44| Neuropsych Bite: Creutzfeldt-Jakob Disease – With Dr. Joel Kamper

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NAVIGATING NEUROPSYCHOLOGY

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Speakers: Joel Kamper, Ryan Van Patten, John Bellone

Intro Music 00:00

Ryan Van Patten 00:17

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

John Bellone 00:24

..and I'm John Bellone. Today we have a returning guest on NavNeuro. We're speaking with Dr. Joel Kamper, a board-certified neuropsychologist at the James Haley VA in Tampa, Florida.

Ryan Van Patten 00:35

Today is our newest so-called "Neuropsych Bite", and the first in a series of conversations with Joel about rare neuropsychological syndromes. Today is Creutzfeldt-Jakob disease, or CJD. We have upcoming episodes on Balint's syndrome, moyamoya, and limbic encephalitis - so stay tuned for those.

John Bellone 00:56

We're going to continue to release full length episodes as well, but we'll sporadically be releasing these "Neuropsych Bites". This episode is shorter than our first "Bite". That was the conversation with Dr. Maggie Lanca on state-level advocacy for neuropsych and teleneuropsychology. You'll notice that the "Neuropsych Bites" are going to vary a bit in their length, but we'll try to keep them all around 30 minutes or less. So, with that, we give you our "Neuropsych Bite" with Dr. Joel Kamper.

Transition Music 01:25

Ryan Van Patten 01:34

Creutzfeldt-Jakob disease, or CJD, is a rapidly progressive neurodegenerative disease caused by prions. Tell us about the neurobiology, epidemiology, and clinical symptoms of CJD.

Joel Kamper 01:47

Sure thing. So, like you mentioned, CJD - which, I won't be saying the whole name [laughs] - CJD is, yes, caused by prions, which are actually infectious proteins. Not infectious in a traditionally thought of way, like a virus or a bacteria. It's more that they're proteins that are misfolded. Without getting too much into the neurochemistry of it, proteins all get folded a certain way. That's why in Alzheimer's disease, the A-beta proteins stick together - it's because they're cleaved and folded a certain way. In CJD, these proteins that get misfolded, are somehow convincing other nearby proteins to also misfold. And that's sort of how they're infectious. If you were to get some of these misfolded proteins in you, they would start convincing

your proteins to misfold and that sort of thing. It's not like it's a separate organism. It's kind of this biologic process gone awry.

There's a couple of different types. The sporadic, or randomly occurring type, is the most common; although there's been some research into how "random" it really is. It is random, but there are a couple studies that have found that there are groups. So, a couple patients in a geographic area or something like that will get it a couple years apart. And it's rare - it's much greater than what you'd expect. They don't know why or how that works. But, there's some speculation that there's some common factor that they're exposed somehow to these proteins.

John Bellone 03:28
I've heard that as high as 85% of the cases are the sporadic origin.

Joel Kamper 03:33
Yep. 80 to 95%. There is a less common genetic subtype, where there's some genetic risk if it runs in your family - 5 to 15%. And then there's variant CJD, which is the Mad Cow one, which we can talk about, too. But, in general, any sort of prion disease - there's a couple others: fatal familial insomnia, Gerstmann-Sträussler-Scheinker syndrome (GSS), and Kuru - which, Kuru isn't really around anymore, you may be familiar with that one.

John Bellone 03:59
K-U-R-U, right?

Joel Kamper 04:14
Yeah. So, that was in Papua New Guinea. There was this rash of these neurologic conditions in this tribe. The tribe had a habit of eating the brains of the recently deceased as a way to commune with their recently departed loved ones. The speculation is that someone in the tribe at some point got CJD, just the normal way. And then their brain got eaten and it became this propagation, and they got a specific name Kuru.

John Bellone 04:45
That's the other etiology. If you're exposed to brain or spinal fluid of an infected person, then that's an origin for you to get it, too.

Joel Kamper 04:54

Correct. And there's been a couple of symptom clusters. I think there was one a couple years ago with a pituitary growth hormone that was infected and some people got it. I read about a couple of cases years ago with some surgical instruments. These prions, they're not organisms. So, it's not like you can kill them. You can clean surgical instruments, but it's super hard. You need really high heat; you need to basically denature the proteins. So, yeah, there's been cases of surgical instruments that have been cleaned the normal way but infected people. I think there were a couple cases where there were cadaver lens transplants, which is interesting because lenses aren't part of your brain. The symptoms that they caused - the syndrome is a neurologic syndrome, but the proteins are probably more widely distributed than that.

John Bellone 05:49

Right. So these are all different ways of transmitting it. And it's pretty scary, you know, to many people, but I think it's important to remember that this is very rare. I think I've seen one in a million people annually.

Joel Kamper 06:01

That sounds about right.

John Bellone 06:04

So, when we talk about the typical clinical presentation, there's several sequelae of this disease - both cognitive and motor, but also sensory and behavioral. Just walk us through the high-level presentation.

Joel Kamper 06:19

Absolutely. So, as you guys mentioned at the beginning, it's rapidly progressive, quite rapidly progressive often, folks are usually dead within a year. Some studies say three to four months or even less, it can be weeks. Typically, the initial symptom is something like myoclonus. Myoclonus is sort of like the twitches you get when you're falling asleep, that everyone has, but it's not when you're falling asleep - it's during the daytime. It's those fast muscle twitches - those sporadic movements. People will also kind of get what is often termed "confusion". I hate that term because, what does it mean?

John Bellone 07:02

It's not specific.

Joel Kamper 07:02

But, that's often how it's described, but they just seem different. They can have changes in their sleep, they can start having falls, and then oftentimes folks will develop seizures, and then they come in to get evaluated. Sort of the classic presentation would be a rapidly progressive dementia. So, you know, grandpa was fine two months ago, and now he's exceptionally impaired. There's often non focal but specific signs - so, like, apraxias and aphasias and things like that, frontal lobe dysfunction. The sleep problems I think I already mentioned briefly, often it's hypersomnia. Sometimes there's hallucinations. But, the myoclonus and then the seizures, those are the constellation of symptoms that would make me suspicious that something's going on. They can also get rigidity and some extrapyramidal type symptoms, too, but that's not quite as common.

Ryan Van Patten 07:32

And the symptoms vary quite a bit depending on where you have the misfolded proteins in the brain, right? It can resemble different types of neurodegenerative disorders. And, apparently, there's a bit of a problem with misdiagnosis in CJD at times based on how you described it. I could imagine it being confused with a delirium as well.

Joel Kamper 07:58

Yes.

Ryan Van Patten 07:59

You'd want to make sure that the person - not only was this rapidly progressive, but that it's a constant state of cognitive impairment - and not a fluctuating course as we would see in an encephalopathy.

Joel Kamper 08:29

That's an excellent point. Yes, that's very important. Sometimes they're okay, sometimes they're confused. It's: they were fine, they haven't been fine in a while, and it's gotten bad. But, yeah, you're right, the symptoms can vary. There are a couple different subtypes they talk about, and without getting into the weeds, the classic profile is kind of what I just described. There's some folks who have ataxia as sort of the primary feature and the dementia comes later, and they might live a little bit longer. And then there's a couple others - there's a thalamic variant, and there's probably half a dozen subtypes.

Ryan Van Patten 09:02
Right. Given that there are no treatments, Joel, how are people with CJD typically medically managed?

Joel Kamper 09:09
I mean, it's really just a symptomatic and supportive sort of thing. So, the myoclonus, they may put them on benzos. They may treat them with antiseizure drugs - keppra, valproic acid, or something like that. If there's some muscle problems, like a patient with dystonia, they're going to give them some muscle relaxers or something like baclofen. There are a couple treatments that are investigative. The one that popped out was doxycycline, which is something that's already currently in use. But, yeah, there's really no treatment.

Ryan Van Patten 09:43
To what extent are people quarantined or kept away from others? You mentioned this isn't a virus like the flu or COVID-19 that we breathe in. But, it does cluster and we don't know exactly how it's transmitted.

Joel Kamper 09:57
Well, I mean, we know that you have to consume neural tissue of some sort in order to get it. Whether there's other precursors, I don't know. But the established method is any exposure to neural tissue - so brain, spinal cord, things like that. And that's how the variant, vCJD, the Mad Cow disease, got going. Cows got CJD, and somehow neural tissue ended up in ground beef and people ate it.

Ryan Van Patten 10:26
Yeah.

Joel Kamper 10:27
So, you do have to be exposed that way; it's not like you can catch it. They're not typically quarantined. The real dicey part comes - because, really the way to be sure, there's a couple tests they can do for diagnosis, but the way to be sure is on autopsy. And then, obviously, you have to be super, super careful. For the patient we had recently, our VA or the university across the street, University of South Florida, wouldn't do it. So, actually, the patient went up to the National Prion Center in Ohio, and that's where they had it done.

John Bellone 10:59
Yeah, you have to be super careful - the pathologists, too. They used to get this a lot because they would nick their finger and get exposed to the neural tissue.

Joel Kamper 11:08
Right. And, the latency is super long. It can be years or decades before you show symptoms.

John Bellone 11:13
Good point.

Joel Kamper 11:14
At that point, it's like, "Was it that?" I mean, you just don't know.

Ryan Van Patten 11:18
Yeah, fascinating. And tragic, of course. How can we as neuropsychologists be of help to a patient with CJD? When might we see them?

Joel Kamper 11:26

That's a good question. On the face of it, most of the symptoms that I described are things that would be diagnosed and treated by a neurologist. So, it may not seem like we have a lot to offer, but we really do - from a "help me rule this out" sort of thing. So, you get someone who, maybe there's not a lot of history, but they're pretty impaired and showing some of these other symptoms - it's kind of weird. Could this be CJD? How impaired are they? That sort of thing. I think, though, really - because as diagnosticians that's what we do - I think often we're better equipped than other disciplines to identify some of the symptoms and bring it up. So, in the case that we had recently, it wasn't on anyone's radar until my resident, Alicia Vanden Bussche - I'll give her a shout out because I know she'll be listening to this -

John Bellone 12:15
[laughs]

Joel Kamper 12:16

I was actually at INS when he came in. And, I got this text message that they got this patient they think may have CJD. It's like, "Oh, crap". So, she was actually the one who brought it up as a possibility to the team because she was the one who

got a good history from the family. She was the one who saw the video on his wife's cell phone of him, you know, four weeks prior at Disneyland dancing and jumping around. Then she looked at the guy in the bed and was like, "Oh, crap", you know? So, she's the one who brought it up to the team as, "Hey, check this out." And then, when I got back, we did it together. It was us kind of pushing, "Hey, here's what it could be". And the team on the medical floor isn't familiar, so we get neurology. So, we say, "Here's the tests that are typically given", and kind of walk that line between telling them how to do their jobs and being helpful.

John Bellone 13:02
So, tell us more about your case. Just a very high-level, quick overview of the presentation and then the cognitive profile.

Joel Kamper 13:09
So there's two "humps" for CJD. The variant CJD, the Mad Cow cases, tend to hit in early 20s. I think 29 is the mean age. The normal kind, the sporadic kind, hits late around the late 60s, I think. So, our gentleman was maybe 70 or so. He comes into the hospital and he's "confused" and shaking. So, okay. He's got the myoclonus pretty noticeable. He was having some seizures - there was a question of status epilepticus and they ruled that out. But, the wife was saying he was fine three or four weeks ago. And, it's like, "Oh, I don't know" - you know, you hear that. So, he was just on the inpatient unit. They consulted us and - Well, actually, let me backup.

They originally consulted us as an outpatient because he was reporting memory problems two weeks previous. He got kicked to our regular clinic which would have taken a couple months to get him seen because you don't know when it's that early. But, the consult we actually acted on.

So, he's inpatient, he's got some symptoms, he's having some speech problems. Okay. So, we go up there and he is densely aphasic. He's completely disoriented. He's almost in a disorders of consciousness sort of state, almost in like a minimally conscious sort of state. He was very, very impaired. We couldn't really get a cognitive profile of him; but, you could see the twitches, the myoclonus, still happening despite the drugs he was on. He had some decorticate posturing - so, some of that lower level neurologic findings. And they were treating all of that as best they could, because they thought it was seizures. With just seizures, you put them on some anti-seizure meds. Well, some of the twitching stopped, but a lot of it didn't. And, he still didn't improve. So, then the wife showed us this video of him at Disneyland three to four weeks previous. And, he's dancing around - he just looks

like a normal guy. And you look at the guy in the bed in front of you, and it's like, "No way, no way".

So, we actually came back three days later and saw him again. And, at that point, we did a low-level disorders of consciousness eval. So, you know, the nail bed pressure, seeing if he'll respond to noise and all that. He responded to pain a little bit, but when you said his name, he would sort of perseverate and just say his name back over and over again. But that was pretty much all we got out of him. They ran a couple of blood tests and CSF tests that were inconclusive, which is not uncommon. And then about a week later, he was gone.

John Bellone 15:42
Wow.

Joel Kamper 15:43
So, the total course for him was seven weeks, maybe.

John Bellone 15:48
Wow. That's tragic.

Joel Kamper 15:49
Yeah, really severe. But, we were the ones who really helped the family understand what the likely diagnosis was, why it was happening. They were wondering, you know, "Why? What is this?" Or, "I think he's got Alzheimer's disease. It's gotten really bad real quick". Well, no. No, they don't know. So, giving that psychoeducation, listening to them - they were exceptionally appreciative of that. I think that's another way we can be helpful - is just spending a little bit of time explaining what's going on and sort of being the "mouthpiece" of the team, which is what we did in this situation. And they left feeling like they had an answer. And then, once the autopsy confirmed that's what it was, they felt a bit more peaceful.

John Bellone 16:35
They saw the prions on autopsy.

Joel Kamper 16:38
Yeah. So there's this spongiform presentation on autopsy that they can see on histology when they do...

John Bellone 16:45
Sure. Yeah. They look at the gross anatomy and then they look at it under the microscope...

Joel Kamper 16:49
Exactly.

Ryan Van Patten 16:50
Yeah, the spongiform presentation - you can think of like Swiss cheese a little bit, right? That's where that word comes from.

John Bellone 16:56
Yeah.

Joel Kamper 16:56
Correct.

Ryan Van Patten 16:58
There's so much tissue loss in the brain that you have holes.

Joel Kamper 17:02
Yep. You know, one other sign because it's not - there's CSF protein markers and other things - but, the other sign is this cortical ribboning on MRI that a lot of studies will talk about. So, it's the whole lamina of the brain that are involved. You see on DWI and then I think on a T2 or T2-FLAIR as well. You see this whole lamina all the way around the brain is bright.

John Bellone 17:31
Yeah.

Joel Kamper 17:31
And it's, you know, I don't know if that's quite pathognomonic, but it's darn close.

John Bellone 17:37

Right. So you have the MRI, the EEG, the CSF. You have the rapidity of the cognitive and behavioral decline, and the motor issues. So, there's a lot of features, although they can be...

Ryan Van Patten 17:51
They're non-specific.

John Bellone 17:51
...non-specific. Right. But, together, the constellation of them makes you strongly suspect.

Ryan Van Patten 17:56
Yeah, it sounds like in your case, Joel, the clinical interview was essential to identify the rapid course and then rule out other explanations.

Joel Kamper 18:04
Right. Absolutely. And that's another thing I think we do better than most disciplines. And where we really came in handy. Because we were just getting told, "This patient has rapid confusion. His potassium is a little low..." Okay, well, that wouldn't do it - what's going on? Then you get the history, and spend a little time, and yeah. We can be very, very helpful in that sort of way. You're not going to get a profile and some of these other things, but it's our clinical skills that really can make the difference.

John Bellone 18:36
Awesome. Well, thanks for walking us through that, Joel. It was really, really helpful.

Joel Kamper 18:39
Yeah, absolutely.

Transition Music 18:40

Ryan Van Patten 18:45
Well, that does it for our conversation with Joel. Given that this is just our second "Neuropsych Bite", we're very interested in feedback from all of you and your thoughts about this type of episode. It's something new for us. So if you have ideas

or questions or comments, please email us at feedback@NavNeuro.com. We'd love to hear from you. And, as always, thank you so much for listening, and join us next time as we continue to navigate the brain and behavior.

Exit Music 19:15

John Bellone 19:38

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Ryan Van Patten 19:50

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