TINNITUS TALK
PODCAST
EPISODE 15

THE BIONICS INSTITUTE
Objectifying Tinnitus

00:00 Introducing Mehrnaz Shoustarian and the Bionics Institute

Hazel: Hey everyone, I'm joined here by **Mehrnaz Shoustarian** from the **Bionics Institute.** Hi Mehrnaz. Good to have you here today.

Mehrnaz: Thank you for having me.

Hazel: So, you work at the **Bionics Institute** and the reason we asked you to come onto the **Tinnitus Talk Podcast** is because the Institute is working on developing an objective measure of tinnitus. So, we obviously want to hear all about that, but before we start on that could you just tell our listeners a little bit about yourself and your background?

Mehrnaz: Sure, so I'm a researcher at the **Bionics Institute** here in **Melbourne.** I have been working at the Bionics Institute for about five years but doing research for a lot longer and my background is biomedical engineering. I have an interest in looking at different ways of recording brain activity and extracting information from the recorded signals.

Hazel: Right, how did you get interested in that specifically?

Mehrnaz: Well, my great research interest is how we can use technology to non-invasively record brain activity and extract information related to how the brain works or different neurological conditions or the effect of drugs on the brain. So, before the **Bionics Institute** I was involved with a start-up company where we were looking at using another recording technique called an **EEG** that records brain electrical activity and developing a device that could help an anaesthetist during surgery to give them information about how deeply anaesthetised a patient is and if a device was using just a sensor that you could place on the forehead and record information. I just think it is quite amazing that with a single sensor you can give information to a clinician in real time that could help them manage their patient. When I came to the **Bionics Institute,** the Bionics Institute has a strong and long history of hearing research and so my technical experience, and a hearing knowledge, led to one of the researchers there, **Professor Colette McKay,** wanting to look at tinnitus using an imaging technique that we used there**, fnirs**, to look at tinnitus, so it was a natural progression into that project for me.

Hazel: Right, so you kind of rolled from brain research in various areas into this field of tinnitus. What did you know about tinnitus before you started this work?

Mehrnaz: I had done a bit of research on hearing and balance during my PhD at **Monash University** here in Australia and so I knew a little bit and, looking into it further, I realised that there was a lot of work needed in the area even though there's a lot of research that has already been done but it's still, as you know, there is no reliable treatment. There is no clinical test available, so it is really very difficult to develop good treatments for this condition. So, there is a huge need for further research.

Hazel: You're absolutely right of course about the need. Do you have any personal experience of tinnitus? Do you know of people who have it?

Mehrnaz: I personally don't have it, but I do know a lot of people and since I have been doing this research and our research as I'll explain later, is quite data hungry, so we need data from a lot of people so I have been talking to and working with a lot of people who have experienced tinnitus over the past three years, and I can understand what a burden it can be.

Hazel: So, tell us a bit more about the **Bionics Institute** and what it does.

Mehrnaz: **The Bionics Institute** was set up over 30 years ago now by **Professor Graeme Clark** who was the inventor of the Australian cochlear implant and the cochlear implant is, as you may know, a device that provides a sense of hearing to people who are deaf or who have severe hearing impairment so there is a lot of background knowledge in hearing at the Institute developed over many years. But the **Bionics Institute** has also gone into other fields of research such as vision and has looked at conditions such as epilepsy and **Parkinson's Disease,** and these are some of the active projects at the moment and they were all based on the initial knowledge that they had from the cochlear implant.

06:00 Objective measurement of tinnitus

Hazel: And this specific project, let's zoom in on the objective measure for tinnitus. Maybe you can start by explaining to our listeners why it is so important to have this objective measure?

Mehrnaz: Well, currently, there is no reliable, clinical test that a clinician can use to give to help them assess what's happening in the brain with tinnitus. So, what clinicians rely on are reports given by the patients. And while these are very important, subjective reports of how you're feeling because of your tinnitus or what your tinnitus sounds like, is very important. But it's limited. It doesn't give clinicians, for example, information about which part of the brain is affected and lack of an objective measure hinders development of treatments as well. Because without an objective measure it's difficult to know what treatments are actually affecting which parts of the brain and are actually working or not. So, having an objective measure is an important step in developing reliable treatments.

Hazel: Yes, this is something I have heard before and I have even heard people use the argument that one of the reasons for instance that the pharmaceutical industry or healthcare industry is not investing more heavily in developing treatments for tinnitus, even though you would say there is a large need and potential market, is this lack of objective measure because they are worried that they can develop the treatment but we won't really be able to assess how well it works if we don't have an objective measure. Would you agree with that assessment?

Mehrnaz: Yes, that's exactly right and, also, without an objective measure it's difficult for people developing treatments or companies developing drugs, to get through the regulatory steps of getting a drug approved. So hopefully an objective measure will help with that as well.

Hazel: That's an additional element I hadn't even thought of. That's useful additional information. Right, so, we have established that if we can successfully develop a measure that really objectively identifies this person has tinnitus, this person doesn't, it would be a breakthrough and it would help tinnitus research and treatments along immensely.

Hazel: Can you describe what the measure that you working on, that you are developing, what that looks like, how that works?

Mehrnaz: Sure. We are using an imaging technique called **Functional Near Infrared Spectroscopy** or **fNIRS** for short and the way we do the recordings is using a cap that we place on the person's head, a bit like a swimming cap, with sensors on them and the sensors shine light onto the head and detect the amount of the reflected light. And from that the changes in blood oxygen levels can be quantified and from that you can infer brain activity. The reason is when a part of the brain becomes active it needs more oxygen so there is an increase in blood flow and therefore there's an increase in blood oxygen levels. That's how the technology works. We're recording signals at rest, so when the person is sitting there doing nothing and also, we are recording brain responses to sound and also to visual patterns and what we're doing is extracting features from these signals in the different conditions and then using machine learning techniques to combine these features. Machine learning techniques basically generate mathematical equations with many parameters where you can input your signal features and the output would be, for example, that a person has tinnitus. Or that a person has severe, rather than mild, tinnitus. So, what you need to do is provide data to these mathematical equations or machine learning techniques, for them to learn what a signal feature from a person with tinnitus would look like. Then what you do is input, so you do more recordings, input signals that you haven't used to train those mathematical equations, and then see whether it can identify this signal as coming from someone with tinnitus, or not or, for example, someone with severe or mild tinnitus. If it can identify a new data set that means that it's got good accuracy.

12:08 The underlying theory

Hazel: There's a lot to unpack there. I'm trying to wrap my brain around it. So, are you starting from a certain theory or model of how tinnitus works in the brain or really with a blank slate and the machine learning programming itself develops over time that model?

Mehrnaz: Well, the reason why we are doing all this is based on a lot of research done previously by other groups using different imaging techniques, not **fnirs** but other techniques such as **Functional MRI** or **PET scans** which are sort of, more sophisticated and give you more information about different parts of the brain. They have shown there is, for example, they have identified certain parts of the brain that are affected in tinnitus patients. They show differences to people who don't have tinnitus. They have also identified that background neural activity, so your brain activity when you are really not doing anything, it's just really background activity. That shows changes with tinnitus and also the other thing that previous research has shown is changes in how different parts of the brain interact with each other.

We've taken this knowledge from other studies to identify parts of the brain we want to image. So, with our system we can place our sensors on the cap on parts of the brain that we know, or we suspect from other studies, that should show changes with tinnitus. And also, we are looking at resting state and responses in the brain because of that knowledge, that background resting state or background neural activity is affected in tinnitus and that leads to different parts of the brain interacting in different ways compared to controls.

So, with all that knowledge, we have put all that together and identified parts of the brain that we should record activity from and the types of signals that we can use, so resting state signals and responses to brains. Now the advantage of the machine learning algorithms is firstly that they are very good at combining different signal features, so information from different sources. These algorithms are very good at combining these. The other thing is that most of the research on tinnitus has been done using statistical techniques and what you get with statistical techniques are group average differences. So, for example, you would say, on average the signal features from the tinnitus group are higher or lower, were different to a control group. So that gives you group differences. But for a clinical test, what you need is to be able to give your system signals from one person and for the system to tell you with good accuracy that those signals appear to be more similar to the tinnitus group compared to the control group. So, you need to feed in as much information as you can for your machine learning algorithms to learn these patterns and then once you've got data from a single subject it can tell you hopefully with good accuracy what that data is more similar to, a tinnitus patient or not, or a mild or a severe tinnitus patient.

16:23 Measuring mild versus severe tinnitus

Hazel: Let's dig in a bit more to the last thing you said, mild versus severe, because I think also that is also a very important distinction that is also missed during previous studies. How do you make that distinction and how confident are you that you are able to make that distinction and then, how do you validate that you made that distinction correctly? I assume you have to ask the person some questions about their tinnitus severity, or loudness or both and then compare that against their brain activity results. Can you tell us a bit more about that?

Mehrnaz: Yes, that is exactly right. So, to start off with we need the subjective information from the patients as well. We have tinnitus questionnaires, for example, the **Tinnitus Handicap Inventory** or the **Tinnitus Functional Index** where they ask the patient questions about their tinnitus and at the end you get a score of whether these responses are likely from someone with mild, moderate, severe or even just slight tinnitus. To start off with you do need that subjective information to correlate with your signal features to be able to start developing these objective measures. Now, how we validate this. As a first step a study that was recently published looked at a fairly small group of 25 patients, 18 controls so it was really a feasibility study just to show that this approach is showing promise, with fairly good accuracy on this data set to distinguish tinnitus patients from controls and tinnitus patients of different severity levels. What we need to do now is test those algorithms, those models, with further data. So that is what we're doing now, collecting more data to increase the sample size and check that it all holds up. We're still getting good accuracy and we are also looking at the questionnaires that I mentioned but also a person's own rating of how loud and how annoying their tinnitus is. And some of the signal features that we have looked at correlate well, for example, with how loud they have rated their tinnitus but not so well with how annoying they rated it, which is promising because it suggests that we can separate those two effects with the recordings that we are doing.

Hazel: That is very interesting and, indeed, something I've not heard before, that that might be possible, and I do think that a lot of clinicians, when they talk about tinnitus and when they talk about severity they are talking about the impact on person, how distressed the patient is and not the loudness, per se. And it's very interesting to hear that you think you might be able to measure purely the loudness signal.

Mehrnaz: That's right**.** As I said, it's a small data set at this stage but that's what we're hoping for, that's what we've seen signs of, separately, so we need larger data sets to see whether that still is the case.

The other study that we aim to do to validate our findings is a study on a sub-group of tinnitus patients who use a cochlear implant. So, they would use the cochlear implant for their hearing loss but in a large group of people who have a cochlear implant and tinnitus, in a large percentage they report that the cochlear implant helps their tinnitus as well. It suppresses the tinnitus. Now, in some people - it's not in everyone that it improves the symptoms - in some people it actually makes it worse and in some people it has no effect, but that is a very valuable group of patients to study. Because you can change the perception of their tinnitus by turning the cochlear implant on and off. So, you would get signals from the same person with their tinnitus modified, therefore you are no longer comparing two groups. You're not comparing a group of tinnitus patients with a group of controls where the differences that you get might just be because they are different people from different groups, you know, where there might be other things going on. Whereas with a cochlear implant user you would be getting data from the same person with their tinnitus perception modified so that is a valuable data set that we hope to get to validate our findings so far.

Hazel: That is very interesting indeed. I hadn't thought of that group as being so useful in that regard.

22:28 Which areas of the brain are you investigating?

Can you tell us a bit more about the specific areas of the brain you are looking at?

Mehrnaz: Sure, yes, the set up we've got at the moment with our **fnirs** cap, we've got sensors over the auditory parts of the brain, the frontal regions and also the regions at the back of the head, the visual cortex. So, the frontal regions we are imaging because they are associated in a lot of studies with the distress experienced by people who have tinnitus. Auditory regions because tinnitus in a large number of people starts off as a problem with hearing which later on becomes more central and spreads to different parts of the brain. Then there are the visual regions and the reasons we are looking at those is because there is a part of the visual cortex that has been shown in many different tinnitus studies that has abnormal background activity. So, the background neural activity that I mentioned earlier. And also, there are also a lot of auditory visual pathways in the brain, therefore when there are changes in activity in auditory regions with tinnitus, studies have shown that this affects the visual part of the brain as well, so that's why we are looking at that part of the brain. So frontal, auditory, and visual regions of the brain are what we are looking at, at the moment.

Hazel: This might be a little sidetrack, but how much is known about the connections between the visual and auditory processing and how that gets linked?

Mehrnaz: With tinnitus, not a lot is known about what happens in those connections and those pathways with tinnitus but there is a lot of work done on auditory visual integration in, I guess, people without tinnitus so more basic research in that area has been done so that should help us make sense of the signals we are looking at as well. The other thing I guess with this set up that we are using at the moment is we are hoping that with this larger data set that we are collecting and the machine learning algorithms that we are doing, we will be able to pick out which channels, which sensors in which parts of the brain are giving us the most information so it might turn out that we don't need all those regions with all those sensors for a clinical application. We can have a cap with a reduced number of sensors that is easier to set up.

Hazel: Maybe we can also talk a bit more about this resting state activity. I thought that was interesting and if I understand correctly, resting state refers to your brain activity when you are not doing anything, right? You're not responding to anything, you're not receiving major stimuli, is that correct?

Mehrnaz: That's correct, yes.

Hazel: So why is it thought that at resting state the brain of a person with tinnitus looks different and maybe you can talk about both actually also, in the non-resting state or the active state or whatever the other state is called. Why is it important to look at both?

Mehrnaz: Sure. I guess changes in resting state activity is what has been shown using other imaging techniques so, for example, in auditory regions, yes, it would make sense that when you have tinnitus, even when you are not listening to a sound your brain thinks that you are, or is creating activity that creates that phantom sound. In the auditory regions it sort of makes sense and then it's not very clear why so many other parts of the brain get involved as well but a lot of studies have shown that they do and therefore background activity in other parts of the brain also gets affected in tinnitus. And then, why do we need to look at responses? Well, one hypothesis that we have is, and other studies have shown this as well, if there is, for example, increased background activity in the auditory part of the brain, then when you actually hear a sound the response of the nerve cells is going to be different to if that background activity was less. So, the activity that you start off with is going to affect how much of a response the brain can produce. That is why we are looking at responses of the brain as well, and not just resting state. And again, we're hoping that this more sophisticated way of looking at the signals is going to tell us actually which of these conditions is giving us the most information. Do we need to always collect all three conditions from our patients or is resting state alone going to give us enough information? These are questions that we still need to answer.

Hazel: So, regarding the response state, so this is when patients are receiving auditory and visual stimuli and you are looking at what is then going on in the brain, are you able to explain how that processing is different or might be different for someone with tinnitus versus someone who doesn't have tinnitus or even someone with mild tinnitus compared to someone with severe tinnitus. How do they process those stimuli differently?

Mehrnaz: Well, what our data has shown us so far is for auditory responses for example. Even when you have groups, so our two groups were matched for age and also for level of hearing. So we do a hearing test before the brain imaging, so we have an idea of their hearing levels and the two groups were matched for levels of hearing and also age but when you look at the auditory responses the tinnitus group showed a reduced response compared to the control group. And that was the case even with visual responses even if they all had normal vision or corrected vision with glasses and they were age-matched, but the visual responses were smaller in the tinnitus group compared to the control group. And one hypothesis that we think is happening is again because of that increased background activity, there is already activity going on, so when you get a stimulus the response is smaller in the tinnitus group compared to the controls.

Hazel: That kind of intuitively makes sense even to someone who doesn't understand a lot about brain processing. But if you already have a background process going on and there is an external stimulus that you have to process on top of that, it just kind of intuitively makes sense that it would be more difficult.

31:45 Comparison against other objective tinnitus measures

Hazel: How much are you aware of keeping track of other efforts to objectively measure tinnitus? I do think there are some other groups looking at this. Do you follow those efforts and are you aware of how they might be the same or different as compared to what you're working on?

Mehrnaz: Obviously, no single imaging technique, I think, is going to give us all the answers about tinnitus and what's going on in the brain. Every imaging technique has its strengths and weaknesses, so there are groups using EEG (brain electrical activity) to do similar things - develop objective measures of tinnitus. There are groups using functional MRI, PET scans, and each of these has its advantages and disadvantages. What we're using, **fnirs**, has a few sort of key advantages which we think will help translate it to clinical use. And these are that it's non-invasive; it's not radioactive; the systems are failing portable so can easily be set up in the clinic; fairly low cost; and also, compared to, for example, MRIs—if you've ever had an MRI scan, it's quite noisy.

Hazel: Yes, a lot of people with tinnitus are afraid to take an MRI because they're afraid the noise exposure will increase their tinnitus, yeah.

Mehrnaz: That's right, yes, it's not a very suitable technique for hearing research and especially tinnitus, so in that sense, **fnirs**, for example, is very quiet. The other thing about **fnirs** is that because I mentioned we want to validate measure in a group of cochlear implant users who have tinnitus, **fnirs** can easily be used on patients who have a cochlear implant, and that's because, again compared to an MRI, MRIs aren't very compatible with cochlear implants and also techniques like EEG for example that record brain electrical activity. If you do an EEG recording on someone with a cochlear implant switched on, the signals from the cochlear implant are going to interfere with the EEG recordings, so they generate odd effects on the signals. Because **fnirs** is using light to image brain activity, there is no interference from the cochlear implant on the light signals from **fnirs**, so it's possible to use them together. All of these advantages, we think, will help—once the measure is developed and we're confident that it's giving us reliable, accurate measurements, then it'll be possible to translate it to clinical use.

35:31 Current phase of the research

Hazel: How far along are you currently? Which stage are you in, and what still needs to be done?

Mehrnaz: At the moment, we are collecting more data to validate our initial findings—make sure they're reproducible. We also managed to get a bit of funding from a program here in Australia called the medical device partnering program that helped us to work with our collaborators to improve the initial algorithms that we had developed, so at this stage with a larger data set that we are collecting, we will be able to validate those improved algorithms as well—make sure that they are working well. That's our sort of current stage of work.

Hazel: Maybe we should go also a bit more into the whole machine learning aspect because that's really fascinating, and I think it's being used more and more for health research, but it's still relatively unknown, especially to the general public. What are the big advantages of doing this, and then how does one do this well? I think one of the things you mentioned is that the more data that you put into the machine learning program, the better it learns, and the more sophisticated the model becomes. Yeah, can you just talk us through that bit more?

Mehrnaz: Sure. So our machine learning work is mainly done by our collaborators. They are a group at one of Australia's universities, Deakin University and they're an institute called Institute for Intelligent Systems Research and Innovation History. It is headed a professor, who has a great team of experts in machine learning, and we've been fortunate to be able to collaborate with them. So the advantage of using these techniques, as I mentioned, compared to more traditional, statistical techniques, is that they'll be able to give us—they'll be able to quantify how well we can take data from a single subject and classify that to a tinnitus or non-tinnitus group or tinnitus groups at different severity levels. So to start off, we just look at two severity levels, but hopefully with more data, we can sort of refine that a bit to more subcategories, and the reason why we have looked at it machine learning is just that currently, again, its clinical use and also, currently there are a lot of algorithms that are used for different applications—non-health applications that can be easily adapted to health applications as well, and maybe in non-health applications it's easier to collect very big data sets, so those algorithms can be developed for bigger data sets in other areas, but with the right expertise they can be adapted to health applications such as tinnitus.

Hazel: All right there several things there I want to follow up on. So, you mentioned, regarding tinnitus severity, I think, you're currently working with, so currently you're able to distinguish no tinnitus vs. mild vs. severe. Is that correct?

Mehrnaz: Yes, so yes, I guess we asked two questions: can we separate tinnitus from no tinnitus, and we looked at the accuracy we can get from that, and then we looked at mild vs. severe based on a tinnitus handicapped inventory rating, which actually gives you more categories. It's got slight, mild, moderate, and severe and, I think, catastrophic as well. So we group—because of the low numbers that we had—we group slight and mild together and moderate and severe together, and just showed that we could very well classify these three groups.

Hazel: All right, and so if I understand correctly, one of your challenges at the moment is just testing on larger numbers of patients who are willing to participate, and yeah, of course, there's a lot of logistics there as well because people can't travel from too far, etc., so I can imagine this is a big challenge, like the machine learning program needs more input, but yeah, there's some challenges there to get those large sample sizes.

Mehrnaz: That's right, yes, that is a challenge that we are working through at the moment and for that, I guess the things that we need are more funding and more testing sites. So with more funding, we can set up testing sites in different locations and be able to collect data faster. At the moment we are just testing here in Melbourne at the **Bionics Institute**, but we can, yes, there are certainly ways of accelerating the data collection phase that needs a bit of funding and resources.

41:52 Funding and partnerships

Hazel: Maybe this is a good time to segue a little bit more into the organizational business aspect of the work. Can you tell us a bit about how the study is being funded and also are you partnering with any other organizations or people in the study?

Mehrnaz: Sure. I guess almost as difficult as understanding the brain is getting funding for research, so that that's a huge challenge, but at the moment our studies are mainly being funded by the **Bionics Institute** itself internally. As I mentioned, we did get some funding from a government program last year, which was great help—the medical device partnering program. At the very start of the project when Professor Colette McKay was looking at using **fnirs** on tinnitus, we did get a small grant from the UK charity, Action on Hearing Loss, but at the moment the major funding is coming from the **Bionics Institute** itself. We're collaborating; we have our collaborators at Deakin University, as I mentioned, and a machine learning team. They have been very supportive of the project and continue to work with us. The other thing that we need to work on going forward is the hardware side of this objective measure, so at the moment we are using a research system that's sort of general purpose. It can be used in any research field that wants to use **fnirs** for brain imaging, but what we really need for a clinical application is a device that's purpose built for the sensors that we need so with a cap that's got the sensors on the locations of the brain that we need and also has our software and algorithms embedded, so that would bring the cost down a lot it, and we'd be able to sell it hopefully at an affordable price to clinics to clinicians so that they could use it. So that's another part and for that, we're looking at a number of different parts but one of them would be to work with a company that already makes **fnirs** systems, but just to now purpose-build it for this application.

44:46 Future roll-out and commercialization

Hazel: I see. Let's talk a bit more about the future, and can you outline what you expect or hope the coming, I don't know, three years or so will look like and ideally what will have been accomplished in a few years?

Mehrnaz: Sure. So what we're hoping to do is firstly expand our current data set to make sure that the findings that we had in our initial study are reproducible with a bigger data set. The other study we'd really like to do is the cochlear implant study I mentioned, where we can measure the same person's brain activity with and without tinnitus or with their tinnitus perception changed. That will also validate our findings and show that we can track different changes in brain activity with tinnitus in the same person, so that would then show that with potential treatments, if you test the same person as before and after treatment, then you can monitor changes in brain activity related to tinnitus. And then the third aspect that we're also working on is to be able to work closely with groups working on treatments—whether drugs or neuromodulation or other treatments to work closely with them to monitor their patients activity before and after those treatments, which would, again, be an important step in the development of those treatments.

Hazel: It certainly would, yes, and have you been able to start any discussions with anyone on that or is that really still in the future? I'm just interested—are you getting a good response in terms of, oh yes, that is something we would be really interested to buy?

Mehrnaz: Yes, we have started discussions. They're very early discussions but there are certainly opportunities to work with groups developing different types of treatment. We are at the moment we're in discussions with two groups. It's very early on, but there has certainly been a very good response, yes.

Hazel: That's good to hear and that's encouraging and so the **Bionics Institute** is a nonprofit organization, correct?

Mehrnaz: That's right, yes.

Hazel: Yeah, so for me that's always encouraging to hear because clearly you have a social mission, but I mean, ultimately, I assume the plan is to commercialize this tinnitus measurement technique. Have you thought about how to do that in such a way that it becomes widely available and benefits as many people as possible?

Mehrnaz: Yes, that is that is certainly our goal—to get to that stage. Over the past four years, the **Bionics Institute** has focused heavily on commercializing some of its research projects and there are a number of approaches that are being used. Obviously with our project, currently we're at the stage where we are making sure that everything works. We've applied for patent protection for our methods, and then we are open to several different methods for commercialization; we're considering different methods, so one is to create a startup that would then attract investment and allowed us to continue the development of the product with the **Bionics Institute** but also other partners, and that's been used in some of our other projects. Another would be to license the approach to someone that has an interest in the area and then continue the development of the product with a licensee and the **Bionics Institute** supporting it. So that's another approach. And then also if we partner with **fnirs** hardware manufacturers who could help take the device through regulatory approvals and aspects like marketing, then that also would be another path to commercialization. Our management team, our CEO, Robert Klupacs, and our head of development, Dr Erol Harvey, they have a lot of experience in this field. They have been through this path with other projects, but they are considering all of them and also they are happy to talk to other people who are in the commercialization field and have an interest in tinnitus, but all of these are options that we can follow.

Hazel: It's good to hear that you are actively thinking about those different options because even if you would invent the best device ever, that's the next crucial step, right? Getting it out there in the way that it gets taken up widely and people really benefit from it.

Mehrnaz: That's right, that's definitely a big step. Research translation, it's a whole world in itself, but hopefully with the expertise that we have at the Institute, it will help move that forward.

Hazel: Yeah, exactly. Yeah, I can imagine it's not your area of expertise, of course, you're the researcher, the scientist.

51:40 How the tinnitus community can get involved

Hazel: Let's talk a little bit about the tinnitus community, let's say, or people with tinnitus. We've seen on the **Tinnitus Talk** forum some activity discussing the **Bionics Institute** and people are curious, interested, encouraged—or they want to know more; some people want to be directly involved. Maybe we can start with that. If people want to be directly involved in the study, who would be eligible and how could they get involved?

Mehrnaz: So just to mention, since last year, the end of last year, when we had a paper published on our first study and there was a bit of media interest, we had a huge response from individuals with tinnitus who volunteered to take part in the study. And that's just been really great and promising for us to know that there is support because as you mentioned, we need a lot of data in this approach that we're using—we need a lot of data so it's great to know that we have the support and people are willing to put in time and come in and get tested, so that's been really great. At the moment, unfortunately, we only have a testing site in Melbourne, and travel is so restricted with COVID at the moment; we even get calls from other cities in Australia from people who want to come but it's just difficult for them to fly over or drive over. So at the moment we can only test people in Melbourne or very close to Melbourne, but hopefully with further funding we can expand our testing sites and then we could accelerate that equation. And then in other ways, I guess, again, we're happy to explore commercialization parts or hardware development parts, so in that sense we're happy to talk to anyone interested as well.

Hazel: That's good to know. Yeah, you can put out a call right now because, yeah, a lot of people might be listening, so yes, if someone knows any leads for Mehrnaz, please reach out.

Mehrnaz: That would be great. Thank you, yes.

54:27 Expected impact on the lives of tinnitus sufferers

Hazel: So, I think I have gone through most of the questions that I want to ask but maybe I'll end off with a big closing question, and then of course, you're free to talk about anything you still want to mention. What's ultimately your big hope or aspiration in terms of the impact you'd like to have on people's lives?

Mehrnaz: What we're mainly hoping is to be able to give clinicians and researchers the ability to somehow track the complex changes that tinnitus triggers in the brain, and that's critical for the development of new treatments and how tinnitus patients are managed. At the moment the clinical path is really not that clear for someone who has tinnitus. They go from general practitioners to audiologists to ENTs, and really there's nothing concrete that anyone can do or anywhere that they can direct them. So, giving clinicians a tool that gives them more information about the tinnitus and what's happening in the brain, we're hoping, will result in improved management, patient management. The other thing is that at the moment tinnitus is mainly an umbrella term. Everyone who has the phantom sound, regardless of the type of sound differences, you know, they just say they have tinnitus, so if we can use an objective measure to help identify subtypes of tinnitus, you know, in terms of which part of the brain is affected or the type of sound that they hear or whether it's related to hearing loss or not—if an objective measure could help identify those subtypes then again, it would be an important step in giving subgroups the right treatment, so identifying the subtype and giving them the treatment that is appropriate. I think that would help management of this condition.

Hazel: It's interesting that you bring up subtypes because just before we started, it occurred to me I should probably also ask about subtypes and then I forgot, so I'm glad you brought it up. It's an interesting discussion because I think the tinnitus research community for the past few years has sort of labored over this. Some researchers are convinced it's an important concept; others are not so convinced, but I guess the problem is no one has ever been able to very conclusively identify what exactly are these subtypes then and how are they defined. Is that something that you hope might come out of your research as well?

Mehrnaz: Yes, I certainly hope that our research helps with that aspect of tinnitus, identifying subtypes. As I mentioned, our imaging technique, like other imaging techniques, is not going to answer all the questions. For example **fnirs**, we know, it can't image deep parts of the brain. It images the cortex and superficial parts of the brain. That's why we identified specific brain regions that **fnirs** *can* image, but there might be subtypes of tinnitus where the abnormal activity is deeper in the brain and we wouldn't access it with **fnirs**, but again even if there are certain groups that we can identify, then that would help take the patient assessment one step further and say, well, it doesn't look like it's this type or that type but maybe you now need to have—hopefully by then they'll be other clinical tests available as well, and they'll say so now maybe you need to have another clinical test to identify this. So our method would help rule out a subtype and direct them to the next step. I think that would help this condition a lot.

Hazel: Yes, definitely, and I'm very interested to see what's going to happen with your research, and I know many in this community will be following you guys. Is there anything, Mehrnaz, that we didn't cover that you wanted to talk about?

Mehrnaz: I think we've covered everything. I guess just to mention that this is definitely multidisciplinary research so my colleague and our research director at the Institute James Fallon, he also has an engineering in Neuroscience background and has a lot of knowledge in the hearing space and so that's sort of his contribution; it's very important. We have the machine learning engineering type aspects. We are going to have hardware development and we have our clinicians, audiologists, and ENT consultants that we sort of keep in contact with just to make sure we're on the right clinical track. So it's definitely multidisciplinary. There are a lot of people involved. We need a lot of expertise from different sides. There's the commercialization, but I think we have a good team and hopefully with everyone's efforts we can move this forward.

Hazel: Certainly. Let's hope so. Yeah, and I agree that multidisciplinary aspect is so important. I think it's always been one of the challenges in tinnitus research—that tinnitus never neatly fit into one discipline or another; it was always crosscutting. Maybe that's one of the reasons it has been under researched, I don't know, but it's great to see you guys pulling together such a multidisciplinary team. So, Mehrnaz, I want to thank you so much for your time and for the work that you do, and like I said, we will be following your work and we hope to stay in touch.

Mehrnaz: Thank you very much. I hope to stay in touch, too, and thank you very much for doing this interview—this opportunity—it's great to be in touch with this community. I think you have some great knowledge already that's also going to help us, so I wish you the best, as well.

Hazel: Thank you.