106| Sport Related Concussion – With Dr. Michael McCrea

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Speakers: Michael McCrea, 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 00:26
…and I'm Ryan Van Patten. One quick announcement before we get into today's episode, we now have a link on our website to a brief 10 minute survey on psychologists' attitudes and practices concerning teleneuropsychology. The

researchers who created this survey are interested in hearing from any and all licensed psychologists who provide neuropsych assessment even if you don't use teleneuropsych. Profession-wide surveys on important topics such as this one can really drive the field forward in important ways. This survey could inform advocacy for organizational and managed care support for teleneuropsychology, and it could inform issues such as insurance reimbursement for telehealth in our field. Again, the survey only takes about 10 minutes and you can find it at navneuro.com at the bottom of our landing page.

John Bellone 01:17

Today we speak with Dr. Michael McCree about sport-related concussion. Mike is Professor and Director of brain injury research at the Medical College of Wisconsin. He's also a board certified clinical neuropsychologist and the past president of AACN. He is an internationally recognized expert in sport-related concussion and a great person to talk to about this topic. We touched on sport concussion and children back in episode #27 with Dr. Keith Yeates, but we had only spent a few minutes on it back then and there's a lot to cover on this topic.

Ryan Van Patten 01:52

Even spending an hour and a half with Mike didn't allow us to cover everything relevant in sports concussion. We focused primarily on definitions, pathophysiology, recognition and diagnosis, biomarkers, evaluation and retesting, recovery, rehabilitation, and return to sport following an injury. We did touch on long-term effects, but only very briefly at the end. We plan to record a future episode covering the literature on long-term effects of repetitive neurotrauma. We would also like to release an episode covering the 6th International Consensus Conference on Concussion in Sport, which just took place a few days ago in the Netherlands in Amsterdam. Everything we cover with Mike is absolutely up to date in terms of the current state of the science, but we recorded the episode a few weeks prior to the recent conference so we didn't review new updates from the Concussion Sport Group.

John Bellone 02:48

It's also important to mention that sport concussion is a highly public and rapidly evolving area. We recorded this episode just prior to the controversy in the NFL about the handling of head impacts sustained by Miami Dolphins quarterback Tua Tagovailoa, so we don't discuss it directly here. But much of what we cover is highly relevant to decisions made about return to play and recovery following head impacts like those sustained by Tua. Just one final caveat: The INS does not promote or recommend any commercial products that are mentioned in this episode. And, with that, we give you our conversation with Dr. Mike McCrea.

Transition Music 03:29

John Bellone 03:38
Right. Dr. McCrea, thanks so much for joining us on NavNeuro. We're so excited to have you here.

Michael McCrea 03:42
Thanks for having me. I'm delighted to be here with you.

John Bellone 03:45
This is a big topic. Let's start by first defining sport-related concussion or SRC. The Concussion in Sport group consensus statement and the American Medical Society for Sports Medicine physician statement, they've both had a big influence on the field and will help to guide our conversation. These documents both include definitions for SRC, and both of the definitions acknowledge that it's a type of traumatic brain injury, or TBI, which most closely resembles mild TBI. Obviously SRC is sport-related, which differentiates it from non-sport TBI. Some other key aspects of SRC are that the injury is traumatically-induced, it results from biomechanical forces, is associated with a complicated pathophysiology, and it results in clinical signs and symptoms as opposed to so-called “subconcussive blows”, which generally don't. How would you define SRC for us and how do you talk about it in relation to TBI more broadly?

Michael McCrea 04:48
I think that's a great place to start, John. To some extent you've done my job for me, I think, on the definition side but there's an element here that I don't want to leave behind. And that is this conceptual understanding or framework as to where does sport-related concussion fit in the overall rubric of traumatic brain injury. I'm stuck on that just for a second here, if you will, because over the past 30 years that has been all over the place including, believe it or not, some discussion along the way that that was lending itself to the notion that maybe sport-related concussion should just be parked over on the side and removed completely from the rubric or classification of traumatic brain injury, which I think all of us in the in the brain injury medicine and and scientific community thought would be a bad idea but, nonetheless, it was in play there for a bit.

But, let's start with that overall definition of traumatic brain injury and then start to hone in on sport-related concussion. So, as you mentioned, TBI is a traumatically induced injury. It's acquired as opposed to other forms of "brain injury" that are

talked about in hospitals and other clinical settings. The diagnosis of traumatic brain injury, whether you're in civilian, military, or sport medicine, is to a large extent based on clinical assessment of signs and symptoms. Modern day classification systems then build into the classification of TBI additional diagnostic studies like head CT, like MRI, and now that we'll talk about later on, I think, in our discussion here, even the advent of more objective blood and fluid based biomarkers. But really the tried and true right now is the classification of TBI based on clinical signs and symptoms.

Many of your listeners, I'm sure, are familiar with the Glasgow Coma Scale score, the GCS, which has a range of 3 to 15, 3 being the most severely injured patient who's obtunded and in deep coma and 15 being a patient who is maybe slightly confused or had a temporary alteration of their mental status, but for the most part, they're neurologically intact. They're conversational and they're generally coherent in the emergency department. The subclassification of TBI is a GCS of 3 to 8 is considered severe. Nine to 12 is considered moderate, and GCS 13 to 15 is classified as mild. Let me pause there and say, in 2022, it's a little embarrassing for us that the best we can come up with in traumatic brain injury is mild, moderate, or severe, right? Imagine that in the context of cancer or other disease states where they have been incorporating really multidimensional objective biological metrics to classify disease for a long time, but we've just never really gotten off the dime. There are movements afoot, literally, as we speak to come up with improved classification systems for TBI, but for our purpose this afternoon here we're really talking about GCS 13 to 15 classified as mild TBI.

Some systems also incorporate defining characteristics on presence or duration of loss of consciousness, post traumatic amnesia, and then they subdivide that mild TBI cohort into "complicated or uncomplicated." I want to take a second here and pay tribute to a real pioneer in neuropsychology and in traumatic brain injury, Dr. Harvey Levin, who unfortunately passed away earlier this year. Harvey has had a hand in so many advances in traumatic brain injury research, they're countless. I think he probably deserves the credit for the nomenclature around complicated versus uncomplicated mild TBI, which has become commonplace in research and clinical practice for 40 years. I had the opportunity to work side by side with Harvey over the last several years and just a brilliant man. Better person than a scientist, which is saying a lot. He'll be dearly missed. But one of his contributions, again, in mild TBI was this concept of “complicated” meaning identified abnormalities on head CT or brain MRI, versus “uncomplicated” or those with "normal" neuroimaging. We'll come back to how that line has moved between complicated and uncomplicated with our research and in recent years. Then within the confines of "mild TBI" lives this construct of concussion. Really, the two terms are interchangeable.

We do know that all concussions are not created equal or all mild TBI are not created equal based on their severity but also based on their population. Your common sport-related concussion, I think most would agree, are really amongst the mildest of the mild. If we've gone from TBI to mild TBI, your conventional or customary concussion patient or in this case athlete, those injuries really land at the mildest end of the mild category or continuum, which then has implications for the projected recovery trajectory for those patients and their overall outcome. We know, for instance, that even all mild TBIs in the civilian sector are not created equal. If you've got a group of patients with GCS 13 and half of them are CT positive, that's a lot different than a clinic sample of all GCS 15s and everybody in that cohort being neuroimaging normal. So it matters. We can't just lump all mild TBI into one population. It matters based on population, it matters based on severity whether you're talking about civilian, military, or sport-related mTBI.

Ryan Van Patten 11:34

The spectrum within mild TBI, within concussion, thanks for highlighting that. We'll spend a lot of time today when we're thinking about sport concussion and the clinical symptoms - relevant to us as neuropsychologists. But let's start with the pathophysiological cascade for a few minutes. There's been a lot of animal work on this issue. Assuming that an athlete has a sport-related concussion with some acute symptoms, but no brain bleeds, skull fractures, no other neuroimaging findings, what can you tell us generally about metabolic, inflammatory, axonal, and any other common brain pathological changes due to sport concussion?

Michael McCrea 12:12

Well, you're absolutely right. There's been extensive preclinical work and animal models. The extent to which they truly apply to the pathophysiology of sport-related concussion, or as I said earlier, the mildest of the mild, I think, is appropriately been open for debate. Like your conventional preclinical models of TBI, whether that be cortical impactor or percussion models, it's hard to dial down the severity of those without focal lesions and to achieve really the equivalent mechanism of sport-related concussion, albeit in an animal model. But certainly outstanding researchers and groups around the world have made progress toward that in the last three decades or more. You're absolutely right, that there's - this what David Hodgson and Chris Giza at UCLA, really pioneers in TBI and concussion research, coined as the "neurometabolic cascade". The sequence of alterations and functional changes at a cellular level where there's a really drastic shift in ion exchange energy level in the brain and the normal balance and function of neurotransmitters that was typically considered a sequential functional process that

rendered neurons as temporarily dysfunctional, and then it was a reversible phenomenon, coinciding with with neurobiological and clinical recovery.

The good news is we now have advanced technologies through imaging, blood-based biomarkers, etcetera that allow us to transfer that work for decades in preclinical TBI models that had a whole host of pathological hypotheses for concussion and TBI and study that in more real time in humans. We now have the ability to instrument athletes, for instance, with head impact measurement technology that tell us about the magnitude of rotational and translational forces applied to the head that caused the incident injury, or the accumulation of maybe moderate magnitude blows that an athlete sustains during the course of a rugby game or football game. Then our work really has focused on applying advanced imaging and blood-based biomarkers to look at the neurobiological effects of injury within that super acute window, the first 48 hours for instance, and then tracking the time course and trajectory of of neurobiological recovery in athletes and service members and civilians affected by TBI and, in particular, mild TBI or concussion. That work really had nice alignment with, again, the preclinical work and these candidate pathologies of mild TBI and concussion in preclinical models and how it plays out in our imaging and biomarker studies.

John Bellone 15:42
What do we know about the epidemiology of sport-related concussion? How common is it?

Michael McCrea 15:49
Well, concussion is highly common across the general population. We know that athletes participating in contact and collision sports are at particularly heightened risk, as are military service members. But, you know, depending on what epidemiologic source you're referencing, a significant portion of the general population, maybe a quarter to up to a third, have sustained at least one concussive injury in their lifetime. When you start to think about your own experience - your family, your friends - you're like, "Oh, yeah, that bears out," right? Fall on the ice, bicycle accident, trampoline, you name it, gym class - it really affects people of all ages, pediatric, adult, and geriatric in the general population.

Then, certainly, if you start to peel the onion in sport, you can categorize sports into non-contact, and that definition has changed over the years. Non-contact sports are like golf, cross country, whereas sports like basketball are really a limited contact, it's not entirely without contact and when contact occurs, it's usually incidental and not an intentional part of sport. Then, certainly, as you move into high contact or collision sports like American football, soccer, rugby, ice hockey, lacrosse, wrestling

that have a more physical and contact basis to them, that's where we see the highest incidence of concussion. The results are fairly consistent in terms of the highest risk sports for concussion at all competitive levels.

Obviously, for the reasons I just cited, if collision and contact is an inherent part of sport, those sports are certainly going to come with a higher rate of concussion. In studies of American football, for instance, when we do large baseline enrollment of collegiate or high school athletes, somewhere between a quarter and a third of those have sustained at least one prior concussion in that sport of interest, in football for instance, and the same for hockey and otherwise. We know that it's common, really, at all competitive levels from professional to collegiate to high school and pre-high school youth sports. Certainly not confined to males playing American football. There are papers out there indicating that, in fact, rugby, which happens to be a rapidly growing sport for boys and girls here in the US, carries the highest rate of concussion.

Then, lastly, I would add that there's been some reference to that there's an epidemic of concussion out there with steep increases year in and year out. That really is not borne out in the data. Certainly, we have better surveillance systems and athletes are more likely to come forward, but, I think, some of the epidemiologic research out there has indicated that these rates of concussion have been relatively stable.

Ryan Van Patten 19:09

Let's talk about the initial recognition and diagnosis of sport concussion. Of course this will vary to a great extent based on different sports, but if you can use examples and if you can summarize what this looks like for us. So first, tell us about the identification of on-field head impacts that raise concern for sport concussion. This can occur both in real time and based on video surveillance - so there's an observed head impact of some kind and then we're looking for particular signs of sport concussion, some of which are more common than others. We might think of, obviously, loss of consciousness, but also motor incoordination, a convulsion, self-reported symptoms like headache, dizziness, neck pain - we could go on. So talk about broadly the concussion surveillance process across these different sports.

Michael McCrea 20:00

As you can imagine, that's really dependent on resources and the structure in which sport occurs. If you're at your 10-year-old daughter's elite soccer game, certainly grandma and grandpa might be videotaping on their iPhone but you're not going to have broad systems in place for injury surveillance. Some high schools with more

resources might videotape football practice. Certainly most schools are videotaping or streaming their football games or other sporting events. Then there's far more resources in place at the collegiate and professional level. In the NFL, for instance, there are multiple layers of surveillance, including dedicated personnel in the booth, elevated above the field of play, where they can see all 22 players on the field. Their job is to run surveillance and identify high impact collisions or, frankly, anything else that would trigger a call down to the sideline and prompt at least a discussion with the medical staff and the athletic training staff on the sideline, potentially prompting the screening and evaluation of an athlete that takes place not only with the team medical staff but also unaffiliated, independent medical staff appointed by the NFL that are involved in the evaluation and disposition of any athlete with suspected concussion, including the the determination of fitness to return to play the same day or the disqualification of an athlete. Now, you're not going to have that in youth sports, obviously. That said, when I think back to when we first started researching sport concussion in 1994, the level of awareness across all stakeholders, athletes themselves, athletic trainers and other clinical staff, coaches, administrators, parents, sport governing bodies - it sounds bizarre, but when we got involved in this in this space and this subject matter, no one was even out there talking about concussion in sport. Maybe the best indicator of that is that the term you're using today, "sport-related concussion" did not exist. I think Kevin Guskiewicz and I and maybe some others were the first to coin that phrase because in writing papers, we just needed some sort of efficient way to communicate what we were talking about. But that phrase, that terminology, did not exist 30 years ago. Now it's it's really common household discussion between parents and their kids who will participate in sports. It's common in the curriculum for athletic trainers, sports medicine professionals, clinician scientists in the neurosciences, and certainly within our own specialty of neuropsychology. So, we can talk about big technology, resource intensive systems that are used for surveillance and professional sports, for instance, but at the same time, I would argue that the whole world is on alert and keeping a watchful eye for the possibility of concussion during practices and games and then implementing an entirely different approach to assessing those athletes and ensuring their safety through participation in sport.

John Bellone 23:58

I want to talk more about the assessment piece and also management and prevention of it. Once a potential concussive event is identified, the athlete should be withdrawn from play and evaluated. This is something that has changed over the years for sure. That process of pulling the player off the field to do a sideline assessment with them, it's often performed using the Sport Concussion Assessment Tool, or SCAT, currently in its 5th edition. The SCAT's designed for adolescents and adults ages 13 and up, while the child SCAT is for children ages

12 and under. Sideline evaluations typically assess for red flags for a serious brain injury, for cognitive functioning, for cervical spine issues, acute symptoms like headache, irritability, etcetera, also neurological vestibular functioning. Can you tell us more about what the sideline evaluation looks like?

Michael McCrea 24:57
Sure, happy to. This might seem as a bizarre reference point for your younger audience members, but quite literally, this was not a Bugs Bunny episode, the standard of care in concussion assessment 30 years ago, maybe even 20 years ago, was literally, “How many fingers am I holding up?”

Ryan Van Patten 25:21
[laughs]

Michael McCrea 25:22
And, “What's your name? Where are we?” I played a lot of sports in high school and college and so forth, including football, and that was my experience. If you were assessed at all, often was not the case, but if you were assessed at all, it was very cursory and a blunt assessment. Because, again, the recognition of this as an injury of any seriousness that would prompt a really urgent decision about removing you from play was really not the mindset at that time. So, um, let me see here. In 1994, I think it was, I was a neuropsychology fellow at Northwestern in Chicago and my mentors at the time, Dr. Chris Randolph, also a neuropsychologist and Dr. Jim Kelly, a behavioral neurologist, all three of us at Northwestern at that time, we literally, and this sounds cliche but it's the truth, we literally scribbled on a napkin one day having lunch the idea of a sideline achievable assessment, a cognitive screening tool for concussion, and we we called it the Standardized Assessment of Concussion. Basically, we took validated approaches to cognitive testing - if you can imagine at that time, common outpatient neuropsych assessments were all day 8-hour evaluations and our sports medicine colleagues, were telling us, "This is a great idea, but if it takes more than 5 minutes, no one's ever going to do it." So we derived a brief orientation test of five questions, a very brief repeated list learning paradigm, word list memory, an orientation test of reverse digits and months of the year in reverse order, and then a delayed recall of the word list learning task. We started studying it, collecting data, both normative and postinjury data. Again, this was really confined to a cognitive screening tool, the SAC, but at the same time, there were symptom checklists being developed out there. Over the years, that “standardization movement” is, as I've called it, has included not only symptom checklists and this cognitive screening tool, the SAC, but also a visual-ocular motor screening, balance tests, and other approaches to standardizing clinical assessment. That really is the backbone of the SCAT, the Sport Concussion

Assessment Tool, now in its 5th and soon to be in its 6th iteration. It's intended as a multidimensional approach that includes, at the very least, symptoms, cognition, balance, and neurologic, including ocular-motor function. It's proven to be, I think, not only highly effective but striking a terrific balance. Certainly, you need a tool with adequate sensitivity and specificity for clinical use and to drive decision making, but, as I said before, it also has to take into consideration really intense situational constraints, right? We're not going to be taking the Wisconsin Card Sorting Test to the football field sideline.

Ryan Van Patten 29:02
[laughs]

Michael McCrea 29:03
By the way, there is a parallel tool called the MACE, the Military Acute Concussion Evaluation, that is used in the austere environment of military conflict and the field of training. It really requires striking an excellent balance between maximum clinical rigor and utility and also the pragmatic considerations of testing in the field, whether that be in sport, military, medicine, or, for instance, the emergency and critical care setting of hospitals and so forth.

Ryan Van Patten 29:41
Thank you. Yeah, so you reviewed the SAC, the Standardized Assessment of Concussion, and its early development. Just to review for our listeners, cognitive functioning is a really integral part of the SCAT, the overall instrument, a sideline testing for concussion. The instantiation of that is the SAC, which has orientation, immediate and delayed memory of a word list, as you mentioned, a few tests of concentration and working memory. Can you speak for a few minutes to the SCAT, including sport-specific orientation questions, the Maddocks questions, and why we need the sport-specific questions rather than our conventional person/place/time questions of orientation?

Michael McCrea 30:21
Yeah, really good question. David Maddocks actually developed that question set around the same time as or maybe shortly after we developed the original SAC in 94 or so. The basic answer to your question is you're trying to increase your signal detection. As I mentioned earlier, sport-related concussion is, I think, commonly considered appropriately as the mildest of the mild in that spectrum of all severity brain injury, which means that the signs and symptoms are also going to be among the most subtle of any signs and symptoms reflective of traumatic brain injury. So, essentially, everybody who is a GCS of 15 with concussion can tell you their name.

They can tell you where they are. They can tell you how many fingers you're holding up unless they have some really focal visual-ocular motor deficit. But we had to raise the signal detection capability and therefore, you're asking sport- and situational-specific questions. "Who scored last?" Some assessments have even asked, "On a certain play, what's your assignment?" Now, that requires somebody from the coaching staff to confirm because otherwise the player can just make it up, but moving beyond really just the most basic questions to questions that are of somewhat more difficult fashion. It proves to really be more effective in drawing out the subtle deficits.

Ryan Van Patten 32:05

People might be wondering what this looks like to have a SCAT administered. Just as an example, in American football these days, we now on TV see a player have a potential concussion, a head impact, and then they disappear into the tent. A lot of us watching [the game] see that and don't know what's going on in there. So describe in some of these professional sports that have the resources to do formal surveillance and testing what it looks like to do a sideline SCAT.

Michael McCrea 32:34

So there's the SCAT, which, as you mentioned, is the tool that was developed by the Concussion Sport Group and now has undergone several revisions. I think, as we said, the SCAT-5 is currently in use and it will likely be followed by a SCAT-6 after the CISG meeting next month in Europe. But there are customized iterations of this. For instance, the National Football League has made some modifications to the conventional SCAT based on their unique needs. But all of these tools have a similar framework: multidimensional, assessing symptoms, cognition, balance, neurologic function, and so forth in screening form in a way that can be conducted in the field. In professional sports, whether that be the NFL, the NHL, the NBA, any player with suspected concussion requires evaluation to confirm or rule out the diagnosis of concussion. If they have suspected concussion, they are then disqualified for the day. I can tell you from my own experience in the NFL as a neuropsychology consultant, the game day evaluation is conducted on a tool very similar to the SCAT, but this is a tool that the NFL refined for their specific purpose in evaluating players on game day. If there's a message down from the booth, for instance, from the eye in the sky that we talked about earlier, that would indicate the need for clinical staff on the sideline to at least engage with the athlete in question, determine whether or not they're experiencing any abnormalities. Many times that happens and there's really no indication of injury at all, but better safe than sorry. If there's a need for clinical evaluation, clinical screening, oftentimes there is a dedicated private area on the sports sideline and you'll see this in collegiate athletics now too, to protect the privacy of the athlete and allow this assessment

take place without distraction of the crowd and the busyness of the sport sideline. So, in the NFL, that's the blue tent that most people are accustomed to. That initial screening takes place in the blue tent. If there is reason for concern that there's the possibility of concussion, then that athlete is required to be removed from the sideline and evaluated in the training room, again away from the distraction of the sideline and the crowd at the event. The same principles apply if injury occurred at practice, for instance. I think for your audience, they probably get their arms around this more readily talking about a game situation. It's then in the training room where this detailed evaluation takes place using the NFL tool akin to the SCAT. That evaluation takes place by the medical staff for the team and by the dedicated unaffiliated neurotrauma consultant that is independent of the club but is integrally involved in the evaluation of the athlete and the determination of whether there's a diagnosis of concussion and whether or not that athlete is either fit to return to play the same day because concussion has been confidently ruled out, or whether or not that athlete should be disqualified from returning to play the same day. So it's a very protocolized and standardized process, which, as you can imagine, is drastically different than how we used to evaluate and manage concussion in all areas of sport 25 or 30 years ago.

Ryan Van Patten 36:57

Sport concussion symptoms are typically present immediately after the head impact, but sometimes they can be delayed and the sport concussion clinical syndrome can evolve over time. So serial assessments can be important. What should we know here in terms of when and how often to perform assessments, which measures to use, and psychometric issues like test-retest reliability, reliable change, practice effects?

Michael McCrea 37:23

Good questions. I think there there's several questions to unpack there. The first, you're absolutely right, and I think this sometimes gets lost, but certainly the most common scenario of concussion - I mean, there's a lot of discussion about delayed symptoms and delayed reporting, but the most common scenario of sport-related concussion is incident injury or mechanism occurs, the athlete is showing signs or symptoms immediately, and those symptoms are commonly headache, confusion, dizziness. We've all seen these, right, during that acute, immediate window. But you're also right that there are at least two other scenarios or pathways that might evolve. The first is the delayed reporter. There have been multiple published studies indicating that a segment of athletes, either due to the very subtle nature of their symptoms or their lack of awareness that what they're experiencing might be representative of the signs and symptoms of concussion or, thirdly, motivational factors because they don't want to be removed from play. At any rate, regardless of

cause, we do know that there's a sizable segment of athletes who don't report their injury until oftentimes the next day. Again, I want to stress that it's not always the case that these athletes are lying to us just to return to play. In fact, that's not always the case. But nonetheless, we know that some athletes will show up in the training room or report to a parent the next day that they're sick to their stomach, they've got headache, dizziness, other common symptoms of sport-related concussion that were from a sport participation encounter the prior day or earlier in the day. This is an important development in the research in recent years. There have been multiple papers now from our group and others indicating that those late reporters end up with a longer trajectory of recovery and to return to play. So what I call the currency exchange then in communication with athletes is, “Listen you playing the "wait and see game," number one, is really not a good idea clinically. There is the possibility that you could have something serious going on and you want to report that as soon as possible.” But even if we take the public health aspect out of this and we talk strictly from a competitive advantage, which is really the language that most athletes speak, “Coming to us sooner is going to result in you returning to play sooner. So it's in your best interest to come forward, report your injury, then we get you in the pathway of treatment and rehabilitation, get you back on your feet, and with a safe return to play sooner than if you would have taken that "wait and see" approach to it.” So that's the late reporter.

There are also reported instances of delayed onset of symptoms. That's been debated over the years. I think, oftentimes, athletes are in a very high adrenaline rush during the heat of a sporting contest. They're not really in tune with what their body might say. This, by the way, isn't confined to concussion, right? There are all sorts of injuries that show up well after a sporting contest when things start to calm down to a normal pace and cadence and they notice that their shoulder or, in this case, their headache is persisting and might be indicative of underlying injury.

Ryan Van Patten 41:31

You had alluded to this earlier, I'd like you to briefly tell us about the current state of the literature in terms of impact monitors like helmet-based or other sensor systems to assess for sport concussion. The last I heard there was not yet good enough evidence to support these systems as impact monitors clinically, but there may be updates since then.

Michael McCrea 41:51

I'm really not aware of any instances where these technologies are being used clinically for injury surveillance purposes. These are strictly research tools. The history and performance of these has been up and down. That's not a knock on the people who have invented and tried to optimize these technologies. This is just an

indication of how hard it is. I've lived through this in the last 20 years where, you know, we want it all. We want a gadget, ideally, maybe no bigger than a nickel. And wearable, so that the athlete doesn't have to do anything special in order for this to work. It has to be accurate. It has to be field deployable. It has to operate on a battery that lasts multiple hours with either Bluetooth or some other mechanism to transmit data in real time. You're talking about an incredible set of wishes that are very difficult to achieve. And then, oh, by the way, it has to be resistant to sweat. It also has to differentiate “real impacts” - and I'm using air quotes there for your audience - “real impacts” from clacks, for instance, where, "Well that was just from me setting my helmet down on the bus", or "That was me jogging and maybe the sensor was being jostled on my skin, in my mouth as a mouthguard, in my helmet." There certainly have been advances. We have used the system called the Head Impact Telemetry System, which has proven to be, I think, the most widely used and credible platform but it only exists for football helmets so the ability to use it in other contact inclusion sports was not there. Other really smart people around the world have attempted to move this technology into wearable sensors, either adhesive patches, headbands, or mouth guards. Then you face a whole assortment of challenges in compliance among athletes, like "Hey, that mouthguard is way bigger than I like and, therefore, I'm not going to wear it." I mean, we're talking about a group of people who how high their socks are versus how low their socks are matters on game day. If we're asking them to wear something that cramps their style, they're just less inclined to do so. It really is proven to be very challenging.

John Bellone 44:28

I'm also curious about the current evidence for fluid biomarkers in diagnosing SRC, which you also had alluded to earlier.

Michael McCrea 44:56

The work in blood-based and fluid-based biomarkers has really been on a pretty incredible trajectory over the last 10 years. Now, let me preface this by saying that no one, not I nor anyone I know, is out there suggesting that anytime soon we're going to be using blood-based biomarkers to "diagnose" brain injury or concussion. But let me just zoom out a little bit and talk about the study of blood-based biomarkers in that all severity spectrum of TBI. The identification of candidate biomarkers and assays, Ryan, was really built off some of that preclinical work that you were referencing earlier where we know, for instance, that axonal injury is really the common suspect in traumatic brain injury in terms of pathophysiological mechanisms. But there's also inflammation and astroglial injury, neuronal cell body damage, again, in more severe forms of TBI. A number of groups around the country and around the world have been identifying blood-based biomarkers that would map on to those common pathological mechanisms of TBI, developing

assays to test them in humans, to test levels of these specific biomarkers, and then conducting clinical validation studies including our group over the last decade or so. Honestly, if you'd have told me 15 years ago, or even 10 years ago, that the performance of these blood-based biomarkers would be as favorable as it is, I'm not sure I would have believed it. But there are a number of blood-based biomarkers that show really steep elevations rapidly within hours after TBI and then most of which have a fairly rapidly diminishing signal over a period of days to weeks post injury. These biomarkers have proven really, highly reliable and valid for instance in differentiating people with traumatic brain injury from trauma controls and healthy controls, while also at a very high accuracy having favorable positive and negative predictive value in and identifying abnormalities on head CT. So one instance of the potential utility is the thought that these simple blood tests could prevent a lot of unnecessary head CTs, which is particularly a big deal in children where radiation exposure is an issue early in life. This work - and again, a lot of it from like the TRACK-TBI study led by Geoff Manley, a trauma neurosurgeon at University of California, San Francisco, and really that group is done pioneering work in all aspects of TBI including biomarkers - where these these biomarkers actually within the first 12 hours of injury proved to have greater diagnostic sensitivity than head CT or even brain MRI, such that they show really significant elevations of GFAP UCHL1 and other acute TBI biomarkers even in a sample of TBI patients who are both CT negative and MR negative, which is pretty amazing. I've had the privilege of being part of the TRACK-TBI effort and the CARE Consortium as well as other studies. The CARE Consortium is the twin sibling of TRACK-TBI but it's focused on mild TBI and concussion in NCAA student athletes and in military service academy cadets. We've enrolled over 60,000 participants in the study and have post-injury data on over 6000 of them, including blood and imaging on several 100 athletes and service members affected by concussion. This is work that I have the privilege of co-leading with Steve Broglio at Michigan, Tom McAllister at Indiana, and Paul Pasquina at the Uniformed Services University, it's been ongoing since 2014. In the biomarker core, we were interested to interrogate whether these high performing blood-based biomarkers from the civilian TBI research setting, patients with more severe grades of injury, would translate to what we called it earlier the mildest of the mild athletes with sport-related concussion. And with the added luxury in this case, we get blood on these participants at time of enrollment, so we have an individual level on each of these participants pre-injury. We published a paper in JAMA Neurology just not long ago - I'm sorry, in JAMA Network Open not long ago, a series of papers indicating, sure enough, spike elevations in these blood-based biomarkers, predominantly GFAP and UCHL1 in athletes with sport-related concussion and military service members who are injured in the line of military training but all of whom have GCS of 15, they're all imaging negative. But, in fact, they show really spike elevations on these blood-based biomarkers within the first 6 to 12 hours that have varied trajectories of recovery and return to normal levels

over a period of days in most instances. The research on validation of these biomarkers has made really enormous progress in the last five years, especially. The name of the game now is clinical translation. You can do everything right in discovery and validation and optimization of your biomarkers to maximize sensitivity and specificity, particularly in positive and negative predictive value but until you have a point of care option to do this in the field, your clinical utility is really limited. There is work underway right now and in partnership with Abbott Laboratories and other groups around the country and around the world to move these biomarkers into a point of care platform where you can use a handheld analyzer, for instance, do rapid assessment of these biomarkers either using serum or, better yet, would even be whole blood to conduct these in the field - whether that's an EMTs in a trauma setting, military medics in the field or the austere environment, or as we're talking about today, in sport. Again, I want to close this where I opened it and make clear that I'm not saying that any time in the very near future we're going to be using a blood test to diagnose concussion on the sports sideline. Number one, that technology is not ready for primetime and number two, blood-based biomarkers, like imaging, like other biomarkers in other areas of medicine, these are meant to augment diagnostic confidence. They're not to replace the clinician or clinical assessment and judgment. But in the setting of mild TBI and concussion, we have forever longed for some objective marker that I can incorporate into my assessment along with the subjective report of the athlete or the patient and my results from clinical testing, for instance. It's moving in an incredibly positive and accelerated direction, but we've got a little ways to go yet before we can translate this to clinical practice.

John Bellone 53:26

Those are all good caveats but it is something that we can look forward to in the future. Good. I want to talk about the utility of baseline evaluations. These would be evaluations completed before the season, presumably when an athlete is healthy and at their peak functioning. Establishing an athlete's own personal baseline might allow for within-person comparison when the same tests are then later administered after a sport-related concussion. For neuropsychologists, cognitive baselines are something that we think a lot about, but from your perspective, under what circumstances are baseline testings useful?

Michael McCrea 54:07

Great question. As neuropsychologists, we are often handcuffed on not really having a great understanding of where our patients started, and that isn't confined to TBI. If you think about neuropsychologists who evaluate patients with stroke, with traumatic brain injury, with brain tumor, with multiple sclerosis, Alzheimer's disease, there's always this nagging question about, "Where did this person, where was their

starting point?" Certainly we have academic achievement tests and measures of premorbid function, but then we've got Jimmy's mom who's saying, "Something's wrong. He had a photographic memory before this happened". Where is ground truth? Well, in most clinical settings, that's just not achievable. Nobody walks into an emergency department with their original Wechsler scale score on the back of their driver's license, for instance.

Ryan Van Patten 55:18
[laughs]

Michael McCrea 55:20
Early on, Jeff Barth, I think, could be credited as being the father of this movement in sport concussion. Jeff Barth and his partner in crime, Steve Macciocchi, at the University of Virginia back in the early 90s, identified what they later called the SLAM model, Sports Laboratory Assessment Model. The cornerstone of it was, we have a readily available cohort that we know to be at-risk of eventual concussion. Why don't we evaluate them before their injury? They're readily accessible to us, they're identified, and we know, in a football setting for instance, if we evaluate them in July, we know that somewhere between 5% and 10% of them are going to sustain a concussion in the next four months. So the baseline assessment model was born. Then several others around the country followed suit in their research, the sport concussion research model for years with the intention of establishing a baseline for research purposes against which to track the effects of injury and measure the trajectory of and time course of recovery. I think a real credit here to neuropsychology is that, over time, that was adopted as the clinical model. So again, early on, it was really intended for research purposes but then athletic trainers and other clinicians in sports medicine realized, "Well, why don't we just do that as our clinical system of care at our school, with our club, for instance? That gives me more confidence as a clinician, because there's a lot of variability in the baseline abilities of athletes, even at the same age, at the same school and, therefore, if I'm really wanting to maximize the accuracy of my assessment of an individual athlete, it would be good for me to know what their starting point was." That movement was really extended beyond the research arena and became the clinical model of care in sport concussion. Now, not every youth sport organization in the world can afford the resources to do baseline testing, but they can at least do a baseline symptom checklist on their athletes and now there's been the advent of computerized assessment modules for sport concussion over the past several decades.

Ryan Van Patten 58:14

If a concussion is not diagnosed on the sideline, then clearly the athlete can be cleared to play. But as you referenced earlier, if a concussion is diagnosed or even strongly suspected, continued participation in sport can be associated with slower recovery and worse outcomes. So if there's a concussion, the athlete should not return to play on the same day. The old recommendation after a sport concussion diagnosis was this prolonged rest in a dark room. But, fortunately, we now know that that's not the best model. This idea of subsymptom threshold aerobic exercise can actually potentially improve recovery after sport concussion. Take a step back for us and talk about this graduated stepwise return to sport strategy from the Concussion Sport Group. Briefly describe the full model and then elaborate on any of the details that are relevant.

Michael McCrea 59:07

Yeah, Ryan, it's been a wild ride...

Ryan Van Patten 59:12

[laughs]

Michael McCrea 59:12

...over the last 25 years with just crazy twists and turns along the way, including, if I can just give a quick snapshot here. In a matter of 15 years or so, starting maybe 25 years ago, we literally went from basically doing nothing, oftentimes not even diagnosing concussion and certainly not any regimented or protocolized approaches to injury management, to then all of a sudden this this crazy concept of what some people were coining as "cocoon therapy" where we were going to put people in a box and and advise total physical and cognitive rest. We never did that, but there were people out there who surely were prescribing that approach, which was counter to essentially everything in medicine, including preclinical studies of TBI. But, you're right. Over time, the research has really supported this contemporary approach to after assessment and diagnosis of concussion. And, by the way, this isn't restricted to sport. This applies in civilian medicine and military medicine. But if we've got an individual, in this case an athlete, with acute concussion, certainly we recommend - well, removal from play the same day is mandatory. Believe it or not, that mandate is not very old. It was maybe only 15 years ago that that started to make its way as a mandatory requirement in sport concussion. If we go back 30 years, there were guidelines that suggested that if you had a grade 1 concussion, you could return in 15 minutes. Returning to play the same day was very common. We published studies back in the early 2000s, indicating that many players returned the same day, an even higher percentage of

them were maybe withheld from play for one day. That has changed dramatically, again, based on the research indicating that, really, the recommended approach now is a brief period of total rest. Usually it's in the order of a couple of days to a point at which symptoms have either resolved or they are stable, meaning they're not getting worse. At that point, we begin to introduce very low intensity, short duration exercise - walking. But the notion of someone having complete cognitive and physical rest for any extended period of time is, thankfully, history and gone by the wayside. Contemporary approach is once that return to play protocol is initiated with, again, very low intensity, short duration exercise. Each day the time and intensity of exercises is throttled up slightly day by day as the athlete is able to tolerate without any recurrent or worsening symptoms. Obviously, all of this is happening in a noncontact setting. Day by day, we then ramp up the time and intensity of exercise based on their heart rate, capacity, and so forth to a point where once we get to the [where] athlete is able to tolerate fairly high intensity exercise for an extended period, then they can return to sports specific activities. Then lastly, return to unrestricted activities, including contact. Current international guidelines in sport really recommend that each stage of that protocol should last at least a day. You shouldn't try to make your way through three stages in one day, for instance, if you're a highly motivated athlete. We know there is some range as to the timing that it takes for athletes to make their way through that protocol. But it has also turned out to have a great impact on clinicians and clinical management. We published a paper in the British Journal of Sports Medicine a couple of years ago really outlining how the management of sport-related concussion has dramatically changed such that, it sounds corny, but in about a matter of about 15 years return to play went from 15 minutes to 15 days and the resultant benefit to athletes has been a major reduction in same season repeat concussions. Our early research indicated that when players were returning too quickly, a very high percentage, like 90%, of repeat concussions were occurring in the first 10 days after initial concussion. Now athletes are given longer to achieve brain recovery and gradually acclimate back to unrestricted activity and the occurrence of same season repeat concussion in the first 10 days has essentially disappeared. These are not research projects that are just sort of science fair ideas. These are studies that have resulted in evidence that have changed clinical practice and improved the health and safety for athletes, like your kids and my kids participating in contact inclusion sports, which is obviously very gratifying.

John Bellone 1:05:10

Do you have an idea of why people were getting repeated concussions within the first 10 days? I have a couple of thoughts, but do we know?

Michael McCrea 1:05:20

Well, if you combine that with what we see in our imaging and our biomarker data, I mean, the theory early on before we had the capabilities of studying this, was that early after a brain injury, a concussive injury, you're really in a state of cerebral vulnerability. We talked about that neurometabolic cascade. If you're returning to an activity where you're going to continue to take additional blows to the head, you're obviously in a vulnerable spot for risk of repeat concussion or worsening of symptoms and signs from your initial injury at the same time. Yes.

John Bellone 1:06:01

There's also a so-called “second impact syndrome”, which is a little controversial. Can you talk about that quickly?

Michael McCrea 1:06:07

The concept of second impact syndrome is that an athlete sustains a concussion, either doesn't report it or reports it and maybe it was overlooked or ignored, not properly assessed. At any rate, this athlete continued to participate or returned to participation within that theoretical window of cerebral vulnerability and, unfortunately, sustained a more severe injury, some followed by really rapid neurologic deterioration on the field and resulting in death or catastrophic outcome, long term disability. As you mentioned, as those case reports were interrogated further, the backbone of second impact syndrome, as it was defined and characterized initially, started to unravel a little bit. There was some question as to whether or not these athletes had initial impact or whether or not that second injury was just really a devastating single injury that resulted, for instance, in a hemorrhage, subdural hematoma or etcetera that resulted in either death or severe neurologic disability. No matter how you slice it, these are really tragic cases. There's people out there still debating whether or not this represents "second impact syndrome." The main focus should be on how we can prevent these preventable injuries. There are certainly going to be instances, people that come to sport with cardiac or brain vulnerabilities that were at risk of catastrophic injury regardless, but we should be focused on the preventable instances of such.

John Bellone 1:08:09

Before we leave the realm of what used to be done and is no longer in vogue, I had heard the old recommendation of waking people up every 30 minutes or some terrible amount of time, which seems awful for the recovery process. Right? That used to be one of the recommendations some people made?

Michael McCrea 1:08:30

Oh, yeah. It was essentially standard practice 25 years ago. I would say it is still the single most common question I get from parents, at least parents who are old enough like me to have lived through that. I can remember an instance where a mom told me that she took a strand of her own hair and laid it across the the nose and mouth of her daughter so that she could look in on her daughter and not have to wake her up, but she could see the strand of hair fluttering and make certain her daughter was breathing. But you're absolutely right. We know that sleep is really critical and of great importance to the recovery process after concussion, just like it is for essentially everything else in life. So the recommendation to wake an athlete with concussion has really gone by the wayside and it is not supported by the evidence. As a matter of fact, you could argue that the evidence is even counterintuitive to waking athletes. That said, some moms and dads just need that peace of mind and still do it, but it's not something that's recommended in modern day guidelines or practice.

Ryan Van Patten 1:09:50

A big area of interest in the scientific literature is acute predictors of better versus worse or complicated recovery. The Concussion in Sport Croup Consensus Statement, the most recent one from 2017, I believe, was clear that the best most consistent predictor of slower, more challenging recovery from sport concussion is initial symptom severity. There's also pre-existing factors, for better or worse recovery like learning disorders, ADHD, mental health history, prior concussion history. What's your broad summary of this literature?

Michael McCrea 1:10:25

This discussion isn't confined just to sport concussion, but we know now that a combination of injury and non-injury related factors combine to predict an individual's trajectory or time course of recovery. If we zoom in on sport-related concussion, yes, there are multiple studies indicating that the severity of symptoms, for instance, within the first 24 hours is highly predictive of the time course of recovery and an athlete's timeline to return to unrestricted activity. But we also know, and we know this from all areas of brain injury research, that it's not all about injury, it's about who comes to injury meaning there premorbid factors or vulnerabilities - history of premorbid depression, anxiety, PTSD, neurologic vulnerabilities such as multiple sclerosis or other neurologic conditions. So it's about who comes to injury. It's about response to injury meaning this kid's got no prior history of anxiety or depression, but they're freaked out because they're going to lose their starting position. Or they go to a school that's on a block curriculum and they miss three days of school, and they're a 4.3 grade point kid. They missed three days of school and they're really wildly anxious and that starts to affect their

recovery. Then we also need to point out that it's also about environments of injury and post injury care. Only a fraction of schools across the country have a dedicated athletic trainer in the training room guiding athletes through the recovery process. So, yes, injury severity in sport concussion is the single strongest predictor of recovery time, but there's also this list of modifiers, premorbid and post injury, that have to be considered because we know that they explain part of the variance in the different recovery times across athletes.

John Bellone 1:12:41

How about some person factors like sex, race, age, etcetera? I've seen evidence that children might take longer to recover than adults. Girls might also have a slower recovery than boys. Anything you want to say about these person factors?

Michael McCrea 1:12:57

There's been mixed findings across those individual factors. I'll speak most directly to the the effect of sex. There were mixed findings across many studies, varied sample sizes, varied methodologies, and oftentimes with the interpretation that women, female athletes I should say, had a longer recovery time after sport-related concussion than male athletes. To my knowledge, the largest study of this sort was conducted by our group at the CARE Consortium. Tina Master, who is a pediatrician and sports medicine specialist at UPenn and CHOP, Children's Hospital of Pennsylvania, led this study where she had the largest sample available anywhere and was able to compare males and females who compete in equivalent sports. So men's soccer and women's Soccer is the same sport. Men's lacrosse and women's lacrosse are not the same sport. They have different rules, different levels of contact that are allowed. Tina did a wonderful job with maximum rigor comparing these two large cohorts. To put this in perspective, I think it's still the case that the CARE Consortium injury database has more female concussed athletes than the largest study of sport concussion prior to the CARE Consortium and that allowed her really great power in assembling this sample. But the long and the short of it is that she found equivalent recovery times between male and female athletes of the same age cohort, collegiate student athletes participating in equivalent sports. What we sometimes find is that their time for clinical recovery is equivalent but clinicians, for socioecological reasons, maybe apply a more conservative approach to return to play in female athletes than in male athletes. So they both have a clinical recovery time, males and females, of six days, for instance, but females might take a day or two longer from the point of clinical recovery to unrestricted activity. But that's not really recovery, that's more about socioecological factors affecting clinician behavior.

Ryan Van Patten 1:15:28

An important term in this space is persistent post-concussive symptoms, or PPCS, which is preferred by a lot of experts over the old term, post-concussive syndrome, or PCS. PPCS can be defined as symptoms lasting longer than the expected period of recovery - so longer than about two weeks for adult athletes and longer than four weeks or so for child athletes. What should listeners know?

Michael McCrea 1:15:55

That's been a bit of a moving target. Even some of the early studies we published, we were seeing athletes report a clinical recovery, on average, of a week or less. As I said, in that day and age, they returned to play essentially the day they were symptom stable or symptom free. Now we've added another week of this graduated exertion and return to play protocol. In our most recent data, we find that the median time of clinical recovery is about a week, but it takes outwards to about four weeks by the time 80% of athletes have achieved a complete recovery and return to unrestricted activities. I guess the long and the short of it is that we have much better data to understand the range, the heterogeneity, and the range of recovery time in athletes. It's not so much that the mean time or average time has recovered. We also know that there's a much wider distribution around that average time for recovery than we originally thought. The good news is that even though the perspective on the average recovery time has expanded, the likelihood of athletes not achieving a full recovery remains extremely low. Even for those athletes who are not completely recovered at 28 days, still the overwhelming majority of them reach a complete clinical recovery somewhere in the next 30 days, which is important for clinicians to know because I think, whether that's in a neuropsychologist office or in a sport training room, everybody starts to get a little anxious and a little frustrated if athlete Jim or Jane is not following the "normal" course of recovery. It starts to go off the rails a little bit and I think it's important for everybody to know that even if you're not recovering in the average or the "normal" timeframe, the odds are still extremely high that you're going to achieve a full recovery even if it takes a little bit longer.

John Bellone 1:18:26

I'm curious what your thoughts are about the role of clinical neuropsychologists in managing sport-related concussion? How can we be most useful?

Michael McCrea 1:18:37

Yeah, so, obviously, I have an inherent bias here about the universal value of neuropsychologists. I'm not joking there. I don't know that there's another specialty out there that understands the combined subject matter of neurologic function and psychological function. Concussion and traumatic brain injury is truly a

neuropsychological construct and injury, meaning, as I said earlier, we know that neurologic injury is the backbone but psychological factors are so critical to a patient's recovery and outcome. We're really the only specialty out there that wears both of those hats. So I tout the value of clinical neuropsychologists across all areas of brain injury medicine and research. As it relates to sport concussion, certainly not every school or youth organization is going to have a neuropsychologist on the sideline or that they have ready access to for acute clinical evaluations and that's probably not necessary. Yet at my own institution, for instance, we have a very busy sport concussion clinic. There are two tracks in that clinic: one is a physician only track where the athletes' symptoms are fairly straightforward, they may not have any cognitive symptoms at all, and there's really not a pressing need for neuropsychological evaluation. But in a large segment of those patients, they are triaged to the multidisciplinary track where the neuropsychologist works closely with sports medicine physicians evaluating those athletes and driving their rehabilitation and return to play process. I guess my point is, we play an important role in all areas of brain injury medicine in civilian, military, and sport, but it's probably not the case that we need to see every single person out there affected by concussion.

Ryan Van Patten 1:20:43

Concussion management is really critical in sport because these injuries are going to happen, we can't prevent them entirely especially, as you've said, in contact and collision sports. But there might be methods for reducing the risk for sport concussion. I'm thinking about things like helmets, mouth guards, neck exercises, even rule changes like body checking in ice hockey or certain types of tackling in American football. Some of these strategies have more support than others. Which methods have the most empirical support for reducing sport concussion risk?

Michael McCrea 1:21:15

That's a great question. Many of your audience members may know that demonstrating the efficacy of prevention strategies with data is not easy but I think there's at least some degree of support and data out there, frankly, to indicate that the most effective prevention strategy in the space of sport concussion has been education. If you watch contact and collision sports in the United States and around the world, the game has changed considerably and how athletes play the game. That's due in large part to this multi-pronged effort toward education and awareness. Athletes certainly now recognize concussive injury as potentially serious and for their own best interest they're avoiding risk of injury to stay on the field of play. We've also had the opportunity to educate through our biomechanics research, for instance, some of the work at Virginia Tech and North Carolina where they've taken these head impact sensor technologies and used them not only to study the biomechanics of head impact exposure and concussion in sport but also

to educate athletes. In our work through the CARE consortium, for instance, the biomechanics core, we had nearly 700 football players instrumented with the Head Impact Telemetry System and we were able to see that, even at the same institution, two football players who play the same football position and are participating in the same practices and same games have wildly different head impact exposure profiles. One tight end, Jim Jones, might have a head impact burden that is three times higher than his tight end teammate, Sam Walton. Then it's time to go to that athlete and say, "Listen, here's what your head impact profile looks like and let's watch you on tape compared to some of the other players." We see, in fact, that Athlete A is playing the entire game with his head down, leading with his head, and it's an opportunity to then educate Athlete A on methods to take their head out of the game more often but be equally as effective competitively. Our work has also resulted in really major policy changes in collegiate football. You and your audience may not be aware of but two-a-days were frankly just a tradition in preseason football training camp when I played. That's no longer allowed in collegiate football. Both collegiate sports and professional sports and many high school governing bodies across the country now limit the number of contact days. This is all intended to reduce the risk of concussion, obviously, but more importantly, it's intended to reduce the level [and] the burden of head impact exposure just through routine participation in sport. We've published a number of papers indicating the effectiveness of those strategies along the same lines.

Ryan Van Patten 1:24:45

So far we've been talking about current athletes who sustained a concussion and what to do about it. Let's move forward and talk about former athletes with concussion histories. This could be someone who played a few years of high school football or retired professional hockey player and everything in between. We're recovering most of the adult lifespan here from people in their 20s and 30s to older adults in their 70s and 80s and beyond. We're talking about professional and non-professional athletes. There are so many important issues in this space like questions about the relationship between concussion history and long-term cognitive, physical, and mental health outcomes. The possible impact of so-called “subconcussive blows,” the highly charged topic of CTE, chronic traumatic encephalopathy, and traumatic encephalopathy syndrome and more. In just one question or one answer here [laughs], give us a broad overview of the long-term effects of concussion.

Michael McCrea 1:25:42

Sure. You first raise a good point that the entire perspective and narrative around traumatic brain injury has expanded from a single event to a lifespan understanding. That's not confined to sport. That work has expanded in all areas of

TBI research - civilian, military, and sport. In the setting of sport concussion, as you are aware and you cited, there have been growing concerns about the potential effects of repetitive concussion or even repetitive head impact exposure on long range neurologic health in former athletes, for instance. Obviously, with the theory that there's a dose response pattern here, that if you played a single year of organized sport you're theoretically at lower risk than someone who played 15 years of collision sports for instance. With respect to that first group, remember that a very large percentage of the general population has sustained at least one concussion in their lifetime. But, at any rate, there have been reports of athletes and retrospective studies of athletes reporting long range neurologic, neurocognitive, neuropsychiatric, and even neurodegenerative changes that have been attributed to prior concussion, repetitive concussion, and head impact exposure. Like in every area of research, the retrospective approach is less than ideal. The literature including the Concussion Sport Group has really called upon the need for truly prospective longitudinal studies. Now, nobody wants to wait seven years for the results of a study where you start researching middle school or high school athletes and follow them across the lifespan. So there are currently a number of efforts ongoing, including our work in studying former high school, former collegiate, and former professional football players and contact sport athletes to truly prospectively assess the trajectory of their health over a period of years after they discontinue participation in sport. Like in our discussion earlier, the important thing here is to have a span wide enough to study the effects of concussion and other factors that could be impacting health - psychological health, lifestyle factors, life stressors and that's really the approach that we're taking. I think there are some assertions out there that this is a foregone conclusion. We certainly know that there's a subgroup of individuals who appear to have problems resulting from prior exposure and these other factors. The likelihood that this is a single cause or a single solution is seemingly unlikely based on the balance of the literature out there. The trick here is to understand, how big is that cohort at risk? Who are they and why are they at risk? Because that would allow us to identify these individuals and preemptively prevent them from any ill effects of traumatic brain injury. Again, not confined to sport but we're doing the same in our civilian studies to identify those who may be at risk of late life problems secondary to TBI.

Ryan Van Patten 1:29:33

Great. Well, thank you so much for all of this. This has been a whirlwind tour of TBI and sport-related concussion in particular. We could keep you on for another three hours with questions but we won't do that to you. Quickly before letting you go, just two quick "bonus questions" that we ask all of our guests. These are about the field of neuropsychology more generally. You're welcome to include TBI in your answer,

but not necessarily so. The first question is: If you could improve one thing about the field of neuropsychology, what would it be?

Michael McCrea 1:30:06
Well, I think my primary answer there is I'd like to see neuropsychology and neuropsychologists more broadly at the table in the discussion of the precision medicine movement. Certainly, as I said earlier, with respect to neurologic injury and disease, we really do bring this total perspective as neuropsychologists to the understanding of neurologic function and psychological function. I think, you know, at least my perspective on the precision medicine movement is this sort of multilevel, multidimensional approach to understanding the person. You know, we're all infatuated with proteomics and genomics and the genetic and physiological makeup of individuals, but I also think that neuropsychologists could play a really valuable role in that movement more broadly.

John Bellone 1:31:16
That's a unique answer. I love it. What is one bit of advice that you wish someone told you when you were training or maybe somebody did tell you that really made the difference? We're looking for an actionable step that trainees can take that they might not have thought of.

Michael McCrea 1:31:33
I guess my main advice, and I'll preface this by saying, I tell people all the time, I never really had a plan. I'm not really promoting that for people out there.

Ryan Van Patten 1:31:48
[laughs]

John Bellone 1:31:48
[laughs]

Michael McCrea 1:31:48
But my bit of advice would be, if you want to do something, just go knock on a few doors and do it. If you're young and ambitious and energetic, someone will gladly take you up on the opportunity. Then along the way, really, the main derivative of that is you will find great mentorship along the way. I literally tell people, my whole story is about someone taking stock and me and then saying, "You know, you should go over here and also talk to so and so." There's just been a thousand of those along the way in my life and my career. Someone, again, taking an interest in

providing me with guidance and good advice along the way. So, you know, take a risk. Go knock on someone's door, pick up the phone and just ask them for five minutes and you stack a bunch of those together and it'll serve you very well. Hopefully as well as it did me over the years.

Ryan Van Patten 1:33:04
Words of wisdom. A great place to close. Mike, thank you so much for being so generous with your time and all the knowledge you've shared today. This has been great.

Michael McCrea 1:33:13
Absolutely. Thanks for having me. This has been a real delight. You guys did a great job squaring up the questions and I hope the audience finds it informative.

Ryan Van Patten 1:33:25
Yeah. We've had a lot of requests for an episode on sport-related concussion. We did one with Keith Yeates a few years ago on pediatric TBI and just barely touched on sport concussion, so we haven't really hit it hard. I think this will be really popular. People like the long form. You know, it's not just an hour. We get, as you experienced, we get really into the weeds. I think it's great.

Michael McCrea 1:33:44
That's awesome. Well, you guys should be proud of what you're doing. This is pretty incredible. Right? And, most importantly, it's elevating the profile for neuropsychology, which we need.

Ryan Van Patten 1:33:56
Yeah.

John Bellone 1:33:57
Thank you for saying that.

Michael McCrea 1:33:58
All right, guys.

Ryan Van Patten 1:33:58
Take care, Mike.

Michael McCrea 1:33:59
Take care. Thanks again.

Ryan Van Patten 1:34:01
Bye.

Michael McCrea 1:34:01
Bye bye.

Transition Music 1:34:01

Ryan Van Patten 1:34:06
Well, that does it for our conversation with Mike. Be on the lookout for upcoming episodes on cerebrovascular disease, digital technology, functional neurological disorders, loneliness, ecological validity, Parkinson's disease, and other topics. And, as always, thanks so much for listening, and join us next time as we continue to navigate the brain and behavior.

Exit Music 1:34:29

John Bellone 1:34:54
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Ryan Van Patten 1:35:05
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End of Audio 1:35:23