[MUSIC PLAYING]

ALICIA SUFRINKO: I think that when most people think of sleep in the context of concussion, you probably think of it as a symptom or a problem following concussion. I don't think a lot of clinicians think of it as potentially a risk factor. But I said, why not look at it as a risk factor? Because we know that healthy individuals, especially our adolescents and young adults, are quite at risk for not getting enough sleep or getting poor sleep, and even athletes. There's some research that suggests our high school athletes don't sleep as much because they're really busy.

And we know that poor sleep is associated with a host of problems, from mental health problems to cognitive, academic problems to higher risk of obesity, Type 2 diabetes in youth that don't sleep enough. So why not? If this is going to affect their overall health, why not could it potentially be a risk factor for worse outcomes following concussion? So we looked at 348 youth and collegiate sports athletes. You can see the age range is what you would expect, many more males than females.

And we had baseline data on these folks, ImPACT and PCSS, and then we have three post-injury time points, two days, five to seven, and 10 to 14. And so by using their baseline data, we characterized them into a sleep symptom group, or those that had multiple complaints of sleep problems at baseline, and then those who had absolutely no sleep complaints to draw contrast of two very different groups. So only 10% had multiple sleep problems.

OK, and we did learn that athletes with pre-injury sleep difficulties perform worse on verbal memory post-injury. It's important to note that, actually, at baseline, they didn't look any different on their verbal memory, which may be surprising if you're familiar with the literature on baseline sleep. It's a really small, but-- I don't want to call it negligible. But we do see some difference on baseline with kids that report very-- less than five hours of sleep.

But in this sample that wasn't thousands of people, we didn't have any statistically significant differences on baseline with any of their neurocognitive scores. So even though they're reporting they're having sleep problems, they actually look the same as the people that don't have sleep problems. However, after injury, for verbal memory at two days post-- so let me see. Yeah, there we are. Two days post, you can see they drop quite a bit more than their control counterparts there. They pop back up and they look similar after that point.

And it's also important to mention that we controlled for non-sleep symptoms. So these just aren't-- going back to Anthony's talk-- just people that are very somatic and have a ton of complaints. Even if you control for the other symptoms that are not related to sleep, you still see this difference. And then we see this also occurs with reaction time. And it's probably more pronounced because it's all three time points that we see this difference.

Again, no difference at baseline, and reaction time higher, worse, as we talked about in prior-- you saw the prior talk. So they slow down a lot more than those athletes that do not have a history of reporting sleep problems. I think this is particularly interesting provided if you go to the sleep literature, looking at what deficits we see with sleep problems, being vigilant, attention, reaction time, and reaction time had the most pronounced changes post-injury, so maybe coincidence, maybe actually because you are getting the affect of sleep in addition to concussion here.

And then no surprise that the athletes with the pre-injury sleep difficulties were more symptomatic both pre- and post-injury. This is their overall PCSS score, but even if you do look at just their sleep score, too, it gets much worse. And that's across time points. So pre-injury sleep difficulties may exacerbate neurocognitive impairment and symptoms following injury, like a diathesis-stress model. And essentially, they may be more vulnerable to having worse sleep problems. And that may show that they decline more. They may be more vulnerable to worse injury.

There's a million different ways to conceptualize it. And we don't know really what's going on yet. So I think the take-home message, clinically, we don't have any specific interventions, but sleep hygiene, if you may. You may want to really focus on these patients right off the bat and make sure that you're paying attention to their sleep and trying to educate and do anything you can so that they don't go down the path of having worse sleep.

And then further research is needed to determine if this is really a risk factor. The PCSS symptoms are nice, but that's certainly not going to diagnose a sleep disorder or tell you all that much about something that was measured in one moment of time. So I think it's a good start and something that's worthy of further investigating.

OK, so we're going to move on to migraine. So personal history of migraine, everyone in here knows, is largely considered a risk factor for sustaining a concussion, like a primary risk factor, and also a secondary risk factor for worse outcomes. There's not a whole lot of research, as Anthony alluded to, but this is-- in the consensus statement, this is something that a lot of clinicians believe.

But I had the question, is family migraine associated with poor outcomes following concussion? And I'm sure I'm not the only one in here that has seen a 16-year-old, soccer-player female who comes in, and Mom's there, and Mom goes, oh, I have migraines. And it's just like she has a migraine. She needs a dark room. Her siblings making noises is driving her crazy. It's just like a migraine.

And so based on prior research with post-traumatic migraine, we do know there is this type of profile. And you heard all about that earlier from Dr. Collin's talk. But essentially, I wanted to know, does having a family history of migraine serve as a catalyst for having a presentation that looks like a migraine post-injury? We know adolescence is a time where you're at risk for onset of migraine.

So we looked at a 153 clinic patients that had a sport-related concussion within the past two weeks. Most of them were seen within the first week. The age was 12 to 18. So we definitely wanted that adolescent group. And we have many more males than females, per usual. They were administered ImPACT PCSS and VOMS. And we defined family migraine as a first-degree relative with reported migraine diagnosis. And then the post-traumatic migraine diagnosis was based on our regular migraine diagnosis of headache with nausea and photo and/or photophobia.

So we learned that family migraine history was associated with post-traumatic migraine symptoms following concussion. So those patients that had family history were 2.6 times more likely to present with the PTM symptoms at that first time point post-injury. So this broke down to over half, being 57% of athletes with family history of migraine had post-traumatic migraine symptoms, compared to only about a third of the athletes with no history.

OK, but I wanted to go beyond this. And we know that post-traumatic migraine is associated with all kinds of poor outcomes, longer recovery, worse performance in neurocognitive testing, especially memory, and so on. But nobody's looked at how it really affects what we see with the vestibular screening. And I also wanted to look at the interaction between family migraine and post-traumatic migraine. Is post-traumatic migraine driving the impairments? Is there a cumulative effect of having also a family history of migraine?

It turned out there was only a main effect for PTM on ImPACT and PCSS as well as VOMS. So it doesn't much matter if you have a history of-- the family history of migraine in what you look like clinically, but it does matter if you have the PTM profile and that symptom presentation. So there was no interaction for PTM and family history.

So, summary, the family migraine history is associated with PTM symptoms following concussion, suggesting perhaps a genetic predisposition for migraine that may serve as a catalyst or a trigger for onset of PTM. And only the presence of PTM, rather than family migraine, was related to the worse neurocognitive in vestibular and ocular motor outcomes. And again, this is a good start. But we don't know as much about recovery and outcomes as we should. We just know at this one time point what the differences are. So it would be very interesting to follow this type of cohort across time and see how they recover, if any differently.

All right, so we're moving on from risk factors to talking-- the primary risk factors to talking more about the injury-related risk factors, presentations post-injury, and how that looks with clinical outcomes. So I'm focusing on an ocular motor problem, near point of convergence, which you'll hear a lot more about tomorrow with Dr. Steinhafel. You've probably heard some today already.

But you can see the little picture. They're measuring near point of convergence up there. So often, we use that little popsicle stick-like target where the patient focuses with both eyes as they bring it in. And you measure the convergence in centimeters at which point there's a deviation of the eye or the object splits into two, so just to give you that background for what I'm talking about.

And we wanted to know, does this-- does your convergence measurement play a role in your outcomes following concussion? So we looked at 78 clinic patients seen, a little bit of broad range here, 1 to 30 days. A lot of them were within about 10 days, but up to a month. And we had a wide age range, 9 to 24-- definitely an adolescent sample for the most part, though-- 45 males and 33 females.

And they were administered three trials of the near-point measurement. And then they also completed neurocognitive and symptom assessments ImPACT and PCSS. So we grouped them by convergence measurements. So those that had less than 5 centimeters were considered normal. And that was 57% of the sample. And then those with convergence insufficiency would be those greater than 5 centimeters. And that was the mean or the average of the three trials.

So you can see this problem seems to be pretty common following concussion. So the first thing we wanted to know, is this reliable to measure in a concussion sample? In normal healthies, the convergence measurement doesn't change much. But we've definitely noticed clinically that you get variable measurements with the convergence-- groups that have convergence problems.

And indeed, that's what we saw with our research in that-- the bottom line-- let's see here. These are people with normal near point of convergence, so less than 5 centimeters. So it looks like they're about 1.8. And they stay at about 1.8. They don't really change. But up at top here, you can see the adolescents that had the convergence insufficiency definitely-- it got worse as they were measured.

So the clinical outcomes-- so the athletes with convergence insufficiency performed worse on neurocognitive testing and they were more symptomatic post-injury. So we did ANOVAs. And they performed worse-- the group that had the convergence insufficiency performed worse on verbal memory, visual motor speed and reaction time, and they had a greater total symptom score.

Now, we also did regressions where we controlled for age, but also for total symptom score. We didn't want to just say, maybe these athletes are more severe injuries. And what we found when we did that was near-point still contributed to reaction time, even controlling for overall symptom severity. But no other composites were significant with the regression model.

So that was a good start. And so more recently, I wanted to look at this same type of patient across time. And interestingly enough, we in clinic often think our patients with convergence insufficiencies recover-- take a longer time to recover. When we actually crunched the numbers-- and again, this is a little bit different of a sample because these were all athletes within seven days of injury. So we got them all very soon, versus when you do 1 to 30 days, you're going to get some chronic people that are just finally coming in because they've had symptoms for three weeks now, right?

And so this sample-- it's not up here, but they had a mean recovery time of about three weeks, so the normal of what we see. But we didn't have any chronic individuals in this sample. And they all looked the same at clearance, you can tell. So even though we replicated this, had a very similar-- actually, all three composites we saw the first time were the same the next time, regardless of when they were seen. If you had that convergence insufficiency, you have this pattern of performance. And then they didn't differ on the recovery time, either.

So athletes with convergence insufficiency have worse neurocognitive outcomes in the acute stage of injury. From a clinical standpoint, personally, and I think a lot of my colleagues-- we really pay attention to the academic accommodations we give this group. They do seem to struggle in school. They get very tired. They have problems focusing, a lot of problems in math, sometimes reading. They have real functional problems, sometimes. And so trying to reduce visual workload, trying to-- audio books, perhaps delaying tests or breaking them up-- this kind of thing can be very helpful for this type-- this trajectory of injury, or this profile.

It did not seem to play a role in recovery duration. However, I'm going to put the caveat of when appropriate treatment is available. So that sample I just showed you-- some of them, if they needed, were seen in vestibular therapy and may have been given exercises. So we don't know the natural recovery of the convergence. Perhaps they would take longer to recover. But at least here, we're really good at getting them into treatment very early. So when you treat it early, most of them can recover in the same duration as someone without this problem.

And then athletes do fully recover from convergence insufficiency. All of them were cleared, had normal convergence in the context of any-- if they had any preexisting issues, they'd still be cleared with that. But they either had a normal convergence and normal scores on testing, so they look equivalent to athletes with and without-- all athletes looked equivalent.

ANTHONY KONTOS: What we were really interested in is, what factors influence these vestibular ocular outcomes that we see as being so important following this injury? Are there certain risk factors that might drive that particular clinical profile? And I hope as you're hearing all of this you're starting to connect the dots yourself in your own head and in your own practices as you leave.

So the VOMS, or Vestibular Ocular Motor Screening, is a tool that came out-- or at least has been published in 2014. It's been in use here for about four or five years before that, at least in some derivation. And now what it focuses on is smooth pursuits, saccadic eye movements, near-point convergence distance, visual motion sensitivity-- that's the one on the bottom-- and then a VOR reflex. And we look at that horizontal as well as vertical.

And the idea here is that we're stirring up the vestibular system with the latter two and looking at what are the symptoms provoked by that. And in the earlier ones, we're looking more at the ocular motor component, and then that convergence insufficiency measure. And the idea is you're getting that symptom provocation here, with the exception of the near-point convergence distance. So that's it. I'm done. Ann, I'm sorry. I didn't mean to steal too much.

So moving on, what do we learn? Well, Mickey said, a lot of the patients we see have this. How many? 60% have at least one of these things going on. The one that's the most common is the VOR. And in this case, we only had the horizontal VOR for some reason in this particular dataset. But that was the most common impairment/symptom provocation we saw.

Interestingly and importantly, we see almost nothing in controls. Only 9% of our controls report something that we would say would be at some level of above zero. So they're almost literally at zero across the board, which is also important to know. We don't want a lot of false positives, right? It's good.

So we developed some cutoffs, which some of you may have already heard. When we look at this sample, it wasn't 50-50 split. So the actual probability to be considered concussed was 44%. So that's what it would look like in a pie graph. My advisor said never use pie graphs, but I'm going to use them, OK?

So when we get to an NPC distance of greater than or equal to 5 centimeters alone-- and notice I said greater than or equal to-- that's it, just that, what we do is we increase it 35%. So now we're about 79% accurate in identifying concussion. Now throw that out the window. And now let's look at symptom provocation.

When we look just at that, if you're at a two or higher on symptom provocation, we see a 50% increase to 94. We actually surprisingly didn't look at what happens when we combine them. We probably should have done that, but we'll do that some other time. So there are some good cutoffs, two for symptoms across each item, and 5 centimeters or above for the near-point convergence.

Is it balance? I always get this question. Aren't you just measuring balance? Everyone always puts, oh, I'm doing a vestibular talk, and then you look, and they're talking about the BES. Look at those wonderful correlations. They're nonexistent. They're not the same thing.

In fact, postural stability across the board-- we're doing other research through the NIH right now. There's nothing there as far as its relationship to the vestibular component. They're totally different systems, totally different outcomes. That Doesn't mean you drop them or one's more important. It means they're different, so they're augmenting. So you should be doing both. The vestibular ocular motor piece, though, hadn't been done up until recently. So I think it's an important addition.

So here's what happens when we look at groups. And I'll thank RJ for-- Dr. Elben for some data here. The high school-- big number there, 468, is from his sample in Arkansas. The colleges are athletes here in Pittsburgh through the DOD study, NCA DOD study. And then we have our original study of high school concussed.

And what we see there is what? The high school kids with concussion are all above those cutoffs because they're concussed. And in contrast, we see virtually nothing going on in our control, both at the early adulthood, college age, and in addition, at the high school age. So that's good, right? We don't want to see them above that line because that would say you have false positives or something like that going on.

But we thought there might be a little bit more to it. And we wanted to look at, really, what is the false positive rate across these measures? And I'll highlight, too. I know these numbers, you're like, oh my god. Which one am I supposed to look at? Those two, OK?

So the first one in the left, 13% in our high school sample, VOR. That's the one where we see the highest rates. So that means 87% across all these items, you're not seeing any positives. So it's 13% false positive rate, if you will. When we look at the college, it's 11%. And interestingly, it's down at near-point convergence distance. It's that measure.

So we were interested-- what is going on with that 13% and that 11%? Why are they reporting that? So when we look at our college-age samples-- so we're going to throw Dr. Elben's sample out for this because we have a little bit better medical history and other data. That's what we wanted to look at. 89% reported zero cutoff.

But there's this group here that had something going on. And some had a lot going on. And we were like, what is going on? Well, 60% of them had motion sickness diagnosed. And we had medical diagnosis for this in their records. So that was kind of a bell. We're like, wait a minute. What other factors might be influencing these VOMS? Because we want to be able to pull those people out so we don't get false positives when we use the VOMS clinically.

So when we look at this, motion sickness is associated with a seven and a half times greater likelihood for, basically, a false positive at baseline on the VOMS. So you need to make sure you know whether or not these patients have a motion sickness history. And if you don't and they don't, you ask them questions about, do you get sick in the car, does this make you sick, et cetera, et cetera. Do you not like shopping in the-- scrolling in the environment? Do you not like walking down the hallway in school, things like this, right?

And then at the end of the day, we see this really, really strong relationship, but not for near-point convergence, just for the VOMS symptom provocation items. So other factors that are relevant-- sex rears its ugly head again. I probably shouldn't say out loud. That didn't sound right.

But in all fairness, here it is. And guess what? It's a risk factor again, which is very specific again here to the VOMS. When we look at the near-point convergence, we don't see a lot going on. And we don't see concussion history or migraine history being significant predictors at baseline. I'll come back to that when we look post-injury.

So what happens post-injury? And I'd like to acknowledge Melissa Womble, who is somewhere in this room in one of the corners, I think-- back in the corner here. She's doing some great work as our fellow here, just about to exit in the next month or two. And she's really helped out looking at post-injury. So now we're looking at, what about those factors I just mentioned on your post-injury VOMS? Does that matter when we look at that?

And lo and behold, we see sex, on-field dizziness at the time of injury, post-traumatic migraine, and fogginess all being significant predictors of a higher vestibular ocular motor score on the symptoms. When we look at near-point convergence distance, it's a little bit different story. But we still see three of them holding here, near-point-- I'm sorry, on-field dizziness, post-traumatic migraine, and fogginess. So those three are a pretty big deal.

But we actually were interested in which particular components of the VOMS are those affecting. Are they just across the board, they just make you higher on all VOMS items, or are they very particular? And so you can start to tie the dots together a little bit. So sex was really only-- only played a role in that VOR component where you're doing gaze fixation while you're moving the head. And then we see nothing, again, for concussion history across any of the individual items.

Migraine history focused more on the saccadic eye movements and, again, on the VOR, not terribly surprising. My wife has migraine history. And I know when she had a concussion about a month and a half ago, which was really interesting to see firsthand the relationship between motion sickness, migraine history, and a concussion-- and she hated the VOMS. Sorry, Ann. She really did. It was brutal. But you know what was great, is she improved very, very rapidly with therapy, which is a whole other research study we need to do.

When we look at the secondary risk factors, we see the same thing again across some other items here, so that on-field dizziness. What happened after the injury also drives whether or not you have these higher scores on the vestibular ocular motor screening tool, with the exception of concussion history and loss of consciousness. We didn't see either one of those factors playing a role in any of this stuff. From the previous slide, concussion history, LOC here.

PTM and fogginess-- these patients are just high across the board. And what we're trying to do now is tease out, just pulling out that component of their global symptom factor, if we can pull that out and look at them, just PTM. And that's really hard to do, but we're trying to do it.

So in summary, the VOMS plays-- or VOMS scores can be affected by these risk factors both in healthy populations-- so some false positives associated particularly with motion sickness and with being female. And when we look at the post-injury, we see some risk factors there as well. So we need to consider these, another set of questions along with somatization, sleep. You'll certainly have so much to do it's going to be a four-hour appointment. But you get the idea here.

Now we're going to wrap up with what I think, at least for me, is maybe-- I'm the researcher, so of course this is all exciting. But this is the most exciting to me, the treatment phase. And we're really moving our research into this area. It's hard to do. That's why you don't see a lot of published studies on treatment. They're very hard to do. It's hard to say we're not going to treat someone.

We wanted to look at what happens when you compare a churn approach, which is really prescribed rest, within different groups. So if you look at one group versus another-- they all have concussion-- do they end up with the same outcome when you prescribe rest of varying degrees to them? And I acknowledge here a couple folks, Danny Thomas, and then, obviously, my colleague here, Alicia Sufrinko. We're working on a secondary data analysis of Danny's really seminal piece of a randomized control trial looking at rest.

What we wanted to do is determine which patients are getting better with rest, if any, and which are getting worse, because we've written a few proposals suggesting that we think you really need to do different things with different patients, especially with regard to activity. So these groups of patients-- and there were 60 males, 33 females. Again, this peds ED, so we're talking about kids, good population. You're seeing a lot of data from this.

Five days strict rest-- one group is randomly assigned to that. The other group was usual care, which was loosely defined as two days and a more progressive returned activity. And then the patients were compared on signs and symptoms only. Those were the two groups we did secondary analysis of. So we went back in the data and said, what if we look at someone who has a higher organic or burden with the injury-- so they had post-traumatic amnesia, a loss of consciousness, disorientation, confusion, these really overt signs at the time of the injury-- versus those who only reported symptoms in the absence of any clinical sign of the injury?

So these are the data that you saw Noel present. And I'll just say that what we see here is that, at four days, we see the biggest difference. The group that gets prolonged rest is actually more symptomatic. Think in terms of more time to ruminate on their symptoms, all these things that we've heard talked about today, contextual framing effect, nocebo, et cetera.

But now, here's the $50 question, if you will. What about if we look at the groups' signs versus the symptoms-only group? Well, if we look at the symptoms-only group, as evidenced by this lighter or gold line in wonderful Panther colors here, we see that that group actually got worse. They're the ones driving this. So if the symptoms-only group is told to rest a lot, they get worse. They actually do better when you tell them to rest, over here, a little bit less and get your butt moving as fast as you can.

In contrast, we see an opposite effect with the early-signs group. So the symptoms group gets worse. The early-signs group with a higher burden-- there's a lot of different ways, more severity. You can think of this different conceptual ways. That group actually got a little bit better with that rest. And so that might be a group that we identify as maybe needing a little bit more of a break. My wife was a good example, where she needed a couple days, not a lot, just a couple days of you're not going to work, you're not doing stuff, but then immediately got into an active approach for her vestibular issues.

So in summary, prescribed rest may not be the best treatment for all patients, as I think we're all starting to jump into. But we have to be careful about which patients we use it for and which patients we don't use it for. And so those with symptoms only, rest is clearly problematic, probably due to some somatization, other symptom issues. Patients with the signs may benefit from a little bit more rest, but we're not talking about a cocoon. We're not talking about that approach. We're certainly not talking about dark rooms, no texting, just a little rest, and then we move on.

Questions to consider-- and this is where we're going next. Do active interventions-- are they more appropriate? Do they work better? If so, when should we use them? How much? How often? And we need to match them with the profiles so that we get the best outcomes, OK?

In conclusion, overall here, I think you're starting to get the idea that we have to ask a lot of questions of our patients to know how we can tie the risk factors to the clinical profiles to the hopeful treatment recommendations and outcomes. And also, I think we need to be very judicious in how we use rest. I think, right now, we're all moving towards a more active approach. That's a good thing. And as we build more data, hopefully we'll be able to be more specific about the when and the how much.

And ultimately, all this hopefully will drive better patient care, as we want to be evidence-based as we move forward. There's a bunch of people, many of whom you met out of the staff in the front that helped out with this, so acknowledge them on this slide.