Kessler Foundation Podcast Transcript: Glenn Wylie on fatigue

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ANNOUNCER: 00:05	[music] Welcome to a Kessler Foundation podcast. The foundation is a global leader in rehabilitation research that seeks to improve cognition, mobility, and long-term outcomes including employment for people with neurological disabilities caused by diseases and injuries of the brain and spinal cord. In this episode, we are talking with Dr. Glenn Wylie. Director of the Rocco Ortenzio Neuroimaging Center at Kessler Foundation. He's also an associate professor at Rutgers New Jersey Medical School. He spoke with Rutgers, the foundation's communications director.
ROB GERTH: 00:43	So you know where I want to start. Jodie our producer who's doing the recording for the people that aren't sitting in the room reminded me that you're a woodworker.
GLENN WYLIE: 00:53	That's right.
GERTH: 00:54	So tell me about that. What does that have to do with your scientific work if anything?
WYLIE: 00:59	Well, I mean, it's a hobby.
GERTH: 01:02	Like what kind of woodwork? Furniture or--?
WYLIE: 01:04	Yeah. I build furniture and-- yeah. And I like to put things together and to build things. I don't know whether that's--
GERTH: 01:16	What's the hardest thing you've built so far?
WYLIE: 01:19	The hardest thing I've built. That's a good question. I built a light. A backsplash for the bathroom that's actually a light. So it comes on when you come into the bathroom and it stays on for a certain amount of time and that's all automatic and it's-- the whole backsplash lights up through tiles we got that are actually made of Onix.
GERTH: 01:44	Oh. So it wasn't wood.
WYLIE: 01:46	So there was wood involved.
GERTH: 01:47	There was?
WYLIE: 01:47	Yeah. There was also stone and some metal.
GERTH: 01:52	Wow. That sounds very difficult. I made a little box once in woodshop in like 11th grade [laughter]. I was six then.
WYLIE: 02:00	It's a good start.
GERTH: 02:00	And my cup's racing card is [inaudible]. I don't think it does. I don't think that counts. That's impressive. And then the other thing that I know of-- now woodworker. And you live in Vermont. You don't do anything easy. You commute to Vermont from New Jersey? Is that--?
WYLIE: 02:16	I go back and forth regularly between the two. Yeah.

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GERTH: 02:19	That's crazy too. And then this leads to my other question about the situation. So you went to school in Canada.
WYLIE: 02:25	Right.
GERTH: 02:25	Are you Canadian?
WYLIE: 02:27	I'm not Canadian but I did grow up in Vermont so--
GERTH: 02:29	Ah, that explains plenty.
WYLIE: 02:30	So I do know where Canada is [laughter]. And I knew that it was an option for school. And actually, so when I started out, I started out going to the school for architecture.
GERTH: 02:41	Really? In Canada?
WYLIE: 02:42	In Savannah, Georgia. At the Savannah College of Art and Design. And I went there for about a year for architecture. And that was great. And I really enjoyed it. But I thought that I should also have a background in engineering probably because I come from a family of engineers.
GERTH: 03:00	Oh, do you?
WYLIE: 03:01	And so I ended up sort of taking a hiatus from that and going and enrolling in an engineering course. And that was in Canada because I had a friend who was going there. And then from there, I took other courses, electives, in psychology and then philosophy and eventually ended up changing my major too. Psychology and philosophy.
GERTH: 03:27	And you ended up in Canada instead of in Savannah?
WYLIE: 03:29	And I ended up staying in Canada. Yeah [laughter]. To finish up my degree. Yeah.
GERTH: 03:33	And then you went over to University of Oxford in England. So what took you over there? How did you make that transition? So wait. Let me ask you. What was your undergraduate degree in then? Psychology?
WYLIE: 03:44	So my undergraduate degree was a combined honors in psychology and philosophy. And I was working on attention and attentional processes. And one of the important thinkers in that literature is a fellow named Allan [inaudible]. And so when I came to the end of my undergraduate degree and I was thinking about doing graduate work, I applied to work with him in Oxford. And that ended up working out, so.
GERTH: 04:17	And at that point, you'd sort of totally given up on the architecture and you were going to-- what? Psychologist or--?
WYLIE: 04:24	Yeah. I was going to-- I had given up on the architecture of buildings and sort of transitioned to the architecture of the brain and the thought.
GERTH: 04:33	Nicely done. Yes.
WYLIE: 04:35	So, yeah. So I mean, yeah. I am interested in how things go together and I think that the woodworking is part of that and architecture is part of that and the work that I do

here is part of that. And what Allan [inaudible] was working on was how do we actually instantiate our intentions? So how does the wheel work? and I thought that was a really awesome question. A really interesting question. And that was a big part of the change from engineering to psychology because in psychology, there's so much that's unknown whereas in engineering, certainly in first-year engineering courses, everything is known. And your job is to find the answer that the professor knows. Whereas in psychology, no one really knows the answers to a lot of questions. And so there's everything to play for and that was a lot more interesting to me.

GERTH: 05:35 How did you make the turn then to where you ended up here? Were there other stops along the way? As far as what you wanted to study. Or do you feel like you are studying what you set out to study right now here? And we'll get to what you're studying here in a little bit.

WYLIE: 05:49 Yeah. I feel like I'm still studying the same basic questions. I've started studying a number of other related things but all in service is the same sorts of questions.

GERTH: 06:08 So at what point did you end up-- so you got your-- you know what, I have to ask you this first before. So with Oxford, you don't get a PhD-- how do you even say it? I'm so ignorant on some of these subjects. How do you even say what you have? What your degree is?

WYLIE: 06:25 So I have a DPhil.

GERTH: 06:27 Which is [crosstalk].

WYLIE: 06:27 Which stands for Doctorate of Philosophy. Now, in Cambridge, you will get a PhD which also stands for Doctorate of Philosophy but for whatever reason, they switched the letters around.

GERTH: 06:38 So DPhil.

WYLIE: 06:39 So, yeah. DPhil is Doctor of Philosophy.

GERTH: 06:40 Okay. I just was curious about that. So then what was your next evolution then after you got your DPhil? I'll say it like I know what it is now.

WYLIE: 06:51 Good work. Yeah. I did a, sorry, a postdoc at Oxford for a year looking at EEGs. Because my PhD or my DPhil, I had worked for the fMRI. And then I also wanted to know about electroencephalography which is looking at the voltage of your scalp when you're thinking. And so I did a year's postdoc in that at Oxford. And then I came back to the US and got a job in the [inaudible] near New York City area in a lab where they were putting together EEG and fMRI.

GERTH: 07:36 Putting it together to do what with it? What was their--?

WYLIE: 07:38 To look at the same questions using both modalities. Because the great thing about fMRI is it gives you really good spatial resolution. You know where thoughts are happening, so to speak, in the brain or where there is brain activity. But it gives really poor temporal resolution. So it's very hard to say exactly when those things happened. Whereas EEG is exactly the opposite. It gives you poor spatial resolution

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	but really good temporal resolution. And so if you put the two together, you can get a really good picture of cognitive processes.
GERTH: 08:16	And then the fMRI-- just for people like me, MRI, you know what that part is. The F part is functional?
WYLIE: 08:24	The F part is functional.
GERTH: 08:25	Tell me how that's different than just an MRI that somebody would get in the hospital.
WYLIE: 08:29	Right. So the MRI that you get in the hospital it's anatomy typically. And that's done by looking at the density of water in your tissues. The fMRI looks instead at blood flow and looks at where the blood is going in your brain. And when you use a region in your brain to do some task, then the neurons there deplete their resources and they need an influx of blood in order to have those resources refreshed. And so by tracking where the blood goes, we can track where neural activity is happening.
GERTH: 09:03	So that's the part of the brain you're using and that's the part you can study like, "Oh, that's where that's happening in the brain"?
WYLIE: 09:08	Exactly.
GERTH: 09:09	Okay. All right. Great. You mentioned your family. Were there scientists in your family or were they artists? Or were they engineers? Or were they all [laughter]?
WYLIE: 09:19	They were mostly engineers. Yeah. So my grandfather was a lighting engineer and my dad actually is a mathematician. And my brother is an engineer as well, so.
GERTH: 09:32	Wow. Smart family. And how did you end up here then at the Kessler-- was it a long hop or was it a lot of stops in between before you got here?
WYLIE: 09:41	No. I came back to the US and did a postdoc that turned into a research position at the [Nathan S. Kline?] Institute. And that's where I was putting together fMRI and EEG. And then a job became available here working with John Deluca. They needed someone to sort of spearhead the neuroimaging effort that they had begun here and I got that job. And I've been here ever since.
GERTH: 10:10	The end of-- so how many years has that been?
WYLIE: 10:14	It's been over 10. Yeah.
GERTH: 10:16	Were you in at the beginning of the fMRI that we have here?
WYLIE: 10:21	Yes.
GERTH: 10:22	Okay. So we'll get to that in a second. I want to work my way to that. Because what I have here is my favorite question I've written since I started doing these interviews. I'm going to read it just because it's my favorite question. Your research seems to fall under three categories, Glenn. Cognitive control, cognitive fatigue, and the neurophysiological effects of cognitive interventions. Why don't you elaborate on that

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	[laughter]? I'm saying that like I know what I'm talking about. I have no idea what-- I know cognitive, right, that's thinking.
WYLIE: 10:50	Right.
GERTH: 10:50	Right? But tell me a little bit about, just in general, the kind of stuff that you do. And give me some examples.
WYLIE: 10:57	Right. So let's start with cognitive control which has been an interest of mine since graduate school. And so that's why I went to Oxford to study cognitive control. And that's really the will. It's really what we're talking about. How is it you're able to instantiate your intentions and your actions? And that's just science-speak for how does the will work?
GERTH: 11:20	How far have we come on that? Do we have any idea of how that works? How that--?
WYLIE: 11:27	We have some idea how it works. And it's not-- maybe it's the most encouraging information. But it looks like you have the ability to hold onto goals in your brain and those goals bias your actions. Because they don't determine your actions. And so this idea of an iron will really is a bit of a myth. Your goals can bias what you do but really a stronger influence is what you've done in the past. So--
GERTH: 12:07	So things are sort of imprinted from what you've done in the past or you--
WYLIE: 12:10	So every time you do something it leaves a trace and it makes it easier to do that again. And so you can-- you know, we have this idea that if you hold onto-- if you have a really strong will you'll be able to avoid temptation. And maybe that's true to an extent, but really, probably what it is is that if you're not tempted by chocolate, it's going to be pretty easy for you to avoid chocolate. Whereas the people who've always been tempted by chocolate, you're probably going to have a piece of chocolate.
GERTH: 12:45	And my communications degree theory is that it's all genetic. It's like if you're--
WYLIE: 12:52	Genes have a part to play. Absolutely.
GERTH: 12:53	Do they? Oh, well then. I guess I should have taken a postgraduate degree in something else then. I just think that we're machines and that we're just operating based on the program that we have programmed into us and that's all there is to it. That's my simple philosophy.
WYLIE: 13:09	I think that there is truth to that.
GERTH: 13:11	I'm not far off? I should write a book.
WYLIE: 13:13	Yeah. You come into the world with this piece of hardware called the brain. But your experiences do shape that. Your thoughts and your actions and so on. And so maybe you have a predilection to loving chocolate. And so it'd be very difficult for you to avoid eating chocolate. But maybe, even with the predilection to loving chocolate, if you've never been exposed to chocolate, then maybe you wouldn't have-- it wouldn't be difficult for you to avoid eating chocolate.

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GERTH: 13:46	Right. Okay. So that's cognitive control.
WYLIE: 13:50	So that's cognitive control. And what is the one time when you have to exert cognitive control? That's when you're cognitively fatigued. Or fatigued in any way. So how do you run the marathon? How do you keep going? Well, cognitive control is probably a part of it. Another big part is practice, right? Training. People who run marathons train a lot. And that sort of mitigates the role of cognitive control. But still, getting through the day when you are tired requires you to exert cognitive control.
GERTH: 14:31	What do you mean if you've run the marathon like you said earlier that you're imprinting all that-- all that training is what's maybe getting you through it, right? Is that--?
WYLIE: 14:39	I think all that training, yeah, is necessary to being able to do it on the day for sure. We know this. I mean, not only because it builds all the muscles but also, it allows you to know that you can do it. Yeah. And it overcomes that inhibition you might have to doing something that's potentially deadly like running a marathon.
GERTH: 15:02	Right [laughter]? You look like a runner though. Are you a runner?
WYLIE: 15:06	I'm not a runner. I ride horses. So, yeah.
GERTH: 15:09	Oh, okay. I think that's a lot harder than it looks. Like when people are riding horses and they're riding them right - I used to have a horse - it's like, "That looks easy." But it's really not. What's going on is, as you know, is much harder-looking than it looks from-- it's much harder-feeling than it looks from the outside.
WYLIE: 15:26	Yeah. And you use muscles for it that you don't use for anything else [laughter]. Yeah.
GERTH: 15:30	Yes. So neurophysio-- help me here.
WYLIE: 15:34	Neurophysiological?
GERTH: 15:35	Yes, effects of cognitive intervention. So what does that mean?
WYLIE: 15:39	So that is essentially doing before and after-- that is essentially looking at brain activation before and after a cognitive intervention or really any kind of intervention. Which is a lot of what we do here at Kessler. Because we develop interventions to help people in various ways. For example, to help people encode memories better if they have multiple sclerosis or TBI. And we can know that they work because you can ask people whether they can remember the information better. And you can test that and you can see that it works. But if you want to know how it works, if you want to know the mechanism, then you need to do something more. You need to do something like neuroimaging where you can look at the brain and the activation pattern in the brain before they got the intervention and compare that to after they got the intervention and see what's changed and what brain areas are responsible for the change in that behavior that you see.
GERTH: 16:43	And then what can you do with that information? And do you judge the-- whatever it is you had them do, you can say, "Oh, that really worked or that didn't work"?

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WYLIE: 16:57	Right. So there are a couple of things we can do with that information. One is to just better understand how-- let's say memory is a nice example. How memory works. So there is a scientific aspect to it. We changed memory function and, look, these are the areas that were changed. And that [inaudible] for just scientific knowledge. Clinically though, we can also go in and say, "Okay. Given that these subjects got better at memory, the recall of information, and given that these particular brain areas were involved in performance increase, maybe if we activate them more, the effect will be even larger. And so maybe we can use that information to then go back and fine-tune the intervention and make it even more effective."
GERTH: 17:53	And in this case-- is there ever a case where drugs are involved in that or is it all sort of physical activity that--?
WYLIE: 18:04	Yeah. We have looked at a number of different things and we have some drugs that we've done and are doing as well. Because that can be-- we know that pharmacological interventions are useful and powerful. And so, yeah, we have some study looking at that too. But some of the most powerful things that we have found have been things like physical exercise and also teaching people effective ways to encode information.
GERTH: 18:46	Which is applicable to anybody, right? It's not just--
WYLIE: 18:50	It is.
GERTH: 18:50	--to people that have a condition or have a disease. It's figuring out how the brain works the best way regardless of what the situation is. And it's applicable, again, backwards to anyone?
WYLIE: 19:02	That's correct. Yeah. Yeah. This is all stuff that you get taught and fairly introductory. They're psychology questions because we know how memory works. We know what the most effective way is to encode information. And that's just-- it's more deeply you encode it, the better you're going to recall it. And so if I ask you to remember three words, you might say to yourself, "Okay. I'm just going to repeat those words over and over again." Which is a very common way to try to remember information but a very ineffective way. Because it's very shallow. Whereas if you encode it more deeply by trying to generate a picture with those words or trying to think about times that you've encountered those words in your own past, well, that's a much deeper level of encoding and you're going to recall those words better.
GERTH: 19:53	And are those different methods using different parts of the brain? [crosstalk] taking it deeper is using--
WYLIE: 19:56	Yes. So the more--
GERTH: 19:58	Oh, go ahead.
WYLIE: 19:58	The more areas of the brain you use, the deeper the encoding is going to be and the larger the network is going to be. That might not be sure actually. Yeah. The larger the network is going to be that's going to support the later recall of those words. So for example, when I want to recall-- when I'm driving and I want to remember something,

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	I know I will forget if I just say, "Oh, I should remember this." I know I will later forget. I'll even forget that I tried to remember anything. And so I just take my finger and I write out the word on my leg. Because that means that I have to think about how it's spelled. I have to figure out how to make those words, make those letters on my leg and I get a sensory feedback as well. And that ends up being a very much deeper level of encoding and I remember it later.
GERTH: 21:02	I totally forgot my headsets and Jodie said to me, "Don't forget your headsets." And I was like, "Okay. I'm going to go get them right now." And by the time I got back to my desk, didn't have. Now I'm here without my headsets. So let's talk specifically about fatigue for a second. Because you do a lot of work with fatigue, right? Yeah.
WYLIE: 21:17	We do a lot of work with fatigue.
GERTH: 21:18	So fatigue for me is like-- physical fatigue is I worked out too much which doesn't happen often. In mental fatigue, I thought too much in this particular day, also doesn't happen too much. But then I go home and I can watch a black and white movie and I can take a nap. In a couple of hours, I'll feel better. But that's not what you're studying so much, right? It's a different level of fatigue that you're talking about?
WYLIE: 21:40	So, well, that is what we study. But it is also different. So let me explain that a little bit. So we study two different types of fatigue. We study mental fatigue and physical fatigue. And so physical fatigue is a fatigue you feel after you work out or after you've won a marathon. And mental fatigue is the kind of fatigue you might feel after you do your taxes. Right? And for most of us, we do exactly what you do. We rest. We go, we do some other activity and after a while, we're refreshed and we're ready to go again. But for individuals who've had brain injury or disease, that's not the case. They have that fatigue, so the mental fatigue, and they rest, and they get up to go again and it's still there. Maybe it's a little bit less in the morning than in the evening, but it's there all the time. And so that's what we're studying. We're studying what you might call pathological fatigue where there's fatigue that does not go away.
GERTH: 22:46	And is it-- real is the word I want to say but it's not really the word I want to use. Is it a fatigue that's in your head or is it a real fatigue or-- do you know what I'm trying to say? Is it-- go ahead.
WYLIE: 23:01	So--
GERTH: 23:01	Say something and save me here. Yeah.
WYLIE: 23:03	Well, okay. So everything is in your head.
GERTH: 23:06	Okay [laughter].
WYLIE: 23:06	Your brain is underlying all your behavior and all your emotions and all your feelings. And so, absolutely, it's in your head just because everything is in your head. So it is real. And maybe what you're asking is, is it comparable? Is the fatigue that an individual who has [inaudible] an injury feel is comparable to the fatigue you feel?

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GERTH: 23:28	Yeah. Yeah.
WYLIE: 23:29	And I think that it is qualitatively the same but there's more of it. So it's quantitatively different. But I think it's the same stuff.
GERTH: 23:41	And why doesn't the black and white movie and the nap help the person with TBI and it helps me? What's the difference there?
WYLIE: 23:49	We're not totally sure about that. We have some ideas, one of which is that the areas we found to be associated with the fatigue are dependent on dopamine. And we think that maybe there the dopamine neurological circuits are damaged in, for example, multiple sclerosis or traumatic brain injury. Another idea which is not-- these two ideas are not mutually exclusive, is that after something like multiple sclerosis or TBI, everything takes more energy to do. So the brain has to work harder just to get even relatively simple jobs done just because it's damaged. And so the information doesn't flow through it with the same sort of ease and fidelity that it would on uninjured brained.
GERTH: 24:41	So your cognitive control has to work harder?
WYLIE: 24:45	Yes.
GERTH: 24:46	Look at that.
WYLIE: 24:46	There you go.
GERTH: 24:46	You taught me. Was studying fatigue a natural outgrowth of everything else coming up to that or was it something you discovered separately?
WYLIE: 25:00	No. It was something I discovered separately. So when I came to Kessler, I had my own line of research which had to do with cognitive control. But John Deluca was here and still is here, and one of his interests, very strong interests, is in fatigue. And so I started working on that because I was working with John.
GERTH: 25:22	Right. Right. And you took to it, obviously.
WYLIE: 25:25	Yeah. Absolutely.
GERTH: 25:26	Because it did kind of fit in with other things you were studying, right? I mean, with generally looking at the brain and--
WYLIE: 25:32	Yeah. Absolutely.
GERTH: 25:33	So it wasn't too far of a stretch. Now, we talked a little bit about TBI and we talked about MS and I'll throw in spinal cord injury. Does fatigue cross all of those conditions and does it cross it in different ways?
WYLIE: 25:52	So yes. I mean, spinal cord injury I'm not as knowledgeable of the literature there. But you find fatigue to be prevalent after a stroke, for example, and after other kinds of brain injuries and diseases. So, for example, in Parkinson's disease, fatigue is a warning sign that you might have Parkinson's disease.

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GERTH: 26:23 So cross conditions. Is it the same?

WYLIE: 26:29 Actually, we're finding that there are differences across conditions. So we started out this research looking at fatigue and multiple sclerosis and in traumatic brain injury. And although those are very different diseases or injuries, they end up with some really strong similarities. So in both cases, the white matter in the brain is damaged. In traumatic brain injury, it's damaged because you've had an injury. In MS, it's damaged because of these plaques that develop in your brain. And so although they have very different causes, they end up looking very similar. And for those two diseases, the fatigue does look similar. But maybe that's not a surprise because the damage to the brain ends up being sort of similar. We've also looked at fatigue in veterans who have Gulf War illness after returning from the first Gulf War. And for them, their fatigue-- though they suffer from fatigue just like folks with MS, it looks like the brain is-- the brain area that's associated with their fatigue is a little bit different than in MS or in TBI.

GERTH: 27:52 Well, I want to talk about that. The Gulf War illness thing. One second though, I want to just ask do these effects cut across age? Are you studying whether it's age-related or race-related or even gender-related or income-related?

WYLIE: 28:11 We had not looked at that. And I would like to look at that. Yeah. I've looked at it a little bit and not really carefully. I've looked at it because our veterans [inaudible] Gulf War illness are older. They are old and getting to be in their 50s and 60s by this point. So I've looked at their differences in their fatigue relative to younger people that we've scanned, but I haven't had enough data to really look at that properly yet.

GERTH: 28:50 But let's look at the Gulf War illness then. Because when I came here and I saw we were studying and we were recruiting people for Gulf War illness, I was like, "Wait a second. When was that [laughter]? Was it the 90s?" I was like, "Wait, I have the date. 90. Yeah. 1990. August 1990 it started." Tell us what Gulf War illness is and then why it's something that you're studying.

WYLIE: 29:10 Right. So in the early 90s, we sent soldiers over to the Persian Gulf to fight Saddam Hussein. And about 25% of them, later on, complained of a constellation of symptoms that got called Gulf War illness. And that included cognitive complaints, fatigue, widespread pain. Symptoms that were sort of similar to fibromyalgia but not identical. They were sort of similar to the chronic fatigue syndrome but not identical. And 25% of your soldiers start complaining of something, you're going to look at it. And the military did. But they weren't able to find anything that was the common factor. That was the smoking gun so to speak. Because one soldier would report having Gulf War illness and the guy who was standing next to him the whole time when he was deployed was fine.

WYLIE: 30:24 So there was no single cause that seemed to explain why some soldiers got Gulf War illness and others didn't. Which makes it very difficult to study. It still makes it difficult to study. What we wanted to know was what does the fatigue look like in this population? What does the brain activation associated with the fatigue in this population look like? And we found that that fatigue is associated with areas having

to do with cognitive control in their brain. And so it's like they have to exert more control sort of all the time to get through the day. Which suggested there is something-- that their brains have to work harder for some reason. And I don't know what that reason is. But it also validates their experience. Because if I say to you that I'm fatigued, you might take my word for it or you might doubt me. I mean, you can't see my fatigue.

GERTH: 31:27 I would say we're all tired, pal.

WYLIE: 31:29 Right. And so to be able to actually show this brain activation and show that it's different than in veterans who have the same age and also had the same combat exposure but who do not have Gulf War illness, that's pretty powerful because that validates what these guys have been saying for all these years.

GERTH: 31:53 Yeah. And that's huge to those guys.

WYLIE: 31:56 Yeah.

GERTH: 31:56 That's got to be huge to be validated like, "Oh, this is not in my head." Even though everything is in your head--

WYLIE: 32:01 Right. Everything is in your head.

GERTH: 32:02 --it's not in my head. I'm not imagining it is what I should say. Is it a war thing or was it a Middle East-- because you were in the desert? Because you said it had to do with using-- might possibly have to do just using your brain on overdrive because you're in a war situation. Is there a Vietnam War illness? Is there a World War II war illness? Or was that just overlooked do you think?

WYLIE: 32:25 Well, okay. So there are a couple of things in that. So when I say that the brain areas associated with cognitive control are more active in these veterans, I mean now. So I don't know that that was the case then. So now, all these years later, when we scan them and they report more fatigue, there's more brain activation in areas associated with cognitive control. So I don't know about the cause. There is some evidence that soldiers coming back from Afghanistan also have similar complaints. A proportion of them. I don't know whether it's 25% in that case too. But there is sort of anecdotal evidence that it's not confined to that conflict. The Gulf War conflict. It's wider.

GERTH: 33:17 And is it just-- I don't mean to ask too many questions about this but I'm fascinated. Is it something that manifested itself as they were over there or is it something that was--?

WYLIE: 33:27 In some cases, yes, and in some cases, no. And this is another reason why it's difficult to pin it down. Because some veteran or some soldiers who are now veterans started to feel these effects almost immediately. And others were deployed and came back, and symptoms developed only later when they were back in our country.

GERTH: 33:52 And what got you to studying this? Is it a veterans thing for you or is it just a fatigue thing or-- what points you in this direction?

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WYLIE: 34:02	Well, so the East Orange VA, which is close by, contacted us and was interested in forming collaborations with us. And, well, civically, there's a study center there called The War-Related Illness and Injury Study Center that is devoted to studying medically unexplained illnesses like Gulf War illness or chronic fatigue syndrome. And given our interest in fatigue, it seemed a natural fit. So that was kind of--
GERTH: 34:39	It was easy.
WYLIE: 34:40	--how it came about. Yeah.
GERTH: 34:42	Yeah. And have you determined anything or you're still studying? And is it hard--- I'm asking so many questions at once. And is it hard to get volunteers? Because, like you said, their population is getting older.
WYLIE: 34:58	So for the Gulf War illness, we finished our first study and we're ready to start our next one. And the next one we're going to look at the interaction of physical fatigue and mental fatigue in these veterans. Because they have both and we don't know whether those two things are independent of each other or whether there's a common denominator that makes them prone to both types of fatigue. So that's what we're going to study next. They are getting older, it's true. Those veterans are troopers. Really. Honestly [laughter].
GERTH: 35:39	Literally and figuratively.
WYLIE: 35:40	Literally and figuratively. And they want to know what's wrong and they want to help the other Gulf veterans who suffer from the same thing. So they're really motivated to help. So it's not so hard to find them. It's not so hard to convince them to participate once we find them. The hardest thing is to find them actually.
GERTH: 36:04	Let them know we exist and we have a study going on. Yeah. Which if you go to our website, right at the top-right, there's a button, Join the Study. So you can click that and see what studies we have. With anything we're working on but particularly with Gulf War illness. Is there-- this isn't a fair question. But so what have you learned about fatigue, Glenn [laughter]? So I'm trying-- is there some things that-- takeaways that are big takeaways since you've been working on fatigue that you can share like, "Here's a couple of things that we do know"?
WYLIE: 36:39	We do know it's the real thing and there are real measurable changes in your brain when you are experiencing fatigue. So that's one important thing. Because it's not just veterans with the Gulf War illness who are doubted when they say they are fatigued. I mean, folks with MS, their families are not always as understanding as perhaps they could be. So--
GERTH: 37:06	And that validation too. I don't mean to interrupt you but the validation, again, is important to patients. To people living with these conditions.
WYLIE: 37:13	Absolutely. Yes. So that's an important thing. And we have found that the areas associated with fatigue are the same areas that are associated with motivation and reward. And so that's potentially very useful to know because you can start to develop interventions to maybe capitalize on that to alleviate fatigue. So those areas

	are also-- those areas are also relying on dopamine and so maybe a dopaminergic pharmaceutical or intervention might help. And maybe also endogenous dopamine could help by, for example, giving people rewards. And so when you and I go grocery shopping, maybe we feel good about having completely gotten through our list but maybe if you had a cellphone, when you clicked off the last item, I cheered and there were fireworks--
GERTH: 38:20	I was going for ice cream, but okay [laughter].
WYLIE: 38:20	--maybe that would be-- that would make that reward that little bit better and would give your brain a shot of dopamine. It would certainly give your brain a shot of dopamine and mine. But if that happened in someone with MS, maybe that would also-- that shot of dopamine would also reduce fatigue.
GERTH: 38:40	Right. Have we changed the way we're studying fatigue? And I'm going to lead into the whole Kessler Foundation fMRI. But just in general, have we changed the way that we're studying fatigue? Has the science of studying it developed in a certain way or leaning in a certain direction like, "Oh, we're all going here now"?
WYLIE: 39:01	There have been changes. Thankfully. Because we've started to distinguish between different type of fatigue. And so we've always distinguished between mental fatigue and physical fatigue or have for many years distinguished between those two types of fatigue. But there's also what we call state fatigue and trade fatigue. And so trade fatigue is this concept of how much are you given to having fatigue? And so to get at that question, I might ask you questions like, "Over the past two weeks, how much fatigue have you felt?" And that will give me an idea of how much you're given to having fatigue. And a lot of research into fatigue has used that kind of questionnaire. Which is perhaps not as sensitive as it could be because there are a lot of reasons why you might say you have had high fatigue if you just-- or haven't been feeling very good for the past two weeks. Maybe you would say you've had more fatigue and maybe it doesn't have as much to do with fatigue as we might think.
WYLIE: 40:12	The other kind of fatigue is state fatigue or the fatigue you're feeling in the moment. And so that's the kind of-- that's the kind of fatigue that we study here. And we study that because I think that it's more accurate because I'm asking you just to tell me how much fatigue you're feeling right here and right now and not to try to somehow estimate the amount of fatigue you felt over the past two weeks. Which I think is very difficult to ask. And also, we induce fatigue. And so we give people tasks that fatigue them. And we ask them how fatigued they are at intervals and then we see what changes in the brain as their fatigue changes. And that's proven to be a very useful and powerful approach.
GERTH: 41:07	And then the Kessler Foundation - let's talk about the fMRI - had the first - I think, if my research is good - MRI devoted to research. So we have a MRI machine in the basement that is devoted to research. It doesn't sound like anybody else is using it for anything else. The--
WYLIE: 41:26	So we had the first one devoted to research in a rehabilitation facility.

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GERTH: 41:30 Ah, okay. Good to know. So how did that come about? And that's why you came here to be in charge of that.

WYLIE: 41:38 To be in charge of the neuroimaging effort. That was years before we convinced the board to build the MRI Center. But we did convince them to do that and there were a number of people involved in that endeavor and I was one of them. Yeah. And so we refurbished what used to be an aqua therapy pool at the Kessler Institute for Rehabilitation. And we put a [inaudible] in that space and now we have a neuroimaging center devoted to research.

GERTH: 42:17 And we should give props to Rocco--

WYLIE: 42:22 Ortenzio.

GERTH: 42:22 --Ortenzio who is-- is that who it's named after?

WYLIE: 42:27 That's who it's named after. He's on the board of Select Medical and Select Medical owns a number of hospitals around the country including the one here. The Kessler Institute for Rehabilitation. And he donated money towards establishing our center, so.

GERTH: 42:50 And so what's the benefit of having that on the property?

WYLIE: 42:56 Then it makes the research we do into the mechanism underlying the rehabilitation interventions we come up with. It makes that research much easier because we have the scanner right here and we're in control of the sequences we run and the hardware that we use. And it really sort of streamlines the research we're able to do here.

GERTH: 43:27 And you don't have to get in line.

WYLIE: 43:28 You don't have to get in line [laughter]. That's right.

GERTH: 43:29 Which is nice too.

WYLIE: 43:30 Yes. In many places, they have a scanner that does some clinical scans which is lucrative. And then any leftover time goes to research. Which means that there's less--

GERTH: 43:46 [crosstalk] motivated for that.

WYLIE: 43:46 --time for research than for clinical.

GERTH: 43:49 And what makes it an fMRI? Tell me about when you're-- could you just-- so you lie in it like you would a scanner or an MRI--

WYLIE: 43:59 Yes.

GERTH: 43:59 --if you were having your brain examined or something? But what makes it functional? What makes it--?

WYLIE: 44:05 So the functional part is just-- it's just a different sequence. So with an MRI machine, you can acquire data in different ways. Essentially, the scanner runs different

software packages. And these software packages manipulate the protons in the hydrogen atoms in your body in different ways. And if we look at the density of water, that will give us anatomical scan. And we can get high resolution anatomical scans looking at that. And if we use a different sequence, we can look at the iron in your blood and sort of track where that's going and that is what enables us to look at function.

GERTH: 45:03 And is it in real time?

WYLIE: 45:05 We can't do real time fMRI. We're getting some protocols up and running to do that. Most of the work that we do we have people come in and do an experiment and we acquire the data and then we analyze it later. But we are now building out the capability to do real time fMRI. So we'll be able to give people feedback in the moment so to speak.

GERTH: 45:33 And so tell me-- give me as simple sort of-- how it will play out. So what the task is and what did somebody do a task and then how you gather that data.

WYLIE: 45:45 Well, so if we go back to memory, which is probably an easy one to think about, if I asked you to remember three words and then you just repeated them to yourself-- I didn't tell you how to remember them. I just told you to remember them. And you just repeated them to yourself. Then later on, if I ask you to recall these words, you will find that they weren't there. And you wouldn't know that you had used a poor strategy until later when I asked you to recall the words. But what if I could tell you in the moment that the strategy you were using was a poor strategy? If I said, "Okay. Remember these three words," and I was monitoring your brain activity and I could see that the areas associated with memory were not increasing their activity, and I could step in at that point and say, "Okay. Try to use a different strategy because the one you're using is not going to do it for you." Then you wouldn't have to wait until later to find out whether or not your strategy was effective.

GERTH: 46:49 Right. And as you would do that, somebody is laying in the machine you can talk to them via intercom, right? Is that how it goes down?

WYLIE: 46:58 Right. So--

GERTH: 47:01 I'm just trying to get a picture of what it's like to be that patient or subject.

WYLIE: 47:05 Right. so what we would typically do is not step in and tell them but we would give them a graphical representation of the activity in the areas of the brain that we're interested in. So in this case memory. And so they would have let's say, a little thermometer that represented the amount of activation in those memory areas. And they would see three words and they would try to encode those. And if the thermometer didn't go up, they would know that the strategy they were using was not effective and they should switch to something else that made the thermometer go up and get warmer.

GERTH: 47:42 That would drive me crazy I think. That would be a challenge I wouldn't be able to put down. Are there other tools that you're using like the MRI or other big tools?

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WYLIE: 47:54	So we have an MRI compatible EEG system. And so that enables us to acquire EEG data while we're acquiring fMRI data. And so that's a great pairing for the reason that I said before because the EEG data gives you millisecond-level temporal information. You know exactly when things happen. But it's really hard to know exactly where they happen. And the fMRI gives you really good spatial resolution but in very poor temporal resolution. And so by putting those together, we can really hone in on what's happening and where and when.
GERTH: 48:34	And that's the-- is that the little cap that you wear--
WYLIE: 48:38	You put it--
GERTH: 48:38	--that has all the electrodes on it?
WYLIE: 48:40	Exactly. Yeah. Yeah.
GERTH: 48:44	Where do you think it's going? Where do you think the field is going like in the next 5 years or the next 10 years? What do you think you're going to be working with? What equipment are you going to be working with and what things are you going to be looking into?
WYLIE: 48:56	I think that real time fMRI is one thing that's going to be increasingly important especially for people who want to do interventions. Because not every strategy is optimal-- the same strategy might not be optimal for you as is for me, for example. And so how do we tailor certain interventions to individual differences? And real time fMRI is one way to do that to identify which strategy is most effective for each individual. So I think that's important. And then in terms of analysis, as computers become more powerful, we're able to mine data better and better. And so by using machine learning or deep learning, we're actually able to find things in the data that we wouldn't be able to find on our own because we're not computers and we can't just sort of kind of work through it like a computer can. And I think that's going to show us things we didn't know in those data.
GERTH: 50:18	The data you've already collected and you can just go back through it and go, "Oh, look at that."
WYLIE: 50:21	Yeah. Exactly.
GERTH: 50:23	Yeah?
WYLIE: 50:23	Yeah.
GERTH: 50:23	Okay. Last question. What keeps you here at Kessler? How many years have you been here? Are you [inaudible]? How many years have you been here?
WYLIE: 50:29	Yeah. I came in 2006. So it's been a few years now. And it's a great place, I mean, in a lot of ways. So people are great, the mission is a mission that I believe in and can easily get behind. And we have a board who enables us to do really good quality work and who is interested in enabling us to do that work. And so that means that we have the best equipment that we could ask for, which is a great thing.

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GERTH: 51:15	Nice. All right. Well, thanks, Glenn. I would say that you have some of the best people too.
WYLIE: 51:19	We do. Yeah. Yeah. I mean, I--
GERTH: 51:21	I point to you when I say that.
WYLIE: 51:23	Oh, okay.
GERTH: 51:23	But, yes, you can say that about your co-workers as well.
WYLIE: 51:25	Yeah. Totally.
GERTH: 51:26	All right. Well, thanks, Glenn. I appreciate it.
WYLIE: 51:29	[music] All right. Thank you.
ANNOUNCER: 51:31	For more information about Kessler Foundation, go to Kesslerfoundation.org. Follow us on Facebook, Twitter, and Instagram. Listen to us on Apple Podcasts, Spotify, SoundCloud or wherever you get your podcasts.