[MUSIC PLAYING]

ROBERT KANIECKI: "Cloudy With a Chance of Migraine" is going to focus on the pre-migraine phase. People talk about migraine, they think specifically about the headache. And we're going to talk about the headache. And we're going to talk about the pain.

But migraine's so much more than that. And you guys in concussion-- in this field recognize that concussion's more than headache or dizziness or fatigue. And I think you're beginning, in a sense, to silo people-- certain categories.

Lots of centers seem to be doing that where, all right, we have the dizzy, anxious person. Well, you know what? In migraine, we have the migraine, dizzy, anxiety person, what we call MAD triad, where it's dizzy and anxious and-- so we see some of the same things.

And what I'm going to do is, almost in a sense, maybe break down some of the silos now, which might make a little-- create a little discomfort. You think, oh, now we're finally making sense of this subgroup and this subgroup. And as you know, there's a lot of overlap. So we're going to talk about that.

So first, there's headache. Where's the storm? So when we talk about-- in neurology, we always talk about, where's the lesion? Where is the problem? So where in the nervous system?

So we have pain in the head and neck; nausea; visual changes, both blurring and light sensitivity; cognitive impairment; dizzy; mood changes; fatigue. Sound familiar? Nausea wasn't really quantified in this paper. But if we asked patients with head trauma, "How many of you are nauseated?" it would be a high number as well. So these features overlap.

So migraine is more than a headache. It's a complex neurobiological disorder. Head trauma is a complex neurobiological presentation of a nervous system disturbance, as is migraine. So the lessons we're learning now in migraine, are they going to be applicable to your field? And I believe very much so.

So the headache phase we're going to talk about, because all of you want to talk about, well, how do we manage the headache folks? And I want to give you practical steps of what we do, how we approach it, and what the headache piece is all about. But honestly, the interesting stuff is the pre-headache phase-- maybe not so much the aura, which we'll reflect a little bit upon-- but prodrome, which is the unrecognized clouds before the storm.

So the phases of migraine-- think of migraines-- we can break this down into a series of phases. Prodrome is the first phase. This is recognized, if you ask in a questionnaire, by about 80% of folks. They'd say, yeah, some things.

So yesterday, I had a woman. I said, can you tell me, do you have any symptom before pain, any at all? No, I really don't. Now, do you feel differently in any way before the head starts to hurt? Well, I get this warm sensation right here. And then, I can tell something's brewing was the word-- the word she used.

And I smiled. Because she said, is this funny? And I said, no, it's interesting. Because this phase, you know.

And she said, but you know, doc, I can't always treat there, because I'm busy. I have three kids. I'm flying around. And I don't necessarily connect to this. Now those are the words she uses. I don't connect to this piece until maybe an hour later.

But my job was to then, OK, we need to connect at this phase. Because once she got to headache, all lights were out. I mean, she was going to the emergency room twice a month. She only has four headaches a month. But she's going to the ED twice, because they are completely out of control. Because she's not stopping here and introducing treatment here.

Aura is the next phase. This is the only present in 25% to 35% of folks will have an aura. So an aura is a beautiful event when we see it. We're going to talk a little bit about aura. You guys are going to not see a lot of this. So I'm not sure that aura itself, except in those who definitely have post-traumatic migraine, is really of that much interest to you. So we'll kind of blow through that.

Headache goes through two phases, and you see this. So the post-traumatic patient often has this underlying everyday, low-grade, dull, tension, sinus looking thing. And then, they have the bad ones superimposed. Well, it's the same headache. It's just a matter of how far it goes. And then, the hangover.

We're not going to talk much about the hangover at all, because we know very little about the hangover. However, the headache hangover is perhaps where your patients live. Your patients may be living from prodrome to postdrome constantly and intermittently getting the headache attacks.

So the headache-- let's talk about that. Because again, practically speaking, we want to talk about, how do we manage these folks who actually have the headache phase? When they talk about the pain, what do we want to do?

So here is how we define migraine. The important piece of this is the International Classification for Headache Disorders has a clinical definition, as you see. There are no biomarkers. There's no tests.

MRI sometimes show these little white spots that we call migraine freckles. They're signs of minor damage to the brain of a meaningless-- I use the analogy freckles, because freckling is damage to the skin that's meaningless but it's visible. The migraine spots-- often seen in trauma patients as well-- the migraine spots are meaningless, it appears, but visible on MRI.

But the features, you can see-- unilateral, throbbing, moderate to severe. The point of this is that you don't have to have them all. Some people think, oh, to diagnose migraine, you have to be one-sided. Or you have to throb. Or you have to throw up.

No. You have to have some attacks that do some of these things. But as you can see, the pain could be bilateral and steady, as long as it's moderate to severe and worse with physical activity.

Worse the physical activity is the most specific on this list. Worse with physical activity is exactly what you folks see, right? The headache that gets worse with physical activity. So migraine is very much that. It's an episodic disabling headache disorder, and the disability comes from severity of pain.

But more importantly, pain gets worse when you do stuff. And so that really is what disables folks. I can't go to work. I can't go to school. Because when I do something, I can't go back to the field as soon as I start exercising the head. I can't even walk, doc, because as soon as I get my heart rate up, my head-- so you guys hear these symptoms all the time. So there's the features.

So what hurts? The brain doesn't. So although we can talk about all the brain tracks change with trauma and what happens at axonal levels, really, none of that hurts. The pain comes from the nociceptors that are localized mainly in the membranes, the dura, and the vessels.

So we talk about what hurts. Those are the two spots. And in migraine, those are the two spots that are activated. The periosteum is very likely meaningless.

So we have the dura. So basically, you have the brain. And then, you have a saran wrap layer and a wax paper layer of membranes and then the skull. So I tell patients, all the nerve endings are in the Saran wrap and the wax paper. And that's where the blood vessels are, and that's where the pain is coming from.

So those membranes are disturbed. And the pain's emanating from those. And why does pain get worse? Because those membranes will get-- will be moved when you move. When you cough, when you sneeze, when you bend, when you're physically active, those membranes move.

The brain is tethered, but not fully. It floats. It has movement. You are well aware of that. It moves inside the skull. And that movement is what makes pain worse with physical activity, why it hurts when I bend and I'm physically active.

So the dura and the vessels-- and this is exactly, by the way, where the triptans work. When we talk about sumatriptan, rizatriptan, the mainstays of migraine management, they have receptors in the dura and the vessels. They work directly-- basically, they are specifically targeted to where migraine pain is being generated.

So a little bit about what the pain looks like. So here, you have the trigeminal nerve and the vessels. So the nerve in the membrane-- so this is the-- between the wax paper and the Saran wrap, this is what's going on.

So the nerve endings are agitated. The trigeminal nerve is the one that's innervating these structures. And when it's turned on, when it's activated, it's going to release a series of chemicals. One chemical is CGRP, which is a very potent vasodilator. It will cause the blood vessels to swell.

Substance P will cause the blood brain barrier to break down and to leak. And then the kinins-- inflammatory mediators. So inflammation is a big piece of what we see in migraine. Inflammation is a big piece of what you guys see in trauma.

So this inflammatory cascade causes swelling. The blood vessels are swollen, where you often get a throbbing or worse with physical activity, because the vessels are changing. And the membranes are all swollen. And this is the full effect.

So this is basically sterile meningitis. Those signals are now routed through a series of relay centers, which we're going to really reflect on in a minute. But those signals are sent north. The brain understands this is pain.

So the central projections-- you basically have four stops. So this train has four stops. It starts in the trigeminal nerve there at the bottom. That trigeminal nerve, or TG, trigeminal ganglion is pseudounipolar. It basically has two arms. One arm goes out to the vessels in the membranes. One arm connects into the brain.

So second stop is the spinal trigeminal nucleus, that Sp5. That's in the brainstem. This is a very important structure for you folks. Because this is a very elongated structure that goes through the brainstem into the upper cord.

This is receiving input from here, here, here-- cervical input, intracranial input all integrated in the same spot. There are nerves in this nucleus that have connections to both the dural membranes inside the skull and muscle or joint nociceptors outside the skull integrated in the same spot. And this is what we take advantage of, we think, when we do nerve blocks for people who have intracranial pain, which are very effective. We can talk afterwards a little bit about those.

Third spot is the thalamus. So that's the third stop for this train. And the fourth spot is the cerebral cortex. It has a bunch of stops.

So as you can see, it starts to spread out. Just like you take one bus, then you take it to a central center. Then, you take it more and more options to connect. The key one-- although I just reflect that this spinal trigeminal nucleus-- the second stop, is a really interesting one, it may be the third stop where the money is. So the thalamus and the hypothalamus, deep in the brain midline structures, may be where the money is going to be for all of us.

So what do we do to manage this? So we were very aggressive in migraine. We're very aggressive in migraine that's either genetic or post-traumatic or both. So this nervous system, fundamentally, is more sensitive by nature.

What is migraine? A biological disorder where our brains are different. I have migraines, and our brains are biologically different. We're more likely to be motion sick, even as kids. We're more likely to have colic as babies, irritable bowel. We're more likely to be light sleepers, type A personalities. We're more likely to be anxious. We're more likely to be depressed. We're more likely to be PMS.

We're more likely-- our brains are different. And we're very sensitive to medications, which drives you folks nuts. You can say, I try this. I tried Amantadine, and I didn't sleep for three days. I took a Benadryl, and it kept me up for three days, or it knocked me out for three days. You get both the paradoxical and the real effects at the spectrum.

And this is us. And it's frustrating to us to tell you this, because you think we're nuts. And it's frustrating to you to hear this, because you do think we are nuts. And sometimes, we are nuts.

But this nervous system is different. And so if you understand and say, OK, we're sensitive people-- and you know. we've got the sunglasses. Now, some people take it to the extreme when they come in with the sunglasses and a hat and the big mask. You know, I'm everything sensitive-- to odors, to--

But we have no-- in our waiting room, there's no TV. There's no radio. We've gotten the fluorescent lights out. They're all table lamps.

So the people that aren't migraine people come in and say, boy, I hate this place, because I can't do my stuff, can't read. I don't have a Kindle. I just got a regular book. It's really dark. There's no TV. There's no radio. There's no perfume.

We have it very, very-- de-sensitized the system. That's why, actually, the headache center is the only neurology group that's outside the main Kaufmann Group. Because they've got a fish tank and a TV, and we can't deal with all those kinds of things.

All the rooms are dimmable. All their lights are dimmable in all of our exam rooms so that we can keep everything low. We have natural lighting in all of our offices.

So what do we do with this nervous system? Well, often people, when they get into trauma-- one thing about this-- we're not going to go into too much detail, but if you over-treat it with medication or with caffeine or with sleep for that matter, if you overuse a treatment to treat acute headaches, you're going to find yourself in something we call medication overuse. But I also see nap over use. And caffeine is a drug-- caffeine overuse for these folks. Or Sudafed overuse, because they think it's sinus.

So what do you have to do is really watch out for those that are treating their headaches more than 10 to 12 days a month. OK, there's your cap. So as we go further, whatever your treatment, whatever you're using, we've got to cap it at 10 to 12. Even though if you're having a headache every day, we'll talk about what else to do.

Natural migraine prevention-- and this is where we come down. And I tell them, I'm your coach. I told a young girl this yesterday, 16-year-old, she started crying when I talked to her about going to school all the time. I said, I'm not-- I'd love to be your friend, but I'm not. I'm your coach. I'm here to say, 'atta girl when you did a good thing, and you need to get after it when you don't.

And so what do you need to do? You need to go to school every day, unless you're throwing up, period. There's no lates. There's no-- what we need to do is get to that point.

If I don't give you the tool for your headache that gets you there, OK, that's me. I'm going to work on getting you the right options to get you onto the bus. And a pill's not fast enough, you need to take the injection, period. If you don't, OK, you don't want to. You're still going on the bus. So we need to get you regulated.

And I call it brain boot camp. Everything is regulated. You go to bed and you get up at the same time. There is no nap. There's no sleeping in. You pick six hours a night, that's fine. You pick eight? It's fine. You pick a number, and you stay with that number.

Teens are horrible at this. However, what I tell them, you've got flexibility in the weekend. If you sleep 10:00 to 6:00 in the week, you can do 11:00 to 7:00. You don't have to be on the exact same schedule, but let's get you regimented.

Just regular sleep, regular meals. You eat four to six portions a day-- nothing real heavy, but you don't go long without. I don't care if it's a handful of nuts-- and we say handful is a portion-- handful of nuts, handful M&M's, handful of grapes. I have Raisinets. And I said-- it's not always healthy. I pull a bag of Raisinets, because it's just mine-- out of my-- my recent one, at least-- out of my drawer. I say, this is what I do-- handful of Raisinets and keep going.

You could have a protein shake. You don't have to drink the whole thing. And then, I usually hold it up. I say, it's-- well, it's not the whole beverage. It's what fits in your hand. That's a portion.

So I had a mother yesterday, actually had trauma. She got hit in the head with a hockey stick, because she was spending a lot of time at the rink. And the rink was really there, because she was there for her daughter, who was a figure skater. But somebody swung their bag around and their stick around. Whack.

And she said, I'm at the rink all day. I don't-- I said, what you need to do is bring water. You need to bring food. Regular sleep, regular meals, regular hydration. I keep refilling the water on my own desk. And I'm drinking here in front of you too. [INAUDIBLE] say I practice what I preach.

So you hydrate at least 40 to 60 ounces. I like the trauma people at 60 to 100. And I give the kids Gatorade as an option. Sports drinks, let's go with that, because they're not going to drink that much water.

So regular sleep, regular meals, regular hydration, regular exercise. You can't get there now, you say, every time I exercise, this is what happens, and we do what you guys do. All right, we're going to do five minutes a day. We're gonna do five minutes a day, whether you're doing-- whether it hurts or doesn't hurt, you're doing five minutes. And then you stop.

Next week, you go to 10. Whether it hurts or doesn't hurt, you stop. 15, 20, we wind up, eventually, to get people to 30 minutes a day. Even if it's just walking, we need to get you doing something.

So regular sleep, regular meals, regular exercise, regular hydration, and then regular school or work. That's kind of the recipe of where we go with the left there-- natural migraine prevention. We also then look at, what can we do to modify your diet, if you're overdoing MSG, overdoing caffeine.

So the only dietary restriction I usually place-- most people know if they have a dietary trigger, mind you. I know mine is artificial sweeteners. Automatic-- aspartame, it's a headache. So people usually know. Yeah, mine's bananas. Or mine's wine.

But for the most part, no dietary restrictions, except this-- try to do unprocessed. So if you have ingredients on the package you can't understand, put it back on the shelf. Potato chips is my usually my go-to for an example.

You can get Simply Ruffles, which is potatoes, oil, salt. You can get ranch-flavored Doritos, which is 24 ingredients, half of which you have no idea what they mean. It's nothing of real value in those. So they're less processed. But processing actually is not just unnatural.

Cucumbers hardly ever cause headache, but pickles do sometimes. American cheese or Velveeta or Cheese Whiz-- usually not. I don't know what Cheese Whiz really has. But if you got cheddar cheese or aged cheese, the good stuff-- yeah. Grape juice-- probably not. Wine-- sometimes. So even natural aging or processing-- and what that does is it concentrates the biological compounds that truly can act as triggers in some people.

All right, what about meds? Triptans and non-steroidals, period. These people have other trauma, thought, right? They have rib trauma. They have back trauma. So they're on hydrocodone. They're on Tramadol. They're on a bunch of stuff. Fixing those people is almost impossible.

So right out of the gate, we tell people, if you're on these things every day, we're going to be up against it. They are pro-inflammatory. The opioids are pro-inflammatory, period. They may be helpful for pain, but they irritate inflammation.

There are many people that itch-- they don't even get a rash-- because opioids will cause mast cell degranulation. So lots of people say, oh yeah, I itched with codeine. I didn't really get a rash from it. That's true. It wasn't really an allergy, but it caused inflammation.

They also cause inflammation deep in the brain. So the astrocytes-- which we're not going to really refer to too much today-- astrocytes, basically supportive cells in the nervous system, are doing a lot more than we thought. And they can be irritated by exposure to opioids and cause migraine issues to worsen. So if you're on Tramadol, you're on butalbital, Fioricet, you're on hydrocodone, code we say, we've got to get you off.

If you're willing to do that, great. If you're not willing to do that, go take care of your back. Good luck. Godspeed. Get yourself off the stuff, and then come back when you can get-- we can get after this. Because these are the folks that are really going to be a challenge for you to fix if they're using chronic opioids.

And there are some that need it. They may have had a serious back problem or serious rib fracture. Rib pain's got to be awful. OK, take care of that. And then let's get after the headaches once you're done.

So no butalbitals, no opioids, non-steroidals, and triptans. What do we do? Here are the drugs that have the data, just to give you an idea. But what the point of this is look at the doses. Look at the dose of aspirin that's used in migraine. It's not 325. It's not 650. 900 is the most effective dose.

Remember, we're only doing this fewer than 10 days a month. And you shouldn't do more than two doses a day of anything. One dose should be doing it. So here's the drugs we use. But you you see high-dose naproxen, high-dose ibuprofen, high-dose aspirin, and then diclofenac powder packets. That's Cambia, the brand name Cambia-- not well-covered on most of the insurances, which is the challenge with that one.

And here are the triptans. Look at all the options we have here. These are the drugs of choice. So sumatriptan, zolmitriptan, so Imitrex, Zomig, Amerge, Maxalt, Axert, Frova, and Relpax. The last two are still branded only. This is in chronological order of their release. The last two are still brand only and very challenging to get.

Also, I don't use much of the last two. The last one, eletriptan, has a lot of drug interactions. It's cytochrome P450 3A4 metabolism through the liver. I don't do that one much at all. Plus, it's only brand. It's hard to get.

Frovatriptan's too slow, typically. It's slow of triptan in my mind. It takes three, four hours sometimes to kick in, and migraine people don't like that. They want relief now, yesterday. So we don't do too much of those.

We spend a lot of time with sumatriptan. It's generic. It comes all kinds of versions. We love the injection. There is nothing better, period. There is nothing faster. There's nothing stronger. This is the best treatment on the market for migraine.

And it's not because the brand name Imitrex or the brand Sumatriptan or the molecule sumatriptan is super different from the others biologically. No, it's because it's the only one that's an injection, period. It's the best thing. So it starts working in five to 10 minutes.

Tablets are lucky 30-minute onset. Frovatriptan, again, an hour to two. You just can't. That's time of onset, not time of peak benefit. So we spend a lot of time there on the left, the sumatriptan.

And then naratriptan, this is going to be a good one for you guys. I just want to point that one out specifically. Because the medically-sensitive person that couldn't take sumatriptan, couldn't take Maxalt-- those are the ones on the plans that are generic. So rizatriptan and suma are the two we use a, lot because they're fast. They're strong. But your patients can't take them sometimes.

So half the doses. So if the high dose is too much, just tell them to cut it in half. And if that's still too much, go to naratriptan. Naratriptan, in the clinical trials, the side effects were no different from placebo. Really well-tolerated stuff. It's also generic. So it's on UPMC's plan. It's on Highmark. It's on basically all the plans you'll find. Generic naratriptan held very well. So those are the ones we use.

How about prevention? What are the drugs we should be using? Well, here are the evidence-based guidelines. The anti-convulsants, divalporex sodium valproate, or Depakote band; topiramate, which is Topamax brand. The beta blockers, those are the three that have the most data-- metoprolol, propranolol, and timolol.

I love these in the trauma patients. The beta blockers are really a go-to for us. And I'll you why in a second.

Onabotulinum toxin A, or Botox, is indicated only for chronic migraine, which by definition, you have to have at least 15 days a month, at least eight of which are severe and meet full criteria for migraine. So it's a specific definition. So it's not that you had migraine for a long time.

In our world, in the headache world, chronic means you have headache days more often than not. So more headache days than headache-free days. Whether it's chronic migraine, chronic tension, chronic cluster, the same thing holds true.

So there are the main drugs that we use. Level B Amitriptyline and venlafaxine-- you guys see us using those lot as well-- so Elavil and Effexor, and then the other beta blockers, atenolol and nadalol.

So in the beta blocker family, I like metoprolol and atenolol, because the fewer side effect issue. And again, in your population, propranolol is the most common used-- commonly used beta blocker, but maybe a few more side effects-- mainly fatigue, not a good one for your group, and depression, and sometimes sleep changes-- either hypersomnolence or insomnia. So the beta blockers do have that potential.

So we usually take the ones that are a little more gentle. So atenolol and metoprolol, in my experience, are much better tolerated. And 25, 50 milligrams to start with. So as long as you don't have heart issues, heart rate issues-- bradycardia or hypotension, this is where we go.

Now for the exercise person who's going to look at getting a target heart rate, it's going to affect that. So they just need to be aware of that. Exercise intolerance at our lowest doses is not too common, but it's possible.

The topiramate-- great migraine drug. What's its main side effect? Well, what's the side effect we worry about? Anybody know?

Cognitive, absolutely. Not a great one for your population. So we love topiramate in the typical migraine sufferer. But it's tough in your group. It's really tough.

And you have the student that's at school that's already struggling with grades. Oh, it's a great drug, but this is a potentially double-edged sword. So we go to it if we need to, because it really works well.

But you've got to stay low dose. You've got to work with 15s, the pediatric little sprinkle capsules. You work your way up 15s-- 15 30, 45, 60. You stay below 100 milligrams with that drug, particularly in your teenage group. And this can be very helpful, but you've got to be cautious with it.

So the Amitriptyline-- great for those who can't sleep. And the venlafaxine effects are very good for those who are already sleeping but need to be pepped up a little bit. They're more hypersomnolent.

So that's the group-- those are the groups drugs that we use, just to give you a background. And we'll talk more about therapeutics, if you like, shortly. So that's the headache piece. And that's the one we kind of think about the challenges that are mainly therapeutic.

What about aura? As I told you, I think you're going to learn, watch, and think more about migraine in your patients when we learn about these other pre-headache phases. So aura-- and I put the lightning bolt here, because aura is an electrical phenomenon. It's not a vascular part of the brain not getting enough blood. There are blood flow changes.

But it's an electrical phenomena. It's an electrical storm that may precede the headache. So here you see the main components.

First, it's fully reversible. This is five to 60 minutes. This is what we call the opening act. Now, it can happen during the headache, mind you, but it's an opening act. And it should do something. You should be able to tell me what it does.

So I had a lady yesterday who was great. She said, yeah, I get this little multi-colored Y. And she said, over the span of 15 minutes, it gets a little group of marching multicolored Ys, and they go across this arc.

And they start over here, and they kind of march. There's multi-colored Ys. And then, they go over here. And after 15 minutes, they go off, and then I get my headache.

My favorite is a-- is a boy, who was eight or nine. And he was very thoughtful. I said, do you have something? He said, doc, I got something. And I said-- he was from Uniontown. I remember this kid really well.

And his parents are calling me Doc, and he's calling me Doc. And he said, Doc, I got something. And I said, what is it? He said, I get this fluorescent-- and each time, he's thinking-- fluorescent orange rotating hand-grenade. And he went like this.

So people do it. They do this. They do this. They say sparks and colors. And it should do something. So aura is an event that somebody can describe to you.

Lots of your patients are going to get flashes. Lots of your patients are going to get blurry. Lots of your patients-- but a blurry spot that does something.

Two weeks ago, it's the lady that came in and said, it's a blurry area. I know what-- I could-- you know what it's like? You know when you watch *Cops* and they do that thing to the face of somebody that don't want to show their face? That's what it's like.

I get that, like that thing on *Cops,* where they blur out your face. There's a little blurry. So that's aura. And it should be between five and 60 minutes, can come during the headache.

So it is not just visual, though-- very commonly, tingling and numb. And the third most common is speech language. I can't find the word. I can't tell you what I want to say.

So the visual, or it can be like that. Yeah, I can see in the center, but everything around-- the tunneling-- people will talk about tunneling. Well, tunneling isn't necessarily that everything's black. Sometimes, it's just distorted like this.

Where they'll give you this, again, this-- maybe the colored Ys. Maybe if something is like that. This is the classic scintillating scotoma, which is what this lady was describing.

Or it could be tingling and numb. And it marches. It starts off in the finger, the thumb, and a finger. And it kind of comes up over about five, 10, 15 minutes. And the most common tingling and numb is here-- hand and face. So it starts to get what we call cheiro-oral-- cheiro-oral development.

So what's this about? I said it was an electrical storm. This is truly the weather front. This is, like I said-- I always talk to the kids. I said, you ever watch the Weather Channel? Kids don't watch the Weather Channel anymore.

No one watches the Weather Channel. I guess they took it off my cable, so I can't watch it either. I've got some AccuWeather thing I don't even bother watching. The Weather Channel is kind of interesting.

But in any case, here's the storm. Here's aura. It's a weather front. It's a brain front. And that brain front starts most commonly in the occipital cortex. The occipital cortex is the most sensitive cortex, visual cortex. Why your

People with trauma-- you'd say, well, temporal poles and the frontal lobes are getting all the brunt of this stuff. When we see injuries, that's where the trouble-- no. Those cortices are actually fairly resilient. They can cause seizures more commonly. But the occipital cortex is the one that's really sensitive. And this is where aura is generated.

So guess what? Visual aura, right there-- occipital cortex. That's where the vision change. Where's sensation? Right here. Where's the language piece? Right here. Everything's in the back.

Very rare to get weakness. Patient says they get weakness with their headaches, usually it's heaviness. It feels heavy, and it's not really weak.

But the ones that are truly weak, there's something called hemiplegic migraine, which is rare as hen's teeth. And usually, the people that get this are not headache-related to hemiplegic migraine. They're usually headache that's then functional with a functional component, a conversion symptom. The weakness is more psychogenic than it is biological more often than not.

All right, so this is a wave. It spreads at two to five millimeters a minute across the brain. Just to give you an idea, we can trigger this in animals. And it's been observed. There was a guy-- well, I think it's next. He said, you know what? My visual aura-- and he mapped it out. He was a neurophysiologist. He said, my visual aura moves across my eye, my visual field, about the rate of two to five millimeters a minute in my brain.

So this seemed to correlate directly. You can See this is 1940s. Lashley correlated directly the animal model of what we thought was aura with his own visual aura. So it was really pretty cool. This was a long time ago.

Now, we've got sophisticated techniques that basically show us the same thing. Lashley said, hey, this goes across my brain at a certain period of-- so aura's not in the eyes. The people think it's in their eye, usually. It's in the brain. And it moves across, and we now have, again, velocity of two to five millimeters a minute; changes, blood flow changes that are very clearly aligned to aura.

And there's lots of evidence. And I'm not going to go into details, because this is really sophisticated neuroscience. But we can see aura and make a case that aura triggers the headache. Remember, aura's in the cortex. That's not hurting. But you can make a case that aura can trigger headache through a series of steps.

Genes help you regulate with inflammatory mediators. You see a host of changes in perfusion enzymes. Look at all this. Panx channel, [INAUDIBLE] -- I don't think you want to see any of this, right? ? You don't care about any of this. All the little sophisticated stuff all basically-- all kinds of stuff is happening to, perhaps, connect aura with headache.

And I'm going to get through this. Most migraine sufferers never have an aura. Aura can't be the trigger. That's what people were hypothesizing. Aura is the trigger. And maybe it's silent in some people.

Well, most patients don't have a clinical aura. And when those who have aura will say, it doesn't come with every headache, only once in a while. And aura can come with or without the headache. We know that.

And we know something's happening before the aura. This is where the money is. And this is where I think you guys are going to find it interesting, where we have to learn more about prodrome. Because if we learn more about prodrome, you benefit, we benefit.

So this is prodrome, the clouds. These are the people that tell you in a beginning of a migraine, they know it's coming. So they're normal biologically. They feel they're normal. And then all of a sudden, they start getting these symptoms. And your folks, they have them all the time.

So prodrome is this first phase. It's going to be relevant, because if you can identify, like this lady with the funny feeling, I can treat at that phase. So what I did with her, four ibuprofen when you get this funny feeling. And then, if it gets the full-blown headache, sumatriptan injection, pure and simple.

We've got two levels of care. If you can intercede here, great. Well, you've got this. I trained in St. Louis at Wash U, and it had a lot of population from the south there, particularly from Mississippi, from the old days, Underground Railroad. So St. Louis and then up along the Mississippi was a stopping point. So we had a lot of people from Mississippi and roots in Mississippi. And one of my favorite phrases was, I'm fixing to have a migraine.

[LAUGHTER]

And that's it. I'm fixing to have it. Or like this lady said yesterday, something's brewing. All right? We're going to learn a lot about migraine and trauma, I think, if we learn more about prodrome. And I think you guys are having patients who are in perpetual prodrome.

So what do we know about this? Depends on how you ask. If you ask people, do you have any warning signs beforehand, you get a certain number. If you give them a checklist-- before a migraine, do you ever have nausea, light sensitivity? Before it hurts, do you ever have fatigue? Do you have yawning? Yeah.

Oh boy, you get a checklist, you got up in the 80s. So when people think about it, they'll say, yeah, maybe I do have something. So if you give questionnaires, both adults and kids can recognize this in the majority of cases.

So what do they recognize? This is Les Kelman. He had a database, one of the first big databases with EMR from-- he ran a headache center in Atlanta. And he came up with these characteristics.

32.9 clearly had prodrome. This wasn't soft stuff. This was hard yes. They have identifiable prodrome. The average person had it for at least nine hours. There's a lot of time, folks, before you actually get headache.

What were they? Fatigue, change in mood-- sound familiar-- little nausea, light sensitivity, noise sensitivity, food cravings, neck pain, dizziness. I guess aside from food cravings-- I don't know how often you guys see that-- these other one sounds pretty familiar, don't they?

So food craving is an interesting one, because people would place blame chocolate a lot for migraines. Turns out, more often than not, it was a craving for chocolate that preceded the headache. Whether they got the chocolate or not, the headache was coming. But they blamed the chocolate.

Because they had a craving, they got the chocolate. They said, oh, it's the chocolate. So if you had a Jolly Rancher at the same time, it still would give you a headache, I bet. And sure enough, you test it out, patients say, yeah, it wasn't the chocolate. I was craving the chocolate, and the headache was already in motion. I didn't know that, Doc.

All right. But sometimes you wonder, like chocolate, was that a trigger? Or was it really just the prodrome? So some of those, we see another study by Schulte, just published last year-- because again, we got 40% have prodrome at least two hours that's identifiable and reproducible.

So those who had-- they thought light was triggering their headache were more likely to have photophobia as a present feature, not the light trigger. Those who thought they had odor triggers, which are really common-- one of mine is nail polish remover. And that's a clear trigger, because I don't-- I'm not osmophobic otherwise. I don't have sensitivity to smells.

Actually, there's two. There's another one. It's nail-- or pine cleaner. But I think that's psychosomatic or psychogenic, actually. I'll tell you, I am functional in my own way.

One of my first cases ever in medicine was at the VA. And I took care of a guy that overdosed on Pine-sol And he proceeded to throw up Pine-Sol blood, and vomit all over my brand new shoes that I wore the first day on rotation saying these are-- these are comfortable.

I've got these be comfortable-- that's what I said. One thing you've got to have when you start is comfortable shoes. I had these gorgeous, Cole Haan comfortable shoes. Bam-- vomit, blood, and Pine-Sol So I think that's more psychological.

[LAUGHTER]

Now, we can test prodrome, which is great. You know how you can do it? You can give somebody nitroglycerin. Man, that's not a good thing if you have migraines.

So if you have nitroglycerin, any of you, you'd get a nitro headache. That's pretty immediate. But a migraine suffer gets the double whammy. They get the nitro headache, and then, they get the migraine later.

So you can test migraine. You can put somebody in a scanner, give them nitro. Let's see what happens. You've got to pay them a lot of money, because it's not going to be a lot of fun.

So we can do a PET study. We'll do a PET study before we give you the nitro, and then, we'll see what happens. And is there a prodrome? Can we see what happens in prodrome? So if you have a prodrome, I'm going to bring you into my scanner. I'm going to give you nitro and see what happens in your brain.

So those who had photophobias, light sensitivity, beforehand, guess what? The brain lit up, the visual cortex, before it even started to hurt. So light sensitivity-- the brain, the visual brain is different preceding the headache. Prodrome.

Many of your trauma patients probably had the same stuff. Their visual cortex is turned on. It's more sensitive. This happens temporarily before the headache with us but may be more sustained for you folks.

All right, is it predictable for the headache? What are the most predictable symptoms? Now, how do you test this? You need to have electronic diary where people record their symptom and then the headache comes. But you can't go back. It's time stamped.

So you can't retrospectively say, oh, yeah, I got the headache. This was, all right, symptom, does headache occur? Can you predict it? So how good are you at forecasting in the future?

Just like [INAUDIBLE] in your March Madness bracket. You can't go back and fill it in afterwards saying, oh, I saw who won last night. Let's put them in now. No, it's-- you've got to figure it out in advance.

So this is an electronic diary. These are-- people that get in, you had to have prodrome with at least two-thirds of your headaches, so you had to have symptoms. And 72% had diary symptoms. So let's show you what they had.

What are the symptoms? And do they sound familiar? Fatigue, difficulty concentrating, neck stiffness, and irritability. Wow. Is this your world?

Light sensitivity, noise-- look at the symptoms. And nausea dropped down here. Nausea's not as uncommon. Probably, again, maybe for you folks as well.

Which ones were most predictable, though? Which ones gave you the best chance of predicting the headache? Speech difficulties, reading difficulties. Now, part of this is the visual stuff that you guys deal with that may be convergence insufficiency that, perhaps, is not as big a deal for us in the standard migraine patient. So there is a little bit of that that might be a bit different there. Yawning, emotional changes, blurred vision-- all predictable.

Where's it coming from? Another study-- this is another PET study published in 2014. Where is it coming from? So let me just show you-- get to the-- [INAUDIBLE] the early prodrome.

As I said, we're going to get back to the thalamus and hypothalamus. I think the hypothalamus is going to be where the money is. So the hypothalamus, mid-brain tegmentum, periaqueductal gray-- see a bunch of structures. So there's the big three.

Where the activation was greatest-- the hypothalamus, the periaqueductal gray, which is pain modulation, and dorsal pons, which actually seems to be a migraine-generator. Or it's either gas pedal or brake pedal. We've known about the dorsal pons turning on for decades, actually.

But the hypothalamus-- the hypothalamus is important in cluster headache. They hypothalamus is abnormally activated in cluster. It is abnormally activated in other headaches syndromes that we are aware of. Hemicrania continua-- new daily, persistent headache; chronic paroxysmal hemicrania-- these are all usually tagged in the cluster family, many of them. But the hypothalamus turns on in every one of them specifically.

That hypothalamus is in the middle. It can be shaken. And it's very delicate. It connects to your pituitary gland. That stalk, this area of the brain, it's actually probably very delicate.

We don't think about it much with trauma. We don't see the big hemorrhages there. But these circuits may be much more amenable or much more responsive to trauma and then, perhaps, even to management later.

Late in the prodrome, where do we see? No posterior hypothalamus. So once the brain turns on, its the dorsal pons That's where the headache phase is really triggered on, and that's what we've known for some time. So this just gives you the data. I'm going to kind of go through that.

Nausea, where does that come from? So again, another PET study published in 2014. This is coming from nausea structures deep in the brain. So periaqueductal gray getting turned on. But the nucleus of the solitary track, or the nucleus tractus solitarius, dorsal motor nucleus of the vagus, and nucleus ambiguous-- big brain stem structures that connect south. So these are ones that are visceral connections.

And then prodrome transition to headache. So how do we see this? So here's how I'm going to finish off. I think what we need to do is learn a lot more about what's happening in the hypothalamus and the thalamus.

So what does the hypothalamus do that might turn a headache on? Well we do know that the meningeal vasculature, the vessels, which I said are a big part in pain, the vessels in the dura. Well, the vessels can be altered by the parasympathetic connections.

Remember, that hypothalamus is the master spot. We talk about the pituitary as the master gland. But really, it's the hypothalamus in charge. That's the boss. That's the CEO.

So what you have, that's the owner, general manager. Next step and that general manager may be the pituitary gland. But you've got the owner in charge everything pulling a-- and that's where we think the hypothalamus is, sitting on top of the pituitary gland, sitting on top of all the fight or flight responses, connecting to the vessels in the intracranial circulation, the sympathetic nervous system down further south. We see vasodilation. We see the leakage of the blood brain barrier. By turning the hypothalamus on and its connections to the vessels, we can cause migraine.

And here's where, again, the thalamus may come in. So the hypothalamus must not only deals with the vessels, which I think is important, but it's dealing with the pain modulatory circuitry. It's connected to the system that helps.

And this is what I've used recently, and this is a brand new thing I come up with. My PA always says, I want to hear your newest spiel on this or that. And so my newest one for patients to try to get them focused better on this is to say, think about your nervous system pain transmission, your headache transmission, in two pathways.

You have your pain pathway that I showed you. It has four stops-- trigeminal nerve, trigeminal nucleus caudalis, or the spinal trigeminal nucleus and the brainstem, the thalamus and the cortex. You've got four stops.

And that's, I stubbed my toe, [SWOOSH] ouch-- pain. And that circuit is designed to give you signals quickly so that you don't-- you get off the nail. You get your hand out of the fire, recognize pain quickly. So that's just the pain transmission.

But next to it is pain modulation. And pain modulation can either decrease those signals going through or facilitate them. You can either inhibit pain, or you can facilitate it. And that's what we're taking advantage of. That's what the hypothalamus I think is going to be more connected to. It's going to help modulate those signals going through, increasing the facilitated signals, or saying, suppress them.

And so what we do with migraine people is if you sit home thinking about this-- sometimes, we get away from diaries, because people get so tied up in focusing on their pain that it makes it-- it physically makes it worse. It's not psychologically makes it worse. If you turn your limbic system on at a ten to pain, and you think it's going to be bad, it's going to be worse than if you just ignored it. If you went to work and school and put pain on the back burner, not only is that good a coping skill to learn, but it actually makes pain less very clearly.

So when you see those folks that look like-- they say they have a 10 out of 10, and you look at them and say, you don't have a 10. In your mind, you say that. You probably don't say to them. I have to say it to them sometimes. I have to say to the parents.

I see 10 out of 10. This ain't 10 out of 10. I know that. But what I'm telling you is you feel 10 out of 10, because your pain modulatory circuits are down. Your fences, your barriers are down. We need to build them back up. And that's what the hypothalamus can do.

And that's why-- it's the internal clock. It's fight or flight. But it's also mating behaviors, fly north, fly south, gather nuts, hibernate. This is the part of the nervous system that is very regulated by schedule, by light. And so what we need to do is schedule them. That's where I think the money is. That's why I think people who schedule and do things improve this, is because that hypothalamus connects to the periaqueductal gray. It connects to the thalamus.

Look at the thalamus. The thalamus is getting all this other stuff-- sleep, mood. The thalamus is connecting all this stuff together. The hypothalamus is not connecting. It's in charge of turning this up or down, the gain up or down, here.

But look at all around that dial. And you guys, I guess you're going to have the slide, so I'll put them on. You can look at them at your leisure. But you look around that dial, you say, boy, that's a lot of stuff we've been talking about.

And so I think if we can think about more-- learn more about hypothalamus and thalamus and what it's doing, which are, unfortunately, incredibly complicated structures, both of them. Even to neurologists, our residents, we say, give us-- what does this part of the thalamus do or that part of the hypothalamus do? So these are complicated pieces of neuroanatomy and very small, at least the hypothalamus.

So there are a lot of connections, again, that make a lot of sense to us. [INAUDIBLE] you'll get these-- in and out of systems spots in the nervous system that create these symptoms. And we've seen-- this is not just theoretical. We've seen hypothalamic activation not just in cluster, in paroxysmal hemicrania and these other ones I mentioned, but also in migraine.

So aura was that cortical-spreading depression event, which is kind of neat. And it's electrical, and it's fun. It's nice to hear about. Not particularly relevant.

We can't do anything about aura, by the way. We can't do anything about aura. Once it's a wave, you saw the storm. It's like a stone in a pond. Boom. Once it's done, the ripples are there. You just have to wait them out.

You can't stop aura, as far as we see. You can try to prevent them, but once the ripple starts, it's over. Because people say, oh, I want to get rid of the visual thing as soon as possible. Unfortunately, that's hard.

But prodrome probably is something we can manage. And there have been studies which I didn't go into that looked at managing prodrome. And I had a lady who had cravings and actually could turn her migraine off, because the craving was actually a sign that she was probably hypoglycemic.

But you know what her treatment was? I actually took it off this-- at the end, the last slide, because I didn't think I'd have time. Wendy's loaded baked potato with a Coke. And if she recognized this and would get a Wendy's loaded potato with a Coke, she could stop her headaches.

And it probably was just a version of hypoglycemia that was really part of the headache already starting. So I wouldn't-- if you had to do that 10 times a month to treat your migraines, you might have other problems later in life. But at least short-term was something we found interesting.

So thanks so much. Now, I guess we can open it up to questions.