

Can listening to Mozart help stop seizures in epilepsy patients?

SUMMARY KEYWORDS

epilepsy, music, seizures, brain, electronic music, piece, Mozart, individuals, study, sonata, listening, patients, life, pianos, effect, question, research, people

Heather 00:00

[Your Complex Brain theme music] This is Your Complex Brain, a podcast all about the brain, the diseases that impact it, and the path to finding cures. I'm your host, Heather Sherman, and I have the great pleasure of working alongside the team at Krembil Brain Institute in Toronto, Canada, a leader in brain research and patient care. In each episode, we'll take you behind the scenes into our clinics and our research labs to meet the game-changers of the future, and we'll empower you with the latest research to help you take charge of your own health. You'll also hear directly from patients who are living with brain disease and the care teams who support them. Join us on a journey to unravel the mystery of your complex brain. [Your Complex Brain theme music]

Heather 01:07

[Sonata for 2 Pianos in D Major by Mozart plays] Wolfgang Amadeus Mozart was only 25 years old when he composed his Sonata for 2 Pianos in D Major, also known as K448. [Sonata for 2 Pianos continues]

Heather 01:23

It's one of the few compositions that Mozart wrote to be played on two pianos simultaneously. But, even the master musician could not have predicted that his enchanting melody may one day play a role in helping to reduce seizures in patients who are living with epilepsy. [Sonata for 2 Pianos continues]

Heather 01:52

[gentle electronic music] Epilepsy is one of the most common serious neurological disorders in the world, affecting nearly 300,000 Canadians and 50 million people worldwide. Many experience debilitating seizures, sometimes up to dozens of times a day. Those living with epilepsy often suffer in silence due to stigma surrounding the disease and, in many cases, a lack of effective treatments. That's something our next guests are hoping to change. Dr. Marjan Rafiee is a postdoctoral fellow working in the Neuron To Brain Lab at Krembil Brain Institute, where she leads the Music and Epilepsy Research Project. Dr. Taufik Valiante is a neurosurgeon, a scientist, and director of the Surgical Epilepsy Program at Krembil Brain Institute, as well as co-director of CRANIA, the CenteR for Advancing Neurotechnological Innovation to Application. Welcome, both of you, to the podcast.

Marjan 02:51

Thank you for having us. [gentle electronic music]

Taufik 02:53

Thank you.

Heather 02:56

Dr. Rafiee, I'm going to start with you. There have been a number of studies in the past 15, 20 years, looking at the connection between Mozart and its therapeutic effects for patients with epilepsy and other disorders. So, what have we learned already, and what are you hoping to discover through your work?

Marjan 03:13

So, in the 1980s, a number of computational works led by Gordon L. Shaw, who was a physicist, becoming interested in neurobiology towards the end of his life, looked at the effect of applying electrical pulses to stop seizures, and they predicted that something like this would be possible one day. And then, based on this observation, they expanded their observations and they suggested that listening to music could also have similar effects in individuals with epilepsy. [Sonata for 2 Pianos plays] Eventually, in 1998, this group, they published their first work on the topic of music and epilepsy, looking at the effect of listening to Mozart K448, specifically on reducing seizure-type activities, or interictal epileptiform discharges in individuals with epilepsy. And then, for 15, 20 years after that, a number of clinical studies have been published, which looked at the promising effect of listening to Mozart K448 on reducing seizures and seizure-type activities in individuals with epilepsy. There was still one question unanswered, and that was, "What's going to happen if individuals listen to anything else than Mozart?" and what I'm hoping to understand in this research line is, I'm hoping to get a better understanding about what are the important features in a musical piece that could have such an effect in individuals with epilepsy, to get a better understanding about mechanisms involved in generating such an effect, by looking at the brain recordings. And, ultimately, one day, the dream is being able to create our own music art pieces using a machine-learning algorithm for individuals with epilepsy to reduce their seizures. [gentle electronic music]

Heather 04:44

That is amazing. So Dr. Valiante, what did you think when Dr. Rafiee came to you with this idea? How does it align with the work that you do in your lab?

Taufik 05:03

Well, as you can imagine, Heather, there were a lot of thoughts that went through my mind. First of all, I thought it was cool. I was, kind of, a little bit leaning like, "Are you really sure?" and, you know, I think the argument up to that point was pretty compelling, and the way Marjan had presented it was really more within the context of, sort of, a broader scope of how music is being used in other neurological conditions. And so, you know, from a scientific point of view, it was a little bit hard to imagine that we would actually ultimately see the kinds of effects that we did, and I think that's kind of where the pleasant surprise came. As a clinician, you always think, like, you know, something super-cool, high-tech, esoteric, you know, is going to work, and it may work for very specific individuals, but things that

we can deploy easily in society that are, you know, compliance and enjoyable, even, are really great things that we could use to add on to, you know, the other kind of stuff that we do. So, I think there's a lot of emotions at that point. [laughs]

Heather 06:05

[laughs] That's a good point, though. I mean, we have to be clear that listening to this sonata as part of the study was a supplemental therapy, right? It's not meant to replace medication or other interventions.

Taufik 06:08

No, exactly. But, you know, as a surgeon, I mean, surgery is not the panacea. It is one aspect of care, and I think we all know from, you know, our lives, that it takes, you know, a lot of, sort of, richness to our existences to, sort of, manage every day and get through the day. And so, yeah, I think music is sort of that universal thing which we all have in parts of our existences, and so it is, you know, a piece of a much bigger puzzle, of course.

Heather 06:46

Absolutely. Totally agree. So, Dr. Rafiee, take us through the study, then. How many patients participated, and what, specifically, were they asked to do?

Marjan 06:54

So, there were 13 participants in this study. The first step in our study was to design a control piece, which you could compare to the Mozart piece itself. So, what we did was we randomly shuffled the Mozart piece around. We randomly shuffled the face of the Mozart piece in a way that it had no musicality in it. So, we completely destroyed that rhythmicity in the musical piece and it sounded like noise. [atmospheric, non-melodic music]

Marjan 07:27

And then we asked half of the individuals who started the intervention by daily listening to Mozart K448 for three months per year, and then switching to daily listening to the shorter Mozart for a three-month period. [Sonata for 2 Pianos plays] [atmospheric, non-melodic piece plays] The other group did the opposite. They started the intervention by daily listening to the shuffled Mozart for a three-month period, and then they switched to listening to Mozart K448, once a day, for a three-month period. [atmospheric, non-melodic piece plays] Both groups, they went through an initial and final three-month period in which they didn't listen to any of these pieces, and then we were able to report a reduction of seizure frequencies during the period that individuals were listening to Mozart K448, and not during the period of listening to the shuffled Mozart.

Heather 08:11

So, what kind of a reduction in seizures were you seeing?

Marjan 08:14

On average, we saw around minus 35% reduction on the number of seizures. We had an individual who became seizure-free during the time of listening to Mozart K448. We also had an individual who

showed an increase in the number of seizures while listening to Mozart K448, so we had a wide range of observations, basically.

Heather 08:33

And what do we know about why this particular sonata, why this particular piece of music by Mozart, seems to be so effective?

Marjan 08:41

[amusedly] That's an excellent question, and we're still trying to figure that out. We have a hypothesis. We actually published it in *Epilepsy and Behavior*. It was our last publication, and we had a hypothesis about the importance of the predictability of the rhythmic structure in observing such an effect that we were seeing in Mozart K448 because we were able to see that Mozart K448 has a very unpredictable rhythmic structure comparing to some other pieces such as *Für Elise* from Beethoven. So, that was the starting point of our next work actually. [gentle electronic music]

Heather 09:16

Well, we recently spoke with Scott Dainty, one of the original patients from your study. Here's a little bit more about his story. [gentle electronic music continues]

Scott 09:26

My epilepsy journey did start when I was two, or at least that's when I was diagnosed. Early on, I don't have too many memories of my childhood experiences with epilepsy. A lot of what I do remember started around high school 'cause that's when it was most severe in my life. Going through a lot of hormonal changes, and body changes, and things definitely interfered with, I guess, my brain functioning and my seizures, and so there were some weeks where I was having to go to the hospital two or three times in a week. So yeah, that was a hard time in my life. Going further in school was never really on my radar, but ended up, you know, getting a bachelor's and a master's and going on to be a naturopathic doctor, which I am now.

[pensive electronic music] My seizures happen primarily in my sleep. They're triggered in a sleep state. Kind of a blessing in disguise because I've been able to maintain a driver's license and function fairly well throughout the day, but I never lose consciousness for them so, although they're triggered in an unconscious state, I become conscious and experience them fully. They're all very, just like, muscle-contraction based so, kind of, full-body muscle contractions that are uncontrollable. So, sometimes they can be scary, but I also kind of know, they're always going to pass.

I love music. I've always loved music. It's been one thing that's, kind of, kept me sane throughout my life, even in times where I was having a lot of seizures, and so it's definitely played a big role for me, and that's another reason why I was really drawn to the Mozart study was, you know, if there's something as simple as listening to music, which I already love to do, then I'd love to explore it. [Sonata for 2 Pianos plays] The results of that study were really interesting because, even when they took away looking at averages, and looked at the individuals, my seizures, particularly the experimental groups, decreased in frequency by 30%, so I can't remember exactly the number of nights per month that I would have seizures, and I believe it went somewhere from eight to 10, down to three to five. I felt

pretty good hearing the results. It was definitely encouraging and a really neat thing to present to the world that something as simple as listening to a composition for seven minutes a day, and what whatever further studies find, coming out of this type of area, I find it really promising because it's such a simple intervention to offer to people.

[gentle electronic music] [chuckling] What I've learned about myself throughout this journey is to really, kind of, keep going and keep pushing limits of what people said I could or couldn't do. Some of that translated into education, going further in schooling, and some of that was hockey coaches that told me I was never going to play higher because of my seizures, and then I go on to play for a different team and beat their team next year, and so [laughs] I think part of what I've learned is just to, you know, make your own destiny within the limits that I have. [gentle electronic music continues]

Heather 12:58

Dr. Valiante, you've been treating patients with epilepsy for many years. So, when you hear Scott's story, what strikes you? Is it typical of what you hear from your patients?

Taufik 13:04

From a seizure point of view and the effects of something that is not surgery, I think it is very surprising. Of course, as neuroscientists, we have, you know, the very neuroscientific idea of how brain rhythms are changed by the rhythm of the music, and you know, et cetera, et cetera, et cetera, and then, too, other things, like there's a certain discipline to listening to music at a certain point in the day and so, do you kind of reorganize your life and develop healthy habits? I mean, it highlights, you know, these kinds of the exceptions, but I think that Marjan sort of articulated that, on average, though, the effect was actually quite high. I mean, it was, you know, a 35% reduction. And I think that's what the cool thing is, and I think that, you know, seeing individuals who can benefit like that is comforting in the sense that, you know, you feel, as a clinician, oftentimes, a bit helpless. You know, like, if you've exhausted a treatment, or they've gone through surgery, or they're not a candidate, and then the question becomes, you know, "How else can we help?" and I think that's kind of like the super-exciting thing when you hear his story, that yeah, you know, I think maybe there is something, you know, that we can do in addition to the other things that we do. [gentle electronic music]

Heather 13:12

We talked a little bit about it, but what makes it so challenging to treat patients with epilepsy? You know, what is available to them in terms of treatments right now?

Taufik 14:25

It's funny. In the past, I was often asked to give talks about, you know, advances in surgery, so everybody was kind of expecting, oh a laser, and this and that, and some cool robot, and I'd actually sort of joke with them and say, "You know, the biggest innovation that one would have in surgery would be access." So, I think that's kind of the important thing, which is, sort of, you know, being able to get an individual down the right pathway for helping them, you know, with their seizures and, of course, medications are an important part of that and any kind of lifestyle modification. So, we know that sleep/wake cycle is very important, reducing stressors in the environment, you know, shift work, when you sort of reverse your sleep/wake cycle, it can have deleterious effects on your seizures. So, you

know, all those other kind of holistic things with the medications and then, as a surgeon, of course, surgery becomes an option when you have, kind of, expended every option, when you've tried everything and it doesn't work. Then, if they're not a candidate for that, we think about alternative treatments like neuromodulation, or sort of implantable devices. The cool thing about the music stuff is that it, sort of, can be implemented at any point along there, really. It's something that's easily sort of implementable in one's lifestyle.

Heather 15:38

I want to go over to you Dr. Rafiee. I mean, you obviously have a real passion for music. Do you play an instrument?

Marjan 15:43

[chuckles] Yeah. I used to play a couple of instruments as my hobbies growing up. I used to play piano and cello and, later on, I started to play sitar, which is an Iranian musical instrument. [sitar music plays] So, originally, that was part of the story, my passion for music, basically, when I started to read about these topics.

Heather 16:09

Dr. Valiante, I know you're in a band, so it's obviously in your blood, too. [laughs]

Taufik 16:13

Yeah. I mean, I think it's probably in all our blood. You know, I think one of the cool things is that, you know, it's something so universal.

Heather 16:20

Dr. Rafiee, you did start off as an engineer though, so I'm curious, you know, about your background. How do you marry engineering, neuroscience and, now, this love for music in terms of potential therapy? How do you marry that all together?

Marjan 16:33

It was a series of incidents, to be honest, but originally I remember when I was doing my PhD in Chemical Engineering, there were days that I was feeling that, "I really need to do something more meaningful in my life, and I need to have a career that I can feel that I can improve peoples' lives by the work that I'm doing." And then, when I moved to Canada, I was fortunate enough to find opportunity through Frances Skinner, and Taufik and Krembil in Computational Neuroscience. And, I was just going to different talks back then, just to expose myself to as much possible knowledge, because I was changing fields, and one of these talks was about music therapy in neurological disorders overall, and that made me think. Next to the passion that I have for music and the work that I was doing, focusing on epilepsy and computational neuroscience, I started to just read about these topics and to think about what can be done from our side as an extra step. [upbeat electronic music] And then, I discussed it with Taufik, we developed the idea, and we were fortunate to get funding back then from Epilepsy Ontario to start our research. And then, I was also very fortunate to have some of the most amazing and the smartest people that I've met in my life in our lab, as a colleague, and to get their support as

colleagues, and also collaborators, that we have in this work. So, it was a series of incidents, and I was very lucky, basically. [chuckles] [upbeat electronic music continues]

Heather 18:01

And I guess it says a lot about our team at Krembil Brain Institute, too. I mean, maybe Dr. Valiante, can you speak a little bit about that - the uniqueness of the program and the team?

Taufik 18:08

You know, you don't have to be an expert in XYZ, but the expert is, you know, next door to you or somewhere, and you can go, "Hey," you know, and I think that that's kind of the richness that I try to create in the lab, as well. And, I think, you know, Marjan comes with a very specific interest and skill set, and then, you know, then you have people who are designing, like, devices, and then they're like, "Hey, Marjan. Maybe we can put music into a slice and what do you think that looks like?" And so, we get these pie-in-the-sky kind of ideas where you've got merging different fields, and I think that's the kind of richness that creates just, you know, so much excitement. And, I think it's what I love about the music project. I think it just touches on so many incredible facets, and I think the one other thing I'll just mention - I know I probably could, you know, keep talking forever - but I think it speaks to something which is so near and dear to my heart, which is the idea of raising awareness, and I think, you know, there's an incredible literature in epilepsy that, you know, quality of life is related to the knowledge that one has about their own condition, but also about the knowledge that people have around them about their condition, you know, and I used to sort of -- I don't know if Marjan remembers this, but, you know, we used to talk about sort of, "What are all the potential benefits of this kind of research?" and the one thing we always talked about was that, at the very end of the day, because music is, you know, such a rich and universal thing, is that it will provide us a platform, in fact, to raise awareness and, if at the very least we do that, then I think we've already succeeded, and then, along the way, you know, we have some really cool ideas about exploring the really neuroscientific basis of these kinds of things, and I think that that environment, that kind of community feel to it, you feel it in KBI, of course, but you also feel it with our community partners. So, you know, Epilepsy Ontario has been a strong supporter for us. You know, we work closely with Epilepsy Toronto, as well, and then, you know, Marjan and I do talk about, like, "What about the knowledge translation piece?" and now we already have those connections to our community members and stuff like that, and we have forums like this, you know, with yourself, as well, to sort of create kind of an awareness. And then we can leverage all these partners in different spheres, so I think that's one of the most exciting parts of this, this project, that it just sort of interdigitates with so many things. [laidback electronic music]

Heather 20:33

Dr. Rafiee, what are your thoughts when you think about the collaborations that have happened, and the ones that are possible through this research?

Marjan 20:40

I get very excited. [laughs] That's one of the most exciting aspects of this work because it's interesting to think about, "How did it evolve?" because I remember, at first, it was just us, and then I remember that there was a resistance from the scientific community about this topic, overall, until we saw the results and the rest, which makes sense. It's fine. But, I've been lucky to work with some of the most

amazing collaborators around the world, most recently, and I learned a lot from them, and I'm very, very excited to learn about different things from these people and to see how can we make this topic more challenging and interesting. [laidback electronic music continues]

Heather 21:25

I think we'd better start advocating for a concert hall at Krembil Brain Institute! [Marjan and Taufik laugh]

Marjan 21:31

We should start our own little band actually - The Krembil Band.

Heather 21:32

Actually, that's a great idea! Let's bring in the band. [Taufik laughs] Well, we've spoken in the past about the mysteriousness of the brain and, Dr. Valiante, how much you hope to 'crack that code' through your work in epilepsy. So how much closer do you feel like we're getting to actually understanding more about the brain, with the promise of these new therapies, new technology? Are you optimistic?

Taufik 21:59

Oh, very much so. You know, there are these two large categories of psychology. One sort of looks at the brain, very computer-like in that there are specific parts of the brain that, you know, do language and certain parts, do vision, certain parts do attention, et cetera, et cetera, and then, there's this other, you know, kind of area which I'm very now enamoured by, which is called 'embodied cognition,' which is, you know, the brain doesn't develop just in your head. It develops, basically, as this embodied phenomenon. It's attached to, you know, your body. It has all its senses and interacts with the outside world, and so your brain is really ultimately designed to track and interact with the world, to learn from the world, [uplifting guitar music]. And I think that when we think of music, for example, we think of it in a relatively static way, which is that, you know, I put the music on, I listen to it, it's fun, and, really, this project has changed the way I think about music, largely from the perspective of learning. And so, you know, we have many projects in the lab, which, you know, we exploit specific technologies, whether it's implantable devices, which, you know, we're developing, or the actual kinds of opportunities we have, with our courageous patients who will allow, or participate in, the research that we do, where we have implanted electrodes, and we can uniquely study aspects of the brain which you just can't do in any other way, you know, down to the single-cell level with the kinds of recordings we do, uniquely here at Krembil. We're really the only place in Canada right now that does these types of single-cell recordings. You know, the question that's outstanding is that, "How could you listen to something, you know, one time a day, or maybe a few times a day, and it has permanent, you know, effects?"

Taufik 23:53

But, you know, we have another study where we look at a form of learning, which is called instrumental learning, which was done by Kramay Patel, who, he was actually able to show that a person can learn to control a single neuron in their brain, and the question then sort of that raises is that, "How can you learn to control at such a fine resolution, a specific area, a specific cell in your brain?" And so, it opens up this really crazy potential, which you see, which is kind of like this volitional control of stuff that goes

on, and we kind of understand it, as, you know, mindfulness or, you know, studying. Like, everything is really like you're controlling your brain, but could you explicitly control a certain part of your brain towards a specific therapeutic goal? And I think that that's, you know, something which I had never, sort of, thought about because I think about things in devices so, like, a device will stimulate the brain this many times and it'll cause these kinds of changes in these cells and blah, blah, blah, and on and on. And then, but when you think about something like music, it's much more nuanced. It's got all sorts of things, and I read this fantastic line recently from a scientist at McGill University, which is that, you know, "The music is reward in and of itself." And then, if you think how we learn, well, we learn through reward systems, right? So, if you do something and it hurts, you're probably not going to do it again, or if you have a very positive outcome, you're going to be like, "Oh, I should do that again," and that's really how you learn. And, I think that kind of learning maybe underlies the kinds of things that we think that music could be doing, where you're tapping into the reward system of the brain. And I think that that's something, for me, which is super-crazy exciting because it's an area that I never explored or was part of before, so it opens up incredible avenues, I think, for further collaboration with people who study these types of things. You know, it's funny, because when I was a student, you know, and I sort of try to impress this upon the students in the lab, which is that, you know, every little bit of data that you get is like a portal. It's like a window, a door, and I think that that's kind of what music has done, for me, as a scientific thing is open up a huge portal, because now we have collaborators, you know, international collaborators. It's that kind of richness that the Music Project is bringing, so it's going to help us crack that code. [laughs] [electronic music]

Heather 27:03

That's the beauty of science, right? Building upon each other's work. I mean, the final answer being a cure, I guess, if you get there. Dr. Rafiee, what do you think?

Marjan 27:12

I think Krembil has been a unique institution for me in terms of making me able to expose myself to so many different opportunities, and to work with so many different great people. I try to understand everything from the window of music and the brain. So, in our lab, we have, as Taufik mentioned, we have so many different research works going on, working on implantable devices, and neurofeedback, and different topics, and thinking about these topics and thinking about, "How can we mix it with music? How can we help? How can we use music as a way to get a better understanding about how the brain responds to different conditions, basically?" And, as Taufik mentioned, I also feel really fortunate to be able to work with these collaborators who are working in so many different interesting things, expanding our knowledge, overall, to other neurological disorders, as well, to get a better understanding about how music could help individuals, and how music can provide hope to individuals, basically.

Heather 28:17

Right. It always comes back to the patients.

Marjan 28:19

Yes, always, always.

Taufik 28:21

Totally.

Heather 28:23

So, what's the next step for the research? What would be next for you in terms of new studies coming up? Tell us what's next.

Marjan 28:30

Yeah, we are actually currently planning our next study, which is based on the hypothesis that we mentioned, and we just published a couple of months ago. We're gonna look at the role of the predictability of the rhythmic structure on reducing seizures in individuals with epilepsy. We're currently trying to get our ethics approval and, hopefully, in the upcoming month, one day, we will be able to start our enrollment.

Taufik 28:55

We really want to differentiate ourselves from the literature but also ask a very important question and address a very important question, which is, we don't think there's something specific to a specific musical piece. It's not the piece, itself. There's the structure of it which is important, and we think many musical pieces could have that structure, and so we're not focusing on Mozart alone. That's for sure.

Heather 29:17

Great. So, you're going to be looking at other pieces of music, not just this Mozart sonata.

Marjan 29:21

Exactly. Other pieces. We're not focusing on one specific composer, specifically. We are looking at a range of composers, but we're focusing on structural features of the musical pieces, basically. We are trying to look at the role of the predictability of the rhythmic structure on reducing seizures, and I was actually thinking about, "What do I expect to see?" because I was just, a hint of one of your questions, it made me think about, "What you expect to see in the next work?" I was thinking that it would be very interesting because all these pieces are musical pieces, so I don't know whether we're going to see a reduction only for one group, we're going to see reduction for all of them, or we're not going to see any reduction at all, because this is the scientific world. And then, I assume that any results will be positive results, in that regard, because you're discovering something new, which helps you to plan the next steps, so I can't wait to see the results of that work, actually.

Heather 30:16

Very cool. Well, this is fascinating research. It's been a pleasure chatting with you both today. Thank you so much. [electronic music]

Marjan 30:22

Thanks for your interest.

Taufik 30:24

Thanks, Heather. [upbeat electronic music]

Heather 30:56

[Your Complex Brain theme music] A special thank you to Dr. Marjan Rafiee and Dr. Taufik Valiante for being our guests on today's episode, and to Scott Dainty for sharing his experience as a participant in the Mozart and Epilepsy study. If you'd like to hear more about Scott's story, head to our website, uhn.ca/krembil, and click on the show notes for today's episode.

Heather 30:56

This episode of Your Complex Brain was produced by Jessica Schmidt. Executive Producers are Tobin Dalrymple with Pilgrim Podcasting and Carly MacPherson, with production assistance from Dr. Amy Ma, Twayne Pereira, and Suzanne Wice. For more information about the Krembil Brain Institute, please visit uhn.ca/krembil, and you can reach us by email at krembil@uhnresearch.ca. But please note that, due to privacy regulations, we cannot answer any personal health questions. Thanks for listening. We'll be back in two weeks with another exciting episode. Have a great day. [Your Complex Brain theme music continues]