Transcript of Cerebrum Podcast – Rethinking Youth Sports

**Guest: Michael L. Lipton, M.D., Ph.D., F.A.C.R.,** is a neuroradiologist and neuroscientist at Albert Einstein College of Medicine and Montefiore Medical Center in New York. Lipton received his Doctor of Medicine from Boston University in 1990 and continued his studies at Einstein, where he received his Master of Science with Distinction and his Doctor of Philosophy in Neuroscience. His research program focuses on detecting and characterizing the effects of mild brain injury and the cumulative effects of repetitive subconcussive head injury in sports. Lipton’s work on the effects of soccer “heading” on brain structure and function in amateur soccer players has been reported extensively in the press worldwide. In 2017, Lipton received the Distinguished Investigator Award from the Academy of Radiology and Biomedical Imaging Research.

**Host: Bill Glovin** serves as editor of *Cerebrum* and as executive editor of the Dana Foundation. He was formerly senior editor of *Rutgers Magazine*, managing editor of *New Jersey Success*, editor of *New Jersey Business Magazine*, and a staff writer at *The Record* newspaper in Hackensack, NJ. Glovin has won 20 writing awards from the Society of Professional Journalists of New Jersey and the Council for Advancement and Support of Education. He has a B.A. in Journalism from George Washington University.

**Bill Glovin:** Would you let your son play football? Should you allow your daughter to play soccer, a sport where repeated heading of a ball is an important strategical advantage? Why do some athletes who absorb the same impact to the head suffer symptoms of brain injury while others don’t? This and more will be the focus of today’s *Cerebrum* podcast where we explore topics about brain science with authors of our *Cerebrum* articles.

This month’s guest on the phone with us is Dr. Michael Lipton, someone who has been conducting research in this area long before it was on the radar of the NFL, scholastic and college sports, parents, educators, and the media. Michael founded the Translational Neuroimaging Laboratory in 2000 at the Albert Einstein School of Medicine at Montefiore Medical Center in New York, and is the author of our most recent *Cerebrum* article, “Rethinking Youth Sports,” which you can find at dana.org. I highly recommend it if you have any interest at all in this topic.

Michael's article explores the latest research on what occurs after an individual suffers repeated impacts to the head that do not produce recognized concussion. That's really the key thing here. Most people assume concussions, even mild concussion, can lead to problems. Michael's research tells us why that is not always the case. Mild traumatic brain injury, or mild TBI, is considered the cutting edge of sports head injury research. Welcome to the podcast Michael, and thanks again for the wonderful article. It seems almost fitting that we're talking a day after the start of another NFL season because professional football is probably the main reason this issue has attracted so much attention.
Michael Lipton: It sure is. Football definitely launched the whole topic of traumatic brain injury, and certainly sports-related head injury, into the spotlight.

Bill Glovin: But football just seems to be the tip of the iceberg when it comes to the issue. Why is that?

Michael Lipton: Well, I think that football, and in particular professional football, notwithstanding that it really raised awareness tremendously, it's really a very small piece of the pie when you think about head injury and sports-related head injury worldwide. The number of professional football players or even the number of league football players in the United States is really a very small fraction of the worldwide activity in sports, and it is restricted to very specific populations. It's really a USA phenomenon, it's not a worldwide phenomenon, and it's a sport that to this day is still an almost exclusively male-only sport. A lot of important issues such as the risk to women and girls is really not going to be addressed by a focus on football.

Bill Glovin: Is there too much hysteria surrounding this issue? Should parents consider whether to let their daughters play youth soccer because of the heading issue? In other words, do the positives outweigh the negatives?

Michael Lipton: Well, I think that the available evidence right now is that the positives, in terms of being physically active, are very strong. The information about the negatives is emerging and seem to really be related to what we call excessive exposure or people who have many, many impacts to the head. But the bottom line is that we don't really know exactly where it is that people cross a threshold from lower to higher risk of having a long-term effect of head impacts related to sports. That's something that is going to be very individual. I think that hysteria is never helpful in general, but the truth of the matter is that we don't really know enough yet to make very clear recommendations that are based on evidence.

Bill Glovin: Would you let your son play football?

Michael Lipton: That's a really good question, and one that I haven't had to confront because some of my kids played soccer, my sons have not played football. I would not be an advocate of football in terms of aggressive, full-tackle football. But I'm a pretty conservative person and that's my personal choice. I think that at the peewee level, at the youth level, there's mounting evidence that many, many hits do add up to something bad. But again, it's hard to be able to draw the line in the sand as to where we get to the point where it's clearly too much.

I think that in order for guidelines, that we're talking about what can be done, to ultimately change sports in a way that makes them safer for players, that we really need to do that based on robust evidence. Because the likelihood that we're going to really see uptake on new rules that might modify participation in these types of sports, or that they're really going to stick and have an impact, is
going to be tied to how strong the evidence is. Right now the evidence for something like youth sports is emerging, but it's really being extrapolated from something very different, which is adults who have years of very intensive exposure to impacts.

Bill Glovin: You've been at this for a very long time, long before CTE started to gain notoriety around 2005. What got you interested in this area of research?

Michael Lipton: My interest really comes from my clinical side of what I do. I'm a physician and I'm a neuroradiologist, so I do imaging of the brain. My interest in mild head injury really came from a conundrum in the clinic where we had patients who were referred, as is very common, for imaging of their brain related to, typically, a prior concussion, not necessarily sports related. Those individuals were exhibiting symptoms that didn't resolve. In the field of concussion, somewhere in the neighborhood of 15 to 30 percent of people who experience a concussion will have symptoms that persist and don't resolve. Some of those people they may never resolve, and some of them, they may just take a very long time to resolve.

But when they come in to the imaging center and have a sophisticated MRI of the brain, it looks normal, right? These are not injuries where we see bleeding and dramatic bruising to the brain. That conundrum of a person who clearly has something wrong with their brain function but where we're not able to access what's going on in the brain tissue was really what my initial focus was. That focus was on trying to look at different ways to examine the brain tissue more deeply using brain imaging to understand how the pathology developed in the brain and how that pathology was related to people's functions and outcome.

Bill Glovin: Common sense would tell us that diagnosing the effect of mild traumatic brain injury can be difficult and extremely problematic since there is seemingly no significant event, like a concussion, that brings attention to the problem.

Michael Lipton: We should just clarify, right? Mild traumatic brain injury and concussion are synonyms, right? So mild traumatic brain injury is an event where someone had, there is a discrete event, whether it's an impact to the head or it's a rapid acceleration like in a whiplash or blast exposure. From the time of that event, there are symptoms which will resolve to a variable degree but will resolve in most individuals over a period of time. In the world of sports, I think what we've really been talking about is something that we refer to as subconcussive injury. Subconcussive means that there is no clear discrete event that caused an injury, and rather there has been a series of impacts over time, none of which was recognizable or identifiable as an injury per se. Yet we now know that there can be changes that build up in the brain and affect brain function as a result of those many, many seemingly asymptomatic impacts that accumulate over time.

Bill Glovin: Someone can suffer from CTE without ever suffering from a concussion, but possibly from these subconcussive events that build up?
Michael Lipton: Well, yeah, and I would actually put it a little bit differently. If you look at the index case of CTE, which is Mike Webster, the Pittsburgh Steelers center. He was never diagnosed with a concussion during his lifetime, yet had a very extensive case of chronic traumatic encephalopathy, or CTE. Now, we can look back on this and say that when he was playing in the 70s and 80s, and, really as a starting center for the multiple Superbowl winning team, having numerous impacts to the head over time that he almost certainly had many events that we would classify as a concussion today. But in general, I think that this shines the spotlight on the fact that it's not the overt events that are necessarily the culprit and rather the concussions that we remember may just be an indication, in the setting of a sport like football, of the overall number of impacts that someone experienced.

It's really unclear, or really not possible to disentangle, the clinically obvious concussive events from the numerous hits that happened during practice and play. These players are having so many impacts to the brain that when we make a diagnosis of CTE, which is made after death, right? At the end of a very long period of exposure, you really can't go back and say that it was one or more concussions as opposed to this long chain of repetitive impacts over time. And we know that, in many cases, or at least in some cases I should say, there are people who did not have many, or in some cases not clear that they had any diagnosed concussions yet were ultimately diagnosed with CTE. I think that the field has definitely shifted away from the exclusive focus on concussion and really understanding that repetitive impacts to the head are more likely to be the bigger share of the exposure that leads to the outcome.

Bill Glovin: You touched on the fact that we've really been able to only study the brains of deceased individuals with CTE. A lot of the naysayers say the research is compromised because of that, because we really can't study somebody who is still living in a way that would be accurate. Why is that, and can things change in that regard?

Michael Lipton: Well, the diagnosis of CTE, or the definitive diagnosis of CTE, remains a pathologic diagnosis that can only be made after death. However, that's not unique amongst neurodegenerative diseases. I mean, strictly speaking, Alzheimer's disease, which is the most common form of dementia, is not a diagnosis that can be made definitively until after death when you can actually look at the brain tissue. Yet, in both Alzheimer's, and now emerging in the field of CTE, there are methods and rubrics for coming to presumptive clinical diagnoses based on a patient's signs and symptoms, even during lifetime. But the diagnosis is ultimately not confirmable until after death.

Now, the reason for that is that you need to look at the brain tissue and we don't do evaluations. We can't just give a pathologic evaluation of the brain in a living patient. The obvious route to trying to get around that problem of a lack of ability to look at pathology is to look for a noninvasive measure. There are a couple of ways to get towards that. One of them potentially is by looking for blood biomarkers, and another is looking at imaging.
Both techniques take advantage of the fact that a primary pathologic feature in CTE is the deposition of hyperphosphorylated tau protein in the brain tissue. There are approaches to attempt to detect that either in the blood or in the cerebral spinal fluid, but of great interest is techniques that have been developed and are now being investigated and tested to look at the presence of the tau protein in a living brain using a technique called PET scanning, where an antibody is injected that latches onto the tau protein and is also attached to a radioactive tracer that can be detected by the PET scanning machine. There's now growing evidence that tau can be detected in vivo, in living patients, and may be useful for firming up or enhancing the ability to make diagnoses prior to death, but it's still early days, and the general, clinical use of a tau imaging as a test for that purpose is not really quite here yet.

Bill Glovin: How far away are we?

Michael Lipton: That's a really good question. To juxtapose this, there are similar concepts afoot for examining patients who may have Alzheimer's disease. Now the difference is, in Alzheimer's disease we're looking for a different protein, we're looking for the amyloid beta protein. There are similarly techniques for detecting that amyloid protein in living people just like there are for tau. But in terms of where the science is, I think that if you just contrast a couple of points, it's instructive in terms of how far away we might be.

Today, there are multiple FDA-approved tracer drugs for amyloid that are readily available in the United States and worldwide. Anyone can order and have an amyloid PET scan, yet it's still not clear how the information is actually useful in prognosticating or predicting someone's outcome, or even confirming their diagnosis. Because it became clear, as more and more research was done on amyloid, that we find it in healthy people as well. Other than finding a complete absence, it's not clear how probative it is, so to speak.

On the other hand, if you look at the tau tracers, there are no FDA approved agents right now. It's not clear at all how soon there will be because there are some tricky technical issues to developing a stable and robust tracer for regular clinical use. In concert with that, the studies that are looking at the role of tau imaging are just not nearly as advanced as they are for amyloid yet. Even in the amyloid domain for Alzheimer's disease things really haven't yet gotten to the point where there's a clear prognostic utilization. I think we're years away from a really definitive usage of something like a tau tracer in the clinic for regular clinical use, I would say, at least.

Bill Glovin: What would push that along? Better imaging, more research? Do we need more funding for research, more people doing it?

Michael Lipton: I think that there are two things that are key. Everything ultimately comes down to funding. The question is what will motivate the funding. Unfortunately, I think that, as someone who does clinical brain imaging, the uptake in the clinical world has been anemic for the amyloid imaging agents. Even though they're
FDA-approved, they've been shown to detect the presence of amyloid, and they're safe, and there are actually some clinical indications, it's a test that is rarely compared to other imaging tests. Rarely actually being used in real life. It's also exceedingly expensive, and it's something that is not yet covered by most insurance companies.

So when you think about the development of a totally new approach to image a protein and a neurodegenerative disease along the same lines, the motivation is probably going to be tempered by what the market outlook appears to be. I think that the way to get around that is for there to be large enough studies that can definitively show, one way or another, that the technique is reliable and that it has some impact on treatment. If it's just a matter of detecting the presence of tau in the brain, it's got to do more than that. We have to show that it really gives us sufficient diagnostic information.

Potentially that means stepping the research back and utilizing a test like the detection of tau in vivo to show that it really starts to build up much earlier. In other words, not focused necessarily only on the people who have CTE, but look, at least in a research context, at people who are way, way earlier in that pipeline that ultimately leads to the neurodegenerative disease so that we can come to understand how, if it is the case, that tau starts to build up much earlier, and understand ways, potentially then, to intervene, to preempt the inexorable evolution of the disease.

Bill Glovin: Yeah. That seems like a huge hurdle, and that's, I guess, part of the problem with any kind of Alzheimer's research, because any type of study has to be done over a long span of time. You need to look at people, I guess from maybe, for this, from the age of maybe 12 years old on to 50 or something like that. That would be quite difficult and expensive. Also to even be able to get people to agree to be tested over that long period of time would be a challenge.

Michael Lipton: Yeah, and this is a radioactive tracer, so the idea of using it in research, especially using it repeatedly over time has some safety concerns. It's not trivial, not trivial. We don't actually yet really fully understand the relative prevalence of the problem of tau deposition and CTE. Because if you look at the data that exists from postmortem studies, you have to realize those are postmortem studies, meaning that those are only the brains that came in, in many cases, because there was specifically a concern about CTE. But understanding what is the real prevalence in the population at large is something that would really benefit from a noninvasive approach to detection.

Bill Glovin: I guess the other problem which your article points to, and you mentioned earlier, is that two people can suffer from the exact same collision but have different symptoms.

Michael Lipton: Yes. In that regard it becomes a matter of, when we identify that there is a problem, whether it is simply that someone has a delayed recovery following an impact to the head, or following a season of impacts, or someone has a more
severe adverse outcome, like a onset of neurodegeneration over time. In either case, it really just begs the question as to why that happened to those individuals, whereas many of their teammates didn't suffer those adverse effects. In fact, many of their teammates who seemingly had similar amounts of hits to the head, we don't see that every professional athlete is eventually coming down with CTE. This really gets to the complexity of what confers risk and that it's not just about the head injury itself, but it's what puts certain individuals at risk for having a worse trajectory of recovery, or a worse long-term outcome, or persistent symptoms following their injury.

That by and large, if we look at the whole world of concussion, or if you look at sports concussion in youth sports, most players recover very well rather quickly, but there are some who don't. The area that we don't understand is, what are the factors that make certain individuals susceptible? Is it that girls are more susceptible, or the specific genotype are more susceptible, or some other factor. Being able, again, to be able to detect the pathology as it's evolving, whether it's with a protein deposition type of PET scan or other types of imaging that detect alterations to the brain structure and function, that allows us to then begin to identify who are the risk groups, who are the people that need to be the focus of prevention or the people who need to be targeted and in therapy.

Bill Glovin: So we don't quite even know that yet, which age group is more susceptible or which gender might be more susceptible to mild TBI?

Michael Lipton: Well, there is quite a bit of data available so it's pretty clear that, in general, women are more susceptible to adverse outcomes than men when it comes to concussion. That the extremes of age, very young and very old people, fare worse following something like a concussion. There is data emerging that also indicates that there are certain genes that seem to elevate risk, certainly in more severe forms of brain injury, but now even in more of the mild TBI domain. There's actually lots of evidence that there are a host of factors that confer risk, but it's ultimately the interaction of many of these factors within one individual which determines what the real life outcome is going to be.

That's the next frontier that, on balance, even if we say that, as a group, women have more susceptibility to repetitive head impacts, nonetheless, there are many women who seem to be quite resilient. What's the difference between those individuals? Looking at what we call the interaction of these multiple factors to create a profile of risk that we can then use to triage or assess an individual perhaps prior to deciding on the sport they're going to play, or deciding that they're going to be a combat soldier as opposed to some less risky profession, there are potentially ways to really get traction on who has greater and lesser risk. That's just work that needs to be done, and it requires researching more people.

Bill Glovin: Are there any preventative measures you might recommend?
Michael Lipton: Well, the obvious preventative is to not have injuries to the head, right? We could certainly say that if you don't participate in collision sports, then you are diminishing your risk. That's a true statement, and that's a decision point that people have to cross if they're going to be involved in those. But if we take it as a given that we're going to have people who will be exposed to impacts of the head, whether it's recreationally, occupationally, accidentally, whatever it happens to be, the secondary prevention, or trying to intervene in a way that we can prevent the bad outcome, is really the next point of focus.

That's very relevant in traumatic brain injury because we now know, after many, many years of research, that traumatic brain injury is not an injury that happens just at a moment in time. It's not like when you fall down and break your hand, that bone broke and it's done. Rather, it's an evolution of changes in the brain that are initiated by the force of the trauma. At that point in time, there will be a host of processes. Things that, some of which are covered in the articles, as inflammation or excitotoxicity, which further injure the brain. It's really the elaboration of those different processes that is ultimately likely to be the biggest contributor to the final outcome. In other words, if you have two people and one of them recovers rapidly, and one of them never recovers, a large piece of that is likely to be the extent to which they were or were not able to rein in these adverse responses to the trauma going on inside their brain at the cellular and molecular level.

I think that the real targets for prevention beyond the primary prevention of just not having the injury is really going to be, and we're certainly not there yet, but there's a lot of basis to see that there are points of potential intervention to do things like turn off inflammation, turn off excitotoxicity, or protect cells from secondary injury. Many of these things have been addressed and attempted in rather severe types of injury where they have not shown any success, at least not in the clinic. It's very possible that in part at least, that's because the severity of the injuries were so great that it was beyond the point where we could reasonably expect to get a response by some of these interventions.

If we revisit those with people who have lesser degrees of injury, I'm talking about the difference between someone who's been in a high speed motor vehicle accident and has extensive bleeding and bruising of their brain versus someone who is an athlete that's had a concussion or a series of concussions, we may be able to actually take some of those interventions that have shown promise but have not been effective, perhaps due to the severity of the injury context in which they were tested, and bring them to bear in new studies of less severe degrees of injury.

Bill Glovin: I know in New Jersey, recently they passed the measure to regulate the amount of hitting that can go on in a football practice. Let's say something similar can be done for limiting the amount of hitting that can be allowed in practices involving women's or girls' soccer plus maybe some equipment changes, things of that nature. Do you feel like that could also factor into helping alleviate some of this?
Michael Lipton: I think that, again, limiting exposure, what we call primary prevention, or preventing the impacts, is certainly going to diminish the potential for injury. The only caution that I would add is that it's very important to really understand, from a full circle viewpoint, what the impact of these types of rule changes will be. Just as a quick example, if you make an arbitrary limit that there shouldn't be more than, some numbers that have been thrown around in the past were that there shouldn't be more than 1000 hits per year in tackle football, or there shouldn't be more than a certain number of headers or whatever it is, number of high jumps in a certain period of time.

While well-intentioned, without knowing how much it takes to create the injury, there's really no way to know that there's going to be any impact. If we don't restrict it enough, then the players may still be vulnerable. On the other hand, we could be in a middle ground where the people who are most susceptible will still be receiving too much. Then if we restrict it even further, then there become problems with what will be the acceptance on the part of the players, and coaches, and parents, et cetera. It's not as straightforward as it seems. I think that there is the hidden risk to the overall program of trying to protect the population of making arbitrary cutoffs and points of intervention. This is why I very strongly advocated for research to really define where those thresholds are and how they vary from person to person, or from group of people to group of people.

As far as protective equipment, there is, as I touch on in the article, there's certainly evidence that things like helmets and goalpost padding can essentially eliminate the catastrophic injuries like skull fractures and bleeding inside of the head that led to fatalities, for example, in early American collegiate football. But beyond that, while it would be theoretically possible to create some kind of headgear that would sufficiently attenuate the movement of the head such that the brain was not subjected to enough force to cause an injury, that would likely be a device that would be so large and unwieldy that no one would want to use it.

Bill Glovin: Yeah, we haven't even touched on something like boxing which seems particularly barbaric and just because it's just a lower number of people in the population who participate in that. But it seems like a formula for CTE for sure.

Michael Lipton: The various things that have been suggested in terms of various headgear in soccer and lacrosse, or even the helmets that are used and should be used in football, we have to understand what they can and can't deliver. They can deliver protection, again, from those catastrophic types of injuries. But the idea that those devices are going to sufficiently attenuate acceleration of the brain inside the skull, which is what causes the types of concussive and subconcussive injuries that we've been talking about, that's really not happening with the types of headgear that we're talking about.

Michael Lipton: Well, the original descriptions of CTE, which went by other names such as dementia pugilistica, were originally in boxers. That's really the paradigm for
repetitive head impacts that led to the discovery of neurodegeneration related to repetitive trauma.

Bill Glovin: What is your lab working on at the moment?

Michael Lipton: Our main focus now is specifically looking at individualized risk. We're very interested as we've published a bit in the area of risk of female sex genes and other individual characteristics. Also in trying to understand how the changes in the brain, or brain pathology, actually are unique to each individual. A big limitation of a lot of the imaging research that has been done is that it looks at, for example, a group of hockey players as a group, and essentially goes and looks in the same part of the brain across all those individuals to try to understand the nature of the injury.

But what we've come to learn is that in traumatic brain injury, the parts of the brain that are affected will vary greatly from person to person and from injury context to injury context, simply based on the direction the hit is coming from, how fast it is, how strong it is, how resilient the player is. There are a host of biomechanical features, and we're very interested in trying to understand the way this pathology develops across the brain and how that varies from person to person, which is very important for detection and for being able to ultimately use some of these tests to define prognosis. Because if you're not looking in the right place, then you're not necessarily going to understand the full extent of the injury that someone may or may not have.

Bill Glovin: Well, I think that's a good note to end on. I can't thank you enough for the article and for taking the time to do our podcast. If there's any further interest in this, I highly recommend that you go to our website, which is at dana.org. Again, the article is called “Rethinking Youth Sports” by Dr. Michael Lipton, who's been our guest. You can also find this podcast and all our podcasts in transcript form and on platforms such as iTunes, Spotify, Stitcher, et cetera. Meanwhile, have a great day and thanks for listening.