered. So they look at how variation in one variable is accounted for by variation in another variable. The problem with that approach is it assumes everybody's the same. And when we talk about "Oh, 40% of the variance in X is accounted for by Y." Well, that's across a wide variety of individuals, and actually within an individual that factor may or may not play any role. As clinicians, what we usually are actually dealing with, with an individual kid or adult in front of us, is trying to figure out how they're like other similar types of kids or unlike other types of kids with the same problem. So the notion of phenotypes is going along with the idea that underlying a general population there may be subtypes or subgroups that are identifiable. In this case, we were interested in whether or not they had different prognoses in terms of the likelihood of persistent symptoms. So taking common information from medical history - clinical presentation, symptoms, symptom reports - and looking at whether or not we can recover meaningful subgroups that go on to have different kinds of outcomes. There are a number of techniques around that are more person-centered, which is really the way clinicians think. And while we didn't do it in that particular paper, there is even the ability now to look for subgroups that not only vary by their identifying characteristics, but vary in terms of what predicts membership or variability within that particular subtype. So we're moving to the notion that - and this has always been my feeling with mild TBI in particular, although I actually think it's true of severe TBI - is that the injury may make a lot of difference for one kid and not make a whole lot of difference for another kid. Whereas that other kid may be more influenced by, say, historical premorbid factors and [for] the first kid that's not playing a major role. That's always been the challenge clinically with these populations. What's making a difference for this

individual kid? And this sort of phenotyping approach is just one way of trying to get at that a bit.

Ryan Van Patten 26:13

I love that. It's a challenge when we take research based on groups of people and translate it to individual people. These are all averages. So this approach you're talking about is very, very clinician friendly. Like you said, it's how clinicians think, which makes it more easily translated from bench to bedside, so to speak.

Keith Yeates 26:32

Well, the other thing that I point out at the end of that article, and one of the issues one of the reviewers raised was, “Man, this is complicated.” If you have four subtypes here, and four subtypes here, and seven types here, you wind up with hundreds of possibilities. How is a clinician going to do that? The great thing about electronic medical records when they're done right, is that they can incorporate all this stuff. So you just collect the factors that are there - you get the symptom ratings, you take a history and you make some clinical judgments. You input that as you're collecting the information, which is all part of what a physician or somebody in an emergency would do. That computer spits out, “Here's the subtype that they're most like. And here's their prognosis.” It's not hard to actually do that with current technology. So we may actually get to the point where we already have decision rules that are embedded in EMRs, whether it be about whether to do a CT scan or to take a prognostic rule and apply it. But we may be able to begin to have technology help us when we're sort of saying, “What's this individual kid like?” I mean, I've been talking to statisticians about this issue for 20 years at least, because I was frustrated by the fact that regression coefficients are meant to apply to an entire sample. They imply that it applies to every single kid because it's based on a group average, when I intuitively know as a clinician that regression coefficients in some sense are individual specific. But our stats really don't allow us to get at that. There are now random effects regression models that allow you to get at that. But the challenge with most of those techniques, including the latent techniques we use, is they usually require pretty big samples that are bigger than what we're used to in most of our research.

Ryan Van Patten 28:20

I love this topic in general. I do a lot of thinking about the future, how AI and machine learning algorithms might impact the healthcare industry. I think you're touching on that. The argument that I enjoy hearing and thinking about is that we shouldn't worry about being replaced anytime soon by AI, but that instead, these

algorithms will supplement and augment us as clinicians and help us just as you're saying. We'll have an algorithm that takes clinical information and gives us different profiles, which we can then use to make better clinical decisions. This can apply to TBI and any other health care decision, really.

Keith Yeates 28:56
Yeah. I mean, the AI stuff is going to go a long way. Paul Meehl years ago made the point that actuarial prediction is better than most clinicians. We fool ourselves into thinking that we're good at predicting things, and we're not.

Ryan Van Patten 29:09
[laughs]

Keith Yeates 29:10
It's like, we think interviews are useful. If they're not structured, they're pretty useless, really. So we needed to take that into account. But there are circumstances having more to do with management, probably, and dealing with the human side of things where machines aren't going to cut it. So I think we're silly and stupid if we don't arm ourselves with what technology can do for us because machine learning or any other computer can think far more dimensionally than we can. We have a hard enough time trying to think in three dimensions, much less 10 or 12. So, it can do a lot of things that we can't do. But it's also the case that computers can't totally replace some of the things we do, particularly as neuropsychologists. So, again, I agree it's a matter of figuring out where technology can help us and not being afraid of it. I actually think there's more in medicine that's likely to be almost totally replaced by machines that isn't neuropsychology.

Ryan Van Patten 30:06
Radiology…

Keith Yeates 30:07
Radiology, probably. Pathology. A number of things that are all based on pattern recognition, where machines are just getting better and better and better at it. So.

John Bellone 30:17
We could just ditch the rest of the TBI questions [and] we could focus on the AI stuff [for] the rest of the episode. [laughs]

Ryan Van Patten 30:22
This is a fascinating tangent, I love it.

John Bellone 30:24
Yeah.

Ryan Van Patten 30:25
I guess to be responsible hosts, we will bring it back to TBI, unfortunately. [laughs]

Keith Yeates 30:30
Well, I'll retire before all this stuff happens. So, it won't affect me as directly.

Ryan Van Patten 30:35
Yeah, leave it to others to worry about. [laughs] So I had mentioned earlier, Keith, that John and I are adult neuropsychologists. We've done some work in TBI with adults. We're talking to you about child TBI. I want to be specific about the differences there. Sometimes we can be a little ignorant and assume that children are simply little adults, right? That there's no difference, they're just smaller. Everything I know about adult TBI, you can just apply it to childhood TBI. So tell me why that thinking is wrong and what are some big unique factors about childhood TBI in particular.

Keith Yeates 31:13
I mean, there's differences between kids to begin with than adults and then there are also differences in the injury itself. So, you're dealing with a developing brain, obviously, where there are forces both acting for and against you in terms of the effects of TBI. For you, perhaps there's a certain degree of plasticity, but against you is the fact that plasticity works when you have lots of brain to take over where a lesion has occurred. Where a TBI is a diffuse injury in most cases, you may not have that capacity, and yet you're dealing with an organism that's still learning and still developing. If you don't have the reservoir of experience, education, and so forth that an adult does when they have a TBI, you may actually wind up having a worse outcome. In fact, the literature would suggest that kids are injured at very young ages, perhaps up to 3 or 4 do show worse outcomes relatively speaking than older kids and teens and adults, except until you get to the older adult or elderly. So you have a developing organism whose brain is quite different, particularly as you get into the very young child from an adult. And then you also have - and we can go into all sorts of developmental periods, the whole thing that happens in

adolescence and the extensive development of the frontal lobes in that time period, which also has implications.

Then the injuries themselves tend to be somewhat different. So kids are often involved in lower velocity types of injuries than adults. Their skulls are softer, they tend to have a different lesion pattern as a consequence of both the skull being a different density and the brain having a different distribution of gray and white matter and less myelination in place. So you see differential types of lesions involved. The prediction from lesion to outcome type tends to be a bit different as well. So there's differences in the organism that comes into the injury, there are differences in the nature and mechanics of the injuries, generally speaking, and then there are differences in terms of how that organism and the brain itself responds to a particular injury. So there's multiple dimensions and ways in which childhood TBI and adult TBI, although, again, they're on a continuum. It's not like there's a firm place where a 16 year old looks a lot more like an adult with a TBI than a 4 year old. But there are some important differences that people need to take into account.

John Bellone 33:39

Keith, you mentioned CT before, computed tomography, and I'm wondering how you think about imaging in this population. The decision whether or not to image, obviously there's some cost benefit involved here. I don't know if you feel like the amount of radiation is excessive for a child or if that's not really a factor. The other issue with kids is that they're not going to maybe sit still for an MRI and so you have to consider sedatives. How do you think about this cost/benefit?

Keith Yeates 34:07

CT scan is obviously still the imaging modality of choice in an acute emergent situation, in most cases. I mean, there are some places now that have got rapid MRI and are using them more in an emergent setting, but arguably CT is still the modality of choice because of its sensitivity to blood products, and particularly certain types of blood products that would require emergent intervention, neurosurgically. I think where we've made real progress is not overusing CT, particularly in the mild TBI or concussion population where there is a risk of exposure to radiation. Although in any given individual that increase in risk is relatively small, across a population of enough kids, there's some data to certainly suggest that there's increased risk of cancers and other negative effects. So CT is now used much more judiciously. I have to say with some pride that Canada sort of leads the way here as opposed to the US. And because of risk management issues

in the US, you still see an overuse, arguably, with CT scan. Whereas routinely if you came into the ED 25 years ago and you had what we now call a concussion, or mild TBI, you would get a CT scan, you'd probably be kept overnight in the hospital. CT scan usage in most places in the US and even lower in Canada is under 5% now in that population because there's no findings, you don't find anything. You'll find a lesion if you limit your broad population of these kids with CT, you might find a lesion 2%, 3% of the time, but only a small number of those are actually going to require any kind of neurosurgical intervention. So it's a very small number. So there's no sense in doing CT and, in fact, the most recent CDC guidelines, along with other guidelines, expressly says don't routinely image. We have great decision rules now with nearly 100% negative predictive values that rule out the vast majority of kids even needing CT.

Now I think where we're still struggling in some senses is when is MR indicated in the more severe TBI? You know, CT is a lot less expensive than MR still. It does involve exposure to radiation, whereas as far as we know to this point, MRI exposure doesn't have any untoward effects. But because it's considerably more expensive the question is, “Why would we use it?” And where I haven't seen convincing data, but again, I'm not a neurosurgeon and I don't necessarily have to make these sorts of decisions and I don't look at this literature, is whether or not getting an MR actually leads to changes in management or changes in care. I mean, certainly, we can find more lesions on MR, there's no doubt. Every study that's ever been done, you find 3, 4 or 5 times as many abnormalities on MR after TBI than you do on CT. But does knowing that lead to anything different in terms of outcome? I've certainly seen plenty of cases in my experience where kids were given MR and you went, “Yep, there's abnormality.” And sometimes it was because they were doing worse than expected based on their clinical presentation and you got an MR and "Oh, yeah, we found some things and maybe that explains it", because we don't know for sure. And it didn't lead to any change in management other than to say, "Oh, we have more evidence for an injury than we thought we had." So I think the big pressures that are going to happen over time with the insurance companies, in the US in particular, will be, “How does it matter? What does it do for care?” And I don't know that there's a lot of evidence that widespread use of MR is needed to really manage TBI. There may be specific reasons to get it. Clearly, if you're trying to track a subdural of some sort, if you've got some specific reason to do the imaging, it may be needed. But in many cases, it's not going to actually lead to any change in care.

Ryan Van Patten 38:08
That's really helpful, Keith. Do you have a sense as to how many head CTs a child might have before there's a non-negligible risk of cancer or other negative outcomes?

Keith Yeates 38:21
No, I haven't really read the literature in that much detail. And obviously I'm not a physician and not a radiologist. So it's not - I would always say go talk to your physician about that one.

John Bellone 38:31
I want to talk more about outcomes and recovery. In all childhood brain insults and disorders, there's one potential advantage and one potential disadvantage in terms of recovery. So children have more neuroplasticity than adults, so they have a greater potential for recovery, potentially, following these injuries. This is sometimes referred to as the Kennard principle.

Keith Yeates 38:55
Well, I'll tell you about that one in a sec.

John Bellone 38:57
Okay.

Keith Yeates 38:57
It's not actually her principal. And she didn't say it.

John Bellone 39:00
Interesting, okay. The idea behind the principle [is] that injuries early in life leads to better outcomes. But, kids are also subject to critical or sensitive periods of brain development. We talked a little bit about that, where they might be more vulnerable to the effects of brain injury. So I definitely want to hear your thoughts about the Kennard principle. And then I'm curious also [about] how these competing forces of plasticity versus vulnerability might play out in childhood TBI.

Keith Yeates 39:30
Yeah, you know, it's interesting. Margaret Kennard was an animal researcher and she did some really interesting and elegant studies on the effects of early lesions. Her research did not always show that there was more neuroplasticity in younger

animals than adults. It depended on the particular timing, depended on how many lesions were made, it depended on the extent of those lesions. My former colleague, who passed away a few years back, Maureen Dennis, actually wrote a really nice article about Margaret Kennard's life and about the fact that she was saddled with this principle that was supposedly attributable to her when she never actually believed what it said and didn't feel like it was hers to be credited to.

There certainly is evidence that younger brains retain a surprising degree of plasticity. I think we have to be very careful how we define plasticity, whether we define it at a neural level or a behavioral level because the two are not isomorphic with one another. Plasticity is not inherently always a good thing. The brain's ability to, for example, regenerate or generate new connections sometimes can go awry after an injury and you wind up with connections that are actually more detrimental than they are positive. It doesn't take much to study the effects of early lesions, focal lesions, to know that kids' outcomes after very early focal lesions are quite different than they are in adults. But there was this notion for many years, that early focal lesion was something a kid could just overcome because of plasticity. Well, it turns out that that plasticity often comes with a cost. And that you may not see the focal effects on behavior that you would in an adult with the same focal lesion, but you may see a more general, diffuse lowering of function than you wouldn't in an adult.

The very interesting thing about the focal lesion literature over time is how the outcomes associated with lesions in the same kid can change over time. So you read some of the very interesting work that the folks at UCSD have done on early strokes and the longitudinal work, the outward expression of the lesion can be quite distinct at different age periods as a function presumably of underlying brain development. So, the old notion of "Oh, it's always better to have a brain injury when you're young", doesn't actually tend to hold water totally, particularly for diffuse injuries as I alluded to earlier. Plasticity presumes that there might be the ability either of the damaged area to repair itself in some ways or for undamaged areas to take over function. Those all can be seen in early focal lesion studies. But when you damage the entire brain, or in effect much of the brain as you will in a more severe traumatic brain injury, there isn't the capacity necessarily for that sort of plasticity. You may actually throw the system off in a way that has long lasting effects that are never really recoverable.

John Bellone 42:53
There's the idea of the crowding principle, right?

Keith Yeates 42:57
Yeah.

John Bellone 42:58
Where language might shift to the other hemisphere, but there's going to be consequences, negative consequences of that potentially.

Keith Yeates 43:04
Yeah, I've seen some really interesting cases in my clinical career of what clearly seem to be crowding effects with kids who had early left hemisphere lesions - developed good or reasonably good language skills and really, really bad visual spatial abilities. There was really no explanation that could account for it other than crowding. And that's not unusual. We have plenty of those sorts of cases documented. So that sort of thing certainly can occur. But, if you've damaged both the right and the left hemisphere, as is going to be the case in most severe TBI, and of course a lot of that damage occurs both to the gray matter but also the white matter that connects everything, you've sort of taken your switchboard and put a big dent in it all the way around. It's going to be really hard for any kind of normal connections to be established. It doesn't mean it can't be. Again, as I've alluded to before, there are kids with severe TBI, even younger ones, who do surprisingly well. We don't understand at any sort of mechanistic level why that occurs - why some kids do well and some do much more than we would expect. That's really I think the next frontier in some ways in TBI. We need to not do any more studies that say TBI is bad for you. I mean, we kind of know that. We need to try to figure out where the heterogeneity is coming from and whether we can leverage it at all in terms of promoting better outcomes for the kids that are at risk for poor outcomes.

John Bellone 44:33
So that Kennard, or I guess it's Kennard principle, is maybe not something that we should hold as completely true. It sounds like she wouldn't even want us to do that. And on top of that she gets people like me mispronouncing her name. [laughs]

Keith Yeates 44:46
[laughs] Well, I can't tell you. I've always heard it as Kennard. You know, who knows? It could be Kennard. I don't know.

John Bellone 44:53
[laughs]

Ryan Van Patten 44:53

The focal versus diffuse distinction is helpful, though. I hadn't really considered that myself when thinking about this issue. As you're talking, Keith, I was thinking about the examples, primarily anecdotal, that I've come across where plasticity does seem to really help the young. For example, like a hemispherectomy in an infant where a huge portion of the brain is removed. We think if that happens in an adult, they'll be incredibly brain damaged clinically for the rest of their lives. And when it happens early on, there can be enough reorganization to allow the person to retain some function, but there can still be crowding which is problematic. Like you say, TBI is this diffuse whole brain injury, which may not be better defended by a young brain as compared to an old brain. That's helpful.

Keith Yeates 45:39

Yep. There's a pretty sharp age gradient here too. In that, you're not going to see that crowding or that diffuse effect of a focal lesion in a 16 year old. Again, I mean, there's not a magic button or magic switch that happens and all sudden it's totally different. There's definitely a gradient and a lot of what I was saying applies to younger kids.

John Bellone 46:02

Yeah. Also talking about age, again, what happens in adults is maybe a little bit different than childhood TBI. Because for kids, I guess we often don't see a stark decline the same way that we see a decline from a premorbid baseline in adults. So instead, we see a slowing of the typical neurodevelopment in future months and years. So I'm curious to what extent are cognitive and emotional symptoms present immediately following childhood TBI? To what extent do these injuries tend to stunt the expected development going forward?

Keith Yeates 46:35

It's a good question. There's this interesting, what I think of as a bit of a myth actually, that there are delayed effects of TBI that we don't see for years until afterwards. This notion came out of, again, animal research that suggested [that] at times you didn't see the effects of a frontal lesion until later in development when the frontal lobes are meant to come more online. But that's based on outmoded notions of the frontal lobes, which are not just sitting there doing nothing for 12 years before you start to use them. It's also, I think, based on not very careful thinking about what kinds of outcomes you're talking about. I mean, the vast majority of the literature would suggest that, at least for more moderate to severe TBI, the most pronounced effects are going to be apparent immediately after the

injury, which sort of stands to reason - you don't break your leg and see the worst effects of a broken leg 10 years down the road, you see it right away. That's not to say that it doesn't put you at risk down the road. I think a TBI can put you at risk for a number of things, like emotional difficulty. So when we looked at stuff across time, at least in our research, and I think there are now a variety of other groups that probably would say the same thing, the biggest deficits cognitively, the biggest deficits functionally tend to be immediately after the injury.

You do see cognitive recovery in many cases, at least to some extent. You might see functional recovery. Although one of the things I think that's more interesting about the data that I've looked at with Gerry Taylor and Shari Wade and others is that we see a cognitive recovery occurring in many domains that isn't paralleled necessarily by functional recovery. So if you look at ratings of adaptive function or school performance, you see ongoing problems even though cognitively on our traditional neuropsych tests there's been some recovery. Where you do sometimes see a late onset problem is in the emotional and behavioral area. But I'm a little bit loath to automatically ascribe that to the underlying injury because we see the same thing in concussion. There's more data now to suggest that emotional problems are not immediately seen after concussion, but are seen down the road. To my way of thinking, a lot of that is probably secondary effects of what happens to kids after they have a brain injury, which is they become socially isolated, particularly for more severe injured kids, they have problems in school, they have some sense they're not like what they used to be like, and so forth. They also have a brain that has less reserve, less ability to deal with stress and other things. So as a consequence, there's partly an indirect effect of the injury, but often a lot of it being secondary.

So I think in thinking about what the trajectories are after brain injury, you really have to think about what outcome you're talking about and what period of time you're really looking at. One of my former graduate students, who's actually now a neuropsychologist here at Alberta Children's Hospital, did a nice paper out of Gerry Taylor's data actually looking at this question and looking at profiles of functioning over time. It was what I just said. We saw more evidence of cognitive and functional impairment early. Functional impairment often persisted in those severely injured kids, even after there'd been some cognitive recovery. But we saw more evidence of declines in emotional and behavioral functioning with time. So it very much depends on the outcome and what I think that signals is that the factors that are at play are different for the different outcomes.

Ryan Van Patten 50:09

Gotcha. To move on a bit, I'm thinking about how we might best work with a child who has just had a mild TBI. So, in the past, recommendations in this regard have included extensive rest following mTBI. But we now know that prolonged inactivity can actually have deleterious effects, on both children and adults post mTBI. These days, from what I've seen, the recommendation tends to be to rest for about 24 to 48 hours, followed by a gradual return to normal activities while staying below exertion thresholds, not pushing them to their limit, but slowly tapering up activity be that athletic, academic, intellectual. Is this correct? And is there anything else you'd like to add regarding the impact of rest on recovery?

Keith Yeates 51:04

Fortunately we moved away from the ludicrous notion that we should make kids stay in a dark room for a month after an injury like this, which we don't do to a kid with severe injury, much less acute with a milder injury. I don't know why it took us so long to figure it out. We already knew bedrest is bad for you. So fortunately, the clinical trials that have been done and compared the effectiveness of research clearly have indicated that protracted periods of rest are not good for you after concussion. There is some animal data to suggest that there is a period that's relatively brief that might put you metabolically at more risk. And that's where the 24 or 48 hours is coming from. We also know that the period of time you're most at risk for a second injury is during that period as well. So we've definitely moved away to a much shorter period of rest - 1 to 2 days. Even the notion of gradual return to normal activities is starting to give way, I think, to the notion of active rehab and we're seeing increasing evidence that mild to moderate exercise may promote recovery. Not high level aerobic exercise, but sub-threshold exercise up to about 80% seems to actually promote recovery. So I think we're moving away from a passive, "Let's just wait for somebody to get better" to “Let them rest for a day or two, and let's start to help them get better.” And that's where the guidelines are all headed toward now.

John Bellone 52:34

And the reason for the rest is to avoid a so-called "second impact syndrome.” Would you talk about that?

Keith Yeates 52:42

I don't know that. We have no idea who or which kids are vulnerable to what's been called second impact syndrome. There are still debates about whether it involves a second impact or not. Is it just malignant edema, that there are a few individual

children that are genetically vulnerable to? We really don't know who's at risk for that. And in many of the cases where that was thought to happen, there was no notification of the first injury that occurred by definition. We have some data now to suggest that the rates of second concussion have been pretty drastically reduced, in both NCAA data and other data more generally from the States, to suggest that the institution of a waiting period and a gradual return to play has really had a significant impact on reducing second concussion. The risk of second concussion is a little bit different than the risk of second impact syndrome because second impact syndrome is such a rare phenomenon that we really don't have any ability to predict who's at risk. Even putting that aside, though, we know that multiple concussions are probably not good for you, particularly multiple concussions in short succession. We know that the data was pretty clear [that] the biggest risk is one to two weeks after, but particularly in the first few days after. So having the rest period and then also just having the gradual return, so that if you have a concussion, you shouldn't be back to play with full contact for at least a week avoids that period of vulnerability. That may be one of the biggest benefits of the waiting period - not actually that it promotes recovery, per se, so much as it avoids the second injury.

John Bellone 54:21

Just to clarify the second impact syndrome for people and for myself as well. That's a pretty severe consequence of a second injury, right? That leads to death or significant morbidity. Am I right there?

Keith Yeates 54:33

Yeah. I mean, traditionally, it's involved with some sort of impact close after another one. Often but not always described as being associated with a concussive sort of presentation. Seems to set off a chain reaction of malignant edema and brain swelling that isn't seen in adults generally speaking. You asked the question earlier, “How are kids different?” One of the differences is that kids are more prone to swelling of the brain than adults. I don't know that I totally understand the reason but it's one of the reasons that kids will die of increased ICP at times, because of the swelling. So often the presentation for second impact syndrome [is] somebody who has multiple blows, often did not disclose that they had an initial concussion like presentation, they often collapse on the field or shortly after a game, they have malignant swelling and edema of their brain, and herniates, and they die. So the most famous case in the States is Zack Lystedt , which was out in Washington. That was the case that led to the passage of concussion legislation in all 50 states. There's a famous case up here in Canada, Rowan Stringer, a young woman who died after collapsing at a rugby game where she'd had a concussion, possibly more

than one the day before. She had let a friend know, but didn't tell anybody else and the friend didn't tell anyone, unfortunately. So these are really tragic cases, but they are very uncommon, and are by no means something that you see in a lot of cases of multiple concussions.

Ryan Van Patten 56:08

Circling back to rest, or not so much rest, following mTBI, can you talk about, sort of summarize the guidelines. A child has had an mTBI, they're in school, they play sports, when might they go back to school and return to athletic activity?

Keith Yeates 56:26

I think we've become a lot more common sense about this now, as opposed to making these strict prohibitions about things like, "Oh, they can never have any screen time", or, "Oh, they can't spend any time on the phone with their friends." I think we still want to see a day or two of rest. And then we take a sense of how - and even that differentiation depends a little bit how fast they seem to be recovering. So if they seem to be making a good recovery, it may be only a day of rest. And actually, they may be able to try some school-like activity pretty soon. And if they seem okay, they may go back to school part time on day 2 or 3, many kids can. We shouldn't just have this artificial "Oh, you have to have 40 hours of rest, and then you have to go back to school part time." It really depends on the individual youngster. And the same, to a certain extent, applies to return-to-play, but I think we're more cautious and should be more cautious about returning to contact sport. One of the reasons is that we know it puts them at a much more increased risk of concussion than just going to school does. Secondarily, school is arguably more important to their long-term development than playing a contact sport. But that's why the return-to-sport versus the return-to-play protocols are a little different in that return-to-sport, each step requires at least 24 hours. It doesn't matter how fast you're going, you shouldn't be back to full contact practice and play in less than 6 days, 7 days for full gameplay. Whereas with the school return, I've seen kids successfully return to school after 2 or 3 days. It's really an individual titration of do they seem to be doing okay? Do they need some adjustments? Often you try a half day of school to see how they tolerate it. I think we're also moving away from the notion that you have to be totally asymptomatic to go back to school. I mean, one thing, no kid is asymptomatic. Hardly any of us are asymptomatic. But even the notion you have to be totally back to baseline is probably giving way to the notion that slight symptom exacerbations are to be expected just as a consequence of getting back into things. It's, again, I use the illustration - if you have a badly sprained ankle, you stay off the ankle for a couple of days, and then you start to put

a little stress on it. And it hurts sometimes, but it doesn't mean you go back to totally resting it. I actually think that analogy works somewhat for concussion. You just want to not get too symptomatic. We actually do have some data - I think people realize that, "Oh, if you're symptomatic, you're harming the child and it's going to make them have a more protracted recovery." Actually, the data suggests that's not the case. Mike McCrae's group did a nice little paper that hasn't gotten a lot of attention but they actually looked at symptom spikes and whether it was related to duration of recovery, and they weren't. It sort of stands to reason. I mean, as long as you don't let it get too bad and stay too bad for too long, a few occasional spikes in symptoms is probably just natural variation in the recovery curve. So I think we're moving toward staying cautious about athletic activity because of their increased risk and really take those 6 or 7 days to get back to play. But for school, I think we need to realize the costs that come with not going to school, particularly for teens. I mean, if you have a kid who's in 11th or 12th grade and they miss a week or two of school that can be really devastating in terms of their ability to ever catch up and really can put them behind. So there's a cost/benefit analysis to be done. Like, "Oh, they have a little bit of a headache", but if they're in school and they're staying up with their work, well that's probably better than "Oh, well, their headache is a little worse here and there. Oh, we got to keep them out." So I think we're just developing a bit more common sense about it.

John Bellone 59:59

It sounds like reasonable guidelines to me. I want to talk about post concussive syndrome. Many adult neuropsychologists are familiar with the lack of expected symptomatic recovery after a mild TBI. Symptoms are pretty wide ranging [and] include headaches, sensitivity to light, some cognitive inefficiencies, mood disruption, sleep disruption, many other things. The link, though, between the symptoms and the neuromechanical injury, it's questionable, right? And maybe due to secondary psychosocial issues - you had alluded to that before. People who might be just highly fatigued or stressed, but who haven't experienced a concussion often have symptoms identical. A lot of us, just at baseline, have a lot of the post-concussive syndrome-like symptoms. So can we talk about how common post-concussive syndrome is in children? I've heard that it might be less common than in adults.

Keith Yeates 1:00:54

Well, I tend not to use the term because I don't think we've actually convincingly shown there's a syndrome involved. So I tend to talk about persistent symptoms. Because the symptom profiles are so heterogeneous in concussion - in some folks

it's headache, for others it is dizziness, for others it's mental fogginess, and for others it's emotional distress. So I think we've made a mistake at times talking about post-concussive symptoms as if they're unidimensional, when every factor analysis that's been done of post-concussive symptom measures reveals multiple correlated, but still separable, dimensions. So we have to think about which symptoms we're talking about.

I think in kids the data varies depending on how you define persistent symptoms. One of the interesting things that I've been doing with Andy Mayer is looking at our data sets at different ways of defining whether or not persistent symptoms, and it can really change the estimated prevalence of persistent symptoms from quite low to quite high. I think some of the variability we see in the literature is because of that. But I think it's probably the case that most people would think that somewhere around 20% of kids are still symptomatic at around one month post injury. Is that the cut off? There's no particular time period, I think, that defines when symptoms are persistent. What's clear is there are a lot more kids with acute symptoms and it goes down gradually. Four weeks is a reasonable time because most kids are back to baseline by then. The numbers of kids who are persistently symptomatic at three months is even lower, maybe 10%. But again, as you accepted, if I take a group of kids who had an orthopedic injury, a certain percent of them are going to be persistently symptomatic after their injury as well - lower than kids with concussion, but enough that some of the symptoms that happen after traumatic injury are not specific to the brain, they're just a consequence of traumatic injury.

I think that the reason I got into doing research in this area was partly because back 25 years ago, these kids would come into my office and we widely regarded this injury as totally benign. And yet there were these kids who would come in - many of them had factors I could easily point to, "Oh, you're actually depressed before your injury", or, "Oh, you got a crappy family and that's what you're trying to avoid here". But there were the cases on occasion where a kid presented and I really couldn't think of any other alternative explanation, which is the first thing I try to do in these cases. Then there were other hints based on the severity of the injury or the clinical presentation that there was a real injury that occurred. I mean, something happened to the brain. Like the kid who still had a slight cranial nerve abnormality or a kid who had been unconscious for five minutes. The range of injuries that go into the definition of concussion or mild TBI is quite broad. So what I've been struck by is, again, this heterogeneity. We tend to want to make these generalizations "Oh, it's psychogenic", or "Oh, it's physiogenic." I think, not only is that overly simplistic on average, because there's research and data you can cite to support both of those. But it's quite simplistic when we apply to individual patients, whether they're

kids or adults. In that, in some cases, their persistent post-concussive symptoms are probably entirely related to their premorbid status or how they coped with the injury. Whereas in other cases, the injury really accounts for the difficulties they're having, particularly early on because I do think the balance of factors that contribute changes with time.

So let me give you an example, and then this is the challenge I think we're trying to say it's either/or. You have a kid who comes in, has a blow to the head, is unconscious for 2 minutes, even has let's say they have a post traumatic seizure. No findings on imaging. They report all sorts of mental fogginess, they have new onset migraines, and they're a little dizzy acutely. As time passes, the dizziness isn't there anymore, but they're still having post-traumatic migraine. Their cognitive stuff has cleared up largely but they begin to have emotional distress. And then you find out that in the course of all this, their parents are getting divorced. So when did the injury stop having the effect? Clearly it had an effect acutely. When did the other factors become probably more important? Would they have had the same symptoms from those other factors if not for the injury?

It's this sort of thinking, I think, that leads us to have to get away from this simplistic notion that it's going to be one or the other, or "Oh, it's all psychosocial." In fact, I mean, I find it interesting how much the adult literature tries to say, in some cases, "Oh, it's all premorbid. We can explain this all away." I don't have any reason to think it's fundamentally different in kids than it is in adults. I think there's a bias in some respects, in particular the neuropsychological community to react to the over-medicalization that happens sometimes with a sort of, “Well, you know, they haven't assessed their psychological functioning. We don't know what they were like beforehand”, and almost to take an opposing view just to just to be devil's advocate. I think we don't do ourselves any favors by trying to approach the problem simplistically, and I think that's what my research anyways, that was really what I'm struggling with. Is trying to get a sense of, in getting back to the individual patient notion, of how do we begin to do justice to data in a way that reflects what we intuitively, I think, know as clinicians, which is that generalizations tend not to work as you begin to work with individual patients as opposed to populations.

Ryan Van Patten 1:06:32

Keith, I'm wondering what value neuropsych testing might have in the acute phase of recovery post mTBI and then comparing mTBI to moderate to severe TBI. I've often wondered this myself. I've done some inpatient clinical work with people who have mTBI, comparing that to outpatient work a few months later. What value do

you think we have in a post-acute phase in terms of predicting relevant life outcomes?

Keith Yeates 1:07:01

Well, I don't have any doubt that a good neuropsych assessment makes sense in the post-acute or late-acute period for moderate to severe TBI. I think there's plenty of evidence to suggest that neuropsychologists bring something in terms of added value in documenting the outcomes, because there isn't a one to one correspondence with injury severity from the perspective of clinical presentation or pathophysiology. It's also the case, I think, that we can marshall a fair amount of good evidence to suggest that neuropsychologists and neuropsych evaluations can help predict functional outcomes in a way that the medical side of things won't in isolation. Obviously, it's also a way of tracking recovery. But if you're talking about assessments, at the end of inpatient rehab or sometime in there, I think there's without a doubt substantial value. It's a little trickier in the concussion and mild TBI sphere, because it depends a little bit on what you think the testing is going to accomplish. We've advocated - we being by Mike Kirkwood, me, and a bride of others have advocated [for] a graded approach to neuropsychological assessment in concussion. In that it probably doesn't make sense and certainly isn't feasible from a financial or resource perspective to give every kid who has a concussion a full blown neuropsych assessment at two weeks or a week when most of them are still in a pretty rapid phase of recovery and it's probably not going to make any difference to what you do with them. Where we can do some quick screening, you get a sense of, along with other indicators, a more abbreviated assessment in the post acute period may give us an idea of whether cognitive deficits are part of the picture, because they aren't always, and the extent to which they're there. But I don't think you need to do a full blown assessment to do that. That's where some of the computerized testing or brief abbreviated battery could make sense in a child, particularly if they're still symptomatic after a week to 10 days. Full blown assessments, I think in a mild TBI or concussion spectrum really only become warranted in a kid who's unexpectedly still symptomatic over longer periods of time. Partly not so much to document the effect of the concussion, because aside from our recent data using the NIH toolbox, there isn't a lot of data to suggest that you actually have deficits attributed to the concussion after more than a week to two weeks. But it's really more to try to figure out whether there are premorbid issues that may be interfering with recovery. Certainly in our kids who go undocumented as having learning disabilities or ADHD or other kinds of neurodevelopmental issues that can complicate recovery from a mild injury or account for some of the difficulties a child might be having after an injury. So I think you have to sort of grade the extensiveness of the assessment after a mild TBI or concussion

according to where they are in their recovery curve and what your goals are. I think that you don't have to worry about that quite so much with moderate to severe TBI where there's clearly a need and usually clearly deficits. It's a question of how extensive are they, and how likely are they to pose a difficulty in everyday life.

Ryan Van Patten 1:10:19
What about symptom rating scales and performance validity tests within a neuropsych battery? You find those either and both to be useful and in what ways?

Keith Yeates 1:10:29
I think symptom rating scales are actually absolutely required in all cases of TBI. And again, you won't necessarily use a traditional post-concussive symptom rating scale in moderate to severe TBI, although you certainly could. The kinds of issues that come up after concussion are also seen after more severe TBI without a doubt. I just think that any good neuropsychological assessment takes into account symptomatic presentation. One of the reasons being is that we know that our tests are not necessarily very well correlated with the symptoms that our patients tell us they have. I think there's been a tendency at times for neuropsychologists to downplay symptom reports, almost as if they don't have any validity. But from an existential perspective, they sure as hell do. They have a lot to do with how patients are actually doing in their day to day lives. And maybe we need to be a bit more skeptical about the power of our tests at times. But that's me speaking after 35 years of doing this, where sometimes you got a lot more out of listening to what your patients said their symptoms were then you did out of the testing. Although, again, to me, there's a difference between neuropsych testing and neuropsych evaluation, which is a different issue we could get into. In terms of validity testing, I think they become a standard part of practice without a doubt and deservedly so. It's funny that we tried to tell trainees to make some judgment about how hard they're working just based on watching them and sensing in my own gut that we had no idea by being able to just watch. I mean, you can see obvious indications of somebody not trying. And you can see pretty obvious indications of somebody really working hard, or what seems to be obvious. But all the gray areas in between are very hard to read. The problem, I think, is that we've become a little bit of a victim of our own success with the validity tests. I think we're tending sometimes to apply them uncritically. I tried to talk about that a bit in my presidential address, in that there are different ways to feel those things. Some of them may not actually be attributable to low effort. I think we just need to be a bit careful in how we employ them. But I think in kids 8 and up, where they actually can be used, they probably

should be used routinely. And certainly embedded indicators, at the very least, ought to be part of an overall evaluation.

John Bellone 1:12:43

Without jeopardizing test security or talking too much about the details, can you elaborate a little bit on what you said - that there are ways to fail them, that we should be a little bit more critical?

Keith Yeates 1:12:52

I mean, most of the tests, like any test that is based on a cut off, there's always going to be an error, right? There's always people that are false positives and false negatives. That applies to every testing, just like it does to any sort of testing. The likelihood of those errors goes up the closer you are to cut off, by definition. So there's a difference between - you know, just to put it at an extreme, there's this difference between somebody on any of the forced choice recognition test, which is what most of them are, that performs below chance, in fact, so far below chance it wasn't chance than the person who's just under the cut off. Just as an example, on some of the symptom validity tests, there's pretty good evidence that most populations do very well on them, but they can be actually impaired in folks with dementia or significant memory amnestic disturbance. So, yeah, it's just an uncritical application. It may be that the person who's amnestic looks a lot different, as a group or the group of people with amnestic look different on the test than folks who are actually putting forth low effort. And, in fact, there's some data to suggest that. They both fail, but their overall pattern looks different.

I think we just have to be cautious in kids, where we do have developmental differences in memory. We probably have real differences in effort that need to be taken into account. One of the things I have had very interesting conversations with Erin Bigler about - and this is where I come up against a philosophical issue - is that we know that initiative and effort and the ability to stay focused and so forth is brain mediated itself. There are certainly disorders of brain function or structure that impact one's ability to stay focused, to put forth effort and the like. So we run a bit of a danger sometimes in dismissing a set of data as invalid, when in fact, the invalidity, what looks to be invalidity, is part and parcel of the clinical syndrome. So we just have to think as clinicians rather than uncritically applying tests but I would say that's true of all of our tests. Neuropsychologists are vulnerable to being overly enamored of their tools, just like most disciplines, and we just have to be careful that we don't fall prey to that.

John Bellone 1:14:10

That's an excellent point. We're approaching the end of our time, unfortunately. But can you talk maybe briefly about a couple of psychosocial interventions for kids with mild TBI?

Keith Yeates 1:15:20

You know, there hasn't been a lot done in that area yet. There's been more psychosocial stuff done with kids with more moderate to severe TBI or with adults with concussion or persistent post-concussive symptoms. I think, actually, that's one of the areas that I hope my own research is going to tend to go here in the next couple of years is to begin to look at types of psychosocial interventions that might be helpful. Kelly McNally is a former intern and postdoc of mine, who's done some nice work at Nationwide Children's Hospital doing a combined form of treatment that involves some relaxation, some mindfulness, a little bit of CBT, and has had some nice results, I'll be it not in a formal clinical trial yet. I think the application of those sorts of interventions could be potentially pretty beneficial. And of course, I've been involved over the years with a lot of attempts to do internet based delivery of these sorts of interventions, and Shari Wade's work. I think there's some interesting possibilities for applying that sort of intervention approach to kids with concussion, where it's really hard to get them to come in on a weekly basis for interventions. I think one of the things we're struggling with in the mild TBI concussion area in terms of intervention in general, is [whether] a one size fits all approach is going to

work. Or do we need these sort of super specialized types of multidisciplinary clinics and intervention? So do we need a dizziness specialist and a headache specialist? And I don't think we know the answer to that question yet. Certainly, multidisciplinary clinics are springing up all over the place to try to make money and presumably serve their patients' needs, but I'm not sure every kid needs that sort of intervention.

On the psychosocial side, I wonder sometimes whether a broad spectrum antibiotic type of treatment that combines some of the stuff that gets more specific symptoms, with headache and dizziness being probably the most common, with a more psychosocial approach might work for the majority of kids. We have a paper coming out in Journal of Head Trauma Rehab, where we did cognitive behavioral therapy for insomnia for kids. These were teens who had sleep problems after concussion. The most interesting part of the study to me was not the fact that we helped them with their sleep because this was a validated treatment, it's been tried in lots of populations before. But what was really interesting is we saw the effects on sleep by the end of treatment. At the end of treatment, we didn't see an effect on other other symptoms. So we did a preliminary data analysis. They're like, “Oh,

shucks. Well, we fixed sleep, but we didn't have any other generalized effects." But lo and behold, when we did a further assessment a couple of months later, their sleep maintain was still better, but there are other symptoms that were better, too.

John Bellone 1:15:25
Surprisingly.

Keith Yeates 1:15:27
Well, right. I mean, at some level, it's not a surprise. But I think we tend to sometimes talk about symptoms in concussion as if they're too sociable, which is true to an extent. But it may well be that any intervention that provokes improvement in some symptom domain is going to lead to secondary improvements in a variety of domains. So it might not be that the specificity of treatment needs to be as specific as we think. But I think the jury's still out.

John Bellone 1:18:38
Yeah. And, for the listeners who want more information, we'll link to a couple of studies you mentioned - Wade et al, there's a recent paper, and there are a couple others, the internet based one you had referenced.

Keith Yeates 1:18:51
Shari's actually published at least a pilot of an intervention with mild TBI as well, although most of her work is focused on more severe injury.

John Bellone 1:18:59
Great. Well, we'll link to all those in the show notes.

Well, Keith, you've been so generous with your time, both in New York at INS and today. We really, really appreciate this.

Ryan Van Patten 1:19:08
Yeah. Thank you so much, Keith.

Keith Yeates 1:19:10
You're welcome. I enjoyed it, and I hope you get lots of listeners.

Ryan Van Patten 1:19:13
[laughs]

John Bellone 1:19:13
Yeah, we already have. Your INS New York episode did quite well.

Ryan Van Patten 1:19:18
Yeah. Yeah.

Keith Yeates 1:19:19
Glad to hear that. I suspect most people are listening to help them get to sleep.

Ryan Van Patten 1:19:23
[laughs]

John Bellone 1:19:23
[laughs]

Ryan Van Patten 1:19:25
Whatever benefit we can provide. [laughs]

John Bellone 1:19:28
That's a service maybe for all those mTBI people, they can improve their sleep. [laughs]

Keith Yeates 1:19:33
[laughs]

Ryan Van Patten 1:19:34
Thanks, Keith.

John Bellone 1:19:35
Thanks again.

Keith Yeates 1:19:35
You're welcome. Take care. Talk to you later. Bye bye.

John Bellone 1:19:39

Well, that does it for our conversation with Keith. As always, join us next time as we continue to navigate the brain and behavior.

Exit Music 1:19:46

John Bellone 1:20:10

The Navigating Neuropsychology podcast and all the linked content is intended for general educational purposes only, and does not constitute the practice of psychology or any other professional healthcare advice and services.

Ryan Van Patten 1:20:21

No professional relationship is formed between us, John Bellone and Ryan Van Patten, and the listeners of this podcast. The information provided in Navigating Neuropsychology in the materials linked to the podcasts are used at listeners' own risk. Users should always seek appropriate medical and psychological care from the appropriate licensed healthcare provider.

End of Audio 1:20:39