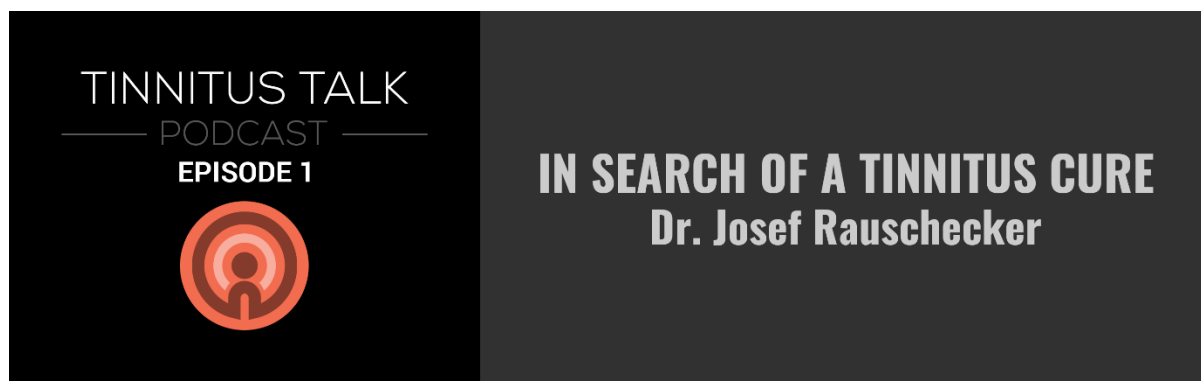




0:00 Jack Straw talks about the podcast and introduces the interview

Sean, aka Jack Straw: Hello everyone, and welcome to **Tinnitus Talk**, a podcast sponsored by [Tinnitus Hub](#). My name is Sean, also known as Jack Straw, and today I'm going to be introducing you to this podcast. To jump right into it, I'm going to talk about what you can expect from it.

Starting off, we're going to have our main focus be interviews. We're going to be interviewing professionals, such as doctors, researchers, PhD's, audiologists, people with tinnitus, pharmaceutical reps... You guys get the idea! It's mainly people that we think are interesting and will provide us, as a community, information that's more cutting edge and at the front lines of tinnitus, which will be fantastic to hear.

Another important part of the podcast will be updates. Keeping everyone up to date on research, treatments and alternative treatments, and making sure that everyone's getting the most recent news as to what's going on in various fields.

Another important aspect is fundraising. A lot of us have to give our own money into these fundraisers to promote research and to help various people push tinnitus into the forefront. That falls on a lot of our shoulders. So, we'll be discussing various fundraisers that are going on and that you should know about.

Another important aspect will be helping everyone who's listening to spread more awareness. You know, it's not very helpful when we are all just sitting on our butts, not really doing much about tinnitus besides complaining. We really have to get out there and do something, if you want to make a difference. So, we're going to be finding ways, at individual and community level, to raise awareness.

Besides that, we'll also have some success stories, taken from the Tinnitus Talk forum and from real life interviews, because we feel it's important. There's a lot of doom and gloom going on, but success is something that does happen, people do achieve it, they do learn to live with their tinnitus. And we think it's important for everyone to hear those types of stories.

Besides that, we'll have some administrative items, where Markku or Hazel can come on and talk about **Tinnitus Hub** or the [Tinnitus Talk forum](#), keeping everyone up to date on new developments there, or asking your help with something, just to bring the community together and have a community talk.

And we'll also have a [Tinnitus Talk podcast forum](#), where we can have questions coming from you guys, we can get feedback, you can suggest future topics, anything like that – we'd love to hear from you guys to make this podcast the best we can!

The last thing you guys are thinking must be: How often will this podcast be coming out? We're going to shoot for once a month. You might get it more than that, or we might have to extend the deadline sometimes. I want everyone to keep in mind that this podcast, and all the work that happens with **Tinnitus Hub** and **Tinnitus Talk**, is all volunteer work; we're all dedicating our own time, going out of our way to make this happen. We're just humans, we

have real life stuff going on as well, we're not professionals. So, keep that in mind, we do have jobs and personal lives beyond our volunteer work.

Just one quick disclaimer: Anything that we talk about on the podcast going forward, anything that our guests say, anything in general that happens on this podcast is not medical advice. We are not doctors; we cannot give you medical advice regarding tinnitus or any other medical illnesses you may have. If you want medical advice, please go to a medical professional.

We do have a great interview for you today. It's with **Dr. Rauschecker**. Hazel got a chance to speak with him and had a fantastic interview. They covered a wide range of topics. You guys put in those questions on the forum, and we compiled the list, and we talked with Dr. Rauschecker and the interview came out fantastic. It's very interesting, I highly recommend everyone to please check it out. You will have a great time, it's very engaging.

I will give you a slight introduction before that begins. But I first just want to thank everyone for listening!

Alright everyone, let's talk about Dr. Rauschecker really quick. He's basically been doing tinnitus research for a very long time. He's currently at **Georgetown University**. He's done various studies over the years, worked with different researchers, and is probably one of the smartest people when it comes to tinnitus. He has a great [TED Talk on YouTube](#) called "Tinnitus – Ringing in the Brain." It's about fifteen minutes; very short, but very informative. It's packed with very interesting information regarding tinnitus. I highly recommend everyone to please go watch that, either before you listen to the full interview or afterward.

Also, Dr. Rauschecker currently has a [fundraiser going on](#) for his research. I highly implore everyone to please donate to his fundraiser, because tinnitus research is very important and that is exactly what he is doing. So without further ado, please enjoy this interview with Dr. Rauschecker and Hazel.

6:40 Hazel and Dr. Rauschecker kick off the interview

Hazel: Welcome everyone to **Tinnitus Talk**, a podcast on all things tinnitus. My name is Hazel, I have tinnitus myself and I work as a volunteer for **Tinnitus Hub**, who are the organisers of this podcast and, amongst others, also run the Tinnitus Talk Online Support Forum. I am very honoured to be here today with Professor Josef Rauschecker. He is one of the most pre-eminent researchers on tinnitus. He is with the Department of Neuroscience at the Georgetown Institute for Cognitive and Computational Sciences.

Hazel: Welcome Dr. Rauschecker – Actually I've been told I can call you Josef? So I will do so!

Dr. Rauschecker: Hi Hazel. Thank you very much for having me and of course you can call me Josef.

Hazel: Thank you. We are so happy to have you join us today and taking some time out of your, no doubt, very busy schedule to engage with the tinnitus patient community.

Dr. Rauschecker: No, it is a pleasure to be there and I look forward to your questions. I have seen some of the prior broadcasts and it seems that you are a very knowledgeable community and that some of the questions might be quite tricky for me to answer but I will do my best.

Hazel: Ok, we'll try to not make it too hard on you.

8:11 Dr. Rauschecker's own experience as a tinnitus patient

Hazel: So, my first question would be: Do you have tinnitus yourself?

Dr. Rauschecker: Yes, I do. I started having it maybe ten/fifteen years ago and started out with just occasional bouts of tinnitus I remember.... And I should clarify, I have noticed that you are pronouncing it 'tinn-EYE-tus'?

Hazel: Yes.

Dr. Rauschecker: I usually say 'TIN-i-tus' and I have checked with the highest authorities in the field, among others, Dr. James Snow who was formerly Director of NIDCD and then ran one of the tinnitus foundations and is a research consultant, and he said absolutely both pronunciations are fine.

Hazel: Good to know.

Dr. Rauschecker: So, I can stick to my 'TIN-i-tus' and you can stick to your 'tinn-EYE-tus' and it's just fine like that.

So, I remember a weekend – can't remember the year, it was probably sometime in the mid to late nineties – when I first got tinnitus, and it was a very disturbing experience. It was not just one of the second-long tinnitus occurrences that everybody has once in a while. It was, you know, I suddenly seemed to have lost hearing a little bit and then the whole weekend I had this buzzing sound.

So, I called my colleague here at Georgetown, the Chair of the Otolaryngology Department, and said: "What's going on?" and he said: "Well, you know, don't worry, it might just go away, it might clear itself but if it persists come and see me." And it did go away after a day or two, it was gone and I was very relieved, but then about a month later it came back.

And what I ended up having for quite a while was what they call intermittent tinnitus – where you have it for sometimes a few days then it goes away again, completely gone, and then it comes back. And I remember talking to someone at a tinnitus meeting and they said: "We know that this form is quite common, but unfortunately the news is bad. The intervals where you are tinnitus free will become less and less and shorter and shorter." And this is exactly what happened, and right now I am at a stage where I have tinnitus almost all the time, except for some days.

You know, some days I wake up in the morning and I'm completely refreshed and have no tinnitus whatsoever, and those are the days where I feel very happy and I feel very relieved and I think: "Maybe it will stay that way." But then often the next day, or two days later, it sets in again and I have tinnitus again.

So the short answer is: Yes, I have tinnitus now, almost constantly, and I think it's been actually a very good teacher for me. As a scientist, I am a good observer, I think, and so I have been using my own experience to draw conclusions from. But we will get into that later.

Hazel: That's very interesting. Were you already studying tinnitus at the time when you got it? Or was it because you got it that you became interested in studying it?

Dr. Rauschecker: No, I already had been interested in it. I have been working on neuroplasticity all my life; how the brain can change with different types of environments or experiences. Part of my Doctoral Thesis was the development of the visual system and how different specialised visual experiences can change the visual cortex part of the brain. And then I became interested in how people who are born with blindness can cope and how their brain changes as a function of their unusual experience.

So tinnitus to me was a form of neuroplasticity as well, a reorganisation that happens if you lose hearing or have partial hearing loss; and that is still part of my concept, that some kind of injury to the nervous system has to precede this experience of tinnitus and perceptual changes. So that was my interest and I actually have written a review paper in Trends in Neuroscience, a high profile review journal, where I compared different forms of plasticity in different sensory systems: visual, auditory and somatosensory; and compared tinnitus with chronic pain or phantom pain in particular, which is a comparison that other people have made as well, and I think it is important to understand that analogy. Again, something that we can get into later.

Hazel: Definitely, we should.

Dr. Rauschecker: So maybe I should continue and be more specific in answering your question.

When I got tinnitus myself, of course my interest became more intense and I said to myself: “You know, how can I use my knowledge that I had up to that point towards understanding my own affliction?” And that often helps. So, I think the experience of having it then influenced my getting into the field more directly, and I got funding and we go on from there.

Hazel: It’s very interesting that it is not a purely academic interest, there is also a personal interest there.

Dr. Rauschecker: Yes, yes of course, and that happens everywhere in every field of science. You know, it is not unusual that people [scientists] are interested in their own afflictions or disorders if they have any.

Hazel: Yes, indeed. We [Tinnitus Hub] did a survey last year amongst participants to the TRI – **Tinnitus Research Initiative** – conference. There were a lot of researchers present, and one of the things we asked them is: “Do you have tinnitus yourself?” I think 40% had it; so that’s much higher than the general population.

Dr. Rauschecker: Yes, sure.

Hazel: Yes, interesting outcome.

15:02 Tinnitus brain mechanisms – Part 1: How tinnitus manifests in the brain

Hazel: So, you started already talking a little bit about tinnitus mechanisms, how it works in the brain. I know your research has focussed, amongst other things, on understanding the brain mechanisms of tinnitus. Can you explain to our listeners what is your current understanding of how tinnitus manifests itself in the brain?

Dr. Rauschecker: Yeah, so there are several levels of involvement of the brain, and when I got serious with my tinnitus research after I developed it myself, about ten or fifteen years ago, I developed this theory which was based on data. You know, it was not just a theory that I took out of thin air, it was definitely based on studies that we did at the time, which we might have done any way, even without my getting tinnitus, because it was just the additional impetus that came from there. But it was really a study that was funded by the Tinnitus Research Consortium at the time and then later by NIH where we used that concept of tinnitus being a form of reorganisation of the auditory cortex and based on an injury that happens in the periphery.

So, there you have already two levels of involvement of the brain: 1) The periphery of the auditory system; you might say well that is still at perceptual level, but the auditory system projects very quickly into the brain stem, so the cochlear nucleus is the first processing station which is part of the brain. It’s just one synapse away from the cochlea and from the hair cells that are receptors, and so they are certainly at a very early level maybe a [brain] involvement because you have damage to the hair cells or some other peripheral station of hearing and something even as early as the brain stem or the cochlear nucleus might change, and there is some evidence for that. 2) But then, we went a step further and said: tinnitus is a conscious experience, so it probably involves at the level of the cortex, where conventionally people think our conscious experiences are represented. And, sure enough, this is the model that has been prevalent for some time now, and this is one of the models that I described in this 1999 review paper, where we say: This input to the cortex changes because some of the ear’s hair cells are damaged and the signal in those frequencies changes. Let’s say somebody who is older gets high frequency hearing loss, so there will be less input coming to the auditory cortex from the cells, from the hair cells in the periphery that represent higher frequencies. That is the most common form of hearing loss.

Then, what happens to that part of the auditory cortex that no longer receives that input? Does it sort of die? Is it deprived of this afferent input? What happens in the most common model, which comes partly from these phantom pain studies, is that – we call them ‘de-afferented’ regions, as physiologists – that these regions actually acquire or stabilise input

from the neighbouring regions. So they don't die; they are actually very much alive, because the cortical cells are still there and, instead of receiving this high frequency input, they receive input now from the neighbouring region, which actually expands into that vacated region. And that's how you get an over-representation of these 'border edge frequencies,' as we call them, and this over-representation then leads to higher activation of these regions than would normally be the case. And this is, in the view of myself and a lot of my colleagues, the ultimate origin of the tinnitus signal. There may be, as I said, there may be more peripheral regions involved, the brain stem or the thalamus, but we think that the reorganisation in the cortex is the decisive fact.

19:41 Tinnitus brain mechanisms – Part 2: The “gating mechanism” and role of the limbic system

Dr. Rauschecker: So that is chapter number one, and I don't know if you want me to proceed with the other part which is actually the more specific part of my theory; then we get to another part of the brain which is actually very crucial.

Hazel: Yeah – of course, I have watched [your TED Talk on YouTube](#) – and I would, by the way, encourage any listener to this podcast to check it out, because it gives, in fifteen minutes, a very clear and succinct summary of your theory – and there you also talk about the second part, which I think is the gateway mechanism. Am I saying this correctly?

Dr. Rauschecker: Yes.

Hazel: So, yes, please tell us more about that.

Dr. Rauschecker: What I am saying there is that.... And you are right, at TED Talk they really coached us to make this short and make it succinct. It's a very interesting experience actually when you have to do these things in 15 minutes where you normally take about 45 minutes at least in an ordinary academic seminar. But it is good to be precise and short about this.

Let me first step back and tell you how my own experience contributed to the understanding of that second part and that is: I noticed, as I mentioned, that I don't have tinnitus all the time. Sometimes it is completely gone, and it's still gone every now and then, and then I wonder what is going on. It can't be that suddenly my hair cells in the inner ear have regenerated that quickly and that my input is normal, or that my auditory cortex suddenly reorganises back to where it was, and the hyperactivity of the auditory cortex is gone and therefore my tinnitus is gone. That is almost impossible to believe.

So, I had the idea that maybe some other mechanism higher up might be important for switching this hyperactivity on and off or switching my perception of hyperactivity on and off. That is what we refer to as the 'gating mechanism.' There is a switch basically, or gate, that can allow the tinnitus sensation to get through to my conscious experience. And in one of these studies, which actually was done in Europe, in Munich, in a collaboration that I had there, they had done structural MRI study of tinnitus patients called **Voxel-based morphometry**, a technique that they used where you can look at density of different parts of the brain. It was a whole brain study where we compared the brain of tinnitus patients with the brains of normal control patients who don't have tinnitus.

And the result was that there was one region that stood out, in that it had a markedly smaller volume in tinnitus patients than in normal controls, and that was a part of the **ventromedial pre-frontal cortex**, and we thought maybe into the ventral striatum or nucleus accumbens. It's a part of the limbic system that was clearly affected in tinnitus patients.

And then you put two and two together and I said to myself: maybe this is where the gating happens. If this region is broken, in addition to the changes in the auditory system, then maybe this is what makes people aware of this [tinnitus] hyperactivity. And if that kind of region might be able to change on a daily basis, it might fluctuate. So if that gating mechanism changes maybe my tinnitus will be gone and if it changes back to where it was it might come

back. So there is a variable there, where the switch actually might happen or where you become aware of these kinds of things or not.

And this might extend to other sensations as well; it might have to do with chronic pain or might have to do with depression; and it is well known that people with tinnitus often have a co-morbidity of depression or anxiety. Not everybody has that, but some people do, and we can get into that as sort of a third path, but I think the gating idea is very important to my theory. And I am still, after ten years, convinced that this is what happens.

24:39 Why not all people with hearing loss develop tinnitus

Hazel: That is very interesting, and it would also explain why not everyone with hearing loss has tinnitus, for instance.

Dr. Rauschecker: Exactly, exactly, that was the other observation when I got into the tinnitus research in more detail, I realised that it's only about 30% of people with hearing loss who end up getting tinnitus, and the explanation would be that their gating system is intact and there is a sort of a second line of defence. The brain holds off that unpleasant sensation because you don't want to have this and so the brain is actually really good at creating this form of homogeneity. It is trying to even out any unusual experiences, so if you suddenly hear a loud noise in your brain, then this higher mechanism thinks: "Well, this is not usual, so we'd better turn the volume down." This is in more lay terms the idea, that in people who don't develop tinnitus that [gating] mechanism works and in people who do develop tinnitus that mechanism is somehow compromised.

26:07 Tinnitus and emotional response – what is cause and effect?

Hazel: Indeed, so that would suggest that the brains of people with tinnitus are somehow significantly different from those without tinnitus. But I wonder: are those differences a cause or an effect of the tinnitus?

Dr. Rauschecker: Yes, this is now the debate of course! The idea that the limbic system is involved in tinnitus is not new. **Pawel Jastreboff** and others before him have brought that up, and it has to do with the observation that people who have tinnitus often are depressed about it. They have anxieties and the conventional explanation is: this is of course a reaction to the tinnitus. Because you have tinnitus you get anxious about what else might happen, you get depressed about your situation.

But our theory turns this around. The new thing about our theory is that we basically turned that around 180 degrees and say: What if that broken gating mechanism is actually the cause of our perception of tinnitus? It is not the cause of the tinnitus signal, that happens in the auditory system. There is no denial of that; I think everybody would agree if you hear something unusual it will have to come out of the auditory system and that's I think well taken by 90% of people in the community now. But the debate is about whether the limbic system involvement is the reaction to the tinnitus or whether it could be the cause. What I am saying is that it is definitely a very important cause.

In science it is often difficult to get through with an idea that has two causes. And in this case, you have a cause in the auditory system that generates the tinnitus signal, and we have a broken gating system which normally keeps the tinnitus signal at bay and people don't even know that they have tinnitus. They might have it for a day or two after a rock concert. They might actually have tinnitus but then the gating system controls it out and kind of turns the signal down, and then you never know that you have tinnitus even though your neurons somewhere might actually fire, and you don't even know about because the gating system – kindly – keeps you healthy and keeps the signal down.

Hazel: That's very interesting, what you said about turning around cause and effect related to the emotional response that people have to tinnitus, because – and this is, I would say, a bit of a controversial issue, also within the tinnitus community – because people feel like they're

being told their tinnitus is their fault because they are reacting emotionally to the tinnitus sound. And people have even been told by their doctors sometimes that the only reason their tinnitus persists is because of their own emotional reaction to it. But you are saying that it is really not that simple.

Dr. Rauschecker: Not that simple. I mean that there may be that additional factor of a vicious circle that starts to take place once you have tinnitus; of course, you get upset about it too and of course that makes it even worse. But I think the original cause – and again this is the second cause, and I am not denying that there is a tinnitus signal generated somewhere in the auditory system – I am actually saying that as a second affliction what tinnitus patients have is this volume loss in the ventromedial pre-frontal cortex and the involvement of the **nucleus accumbens**, which is part of the evaluation system. It has been called the pleasure center, but we have found, and others are now doing a lot of work, that it is also responsible for aversion. So it's not just pleasure, it is also aversion. So if something is wrong in there then you will suddenly put a lot more weight on things that are aversive; this is part of the gating system that the aversion of tinnitus then gets normally fed to the pre-frontal cortex and the pre-frontal cortex then is the one who turns down the signal; and that can't happen if there is a sort of a break in that gating group.

And what I want to add here is that the idea that the emotional response, as you call it, is not a reaction to the tinnitus, but is actually a causal thing, came also from my own observations. I noticed that whenever I had tinnitus – and this is why the intermittent form of tinnitus is so instructive – when I had tinnitus I noticed that I was in a bad mood and when I didn't have tinnitus I was in a good mood, and I was absolutely certain that the bad mood didn't come from the tinnitus and the good mood didn't come from the absence of tinnitus. This was independent of that; I woke up in the morning and I was in a bad mood and I had tinnitus. How can you say this was a consequence of my tinnitus? I was asleep, woke up and had tinnitus, and one day I wake up and had no tinnitus and I was in a good mood.

So, there was clearly a correlation between my mood and the tinnitus signal, and that's where I had the idea: maybe it's the other way around and maybe that system up there that is broken also controls my mood. And you know then the sleep comes in of course; sleep can be the most beneficial thing for or against tinnitus. If you sleep well, this is what I always tell my patients; try to get good sleep, this will regulate down your tinnitus. Absolutely it is the best treatment, together with relaxation in general. So, there is an effect from the limbic system down onto the perception of the tinnitus. There is absolutely no question about it in my mind.

32:34 Variability and fluctuations in tinnitus – what factors are at play here?

Hazel: Perhaps we could explore a bit more the variability in tinnitus that some patients perceive. Actually, my tinnitus is very, very constant. It is just this continuous high-pitched ringing. There is very little variation, but I know a lot of tinnitus patients do experience fluctuations throughout the day or the week or sometimes it's completely off or very much on. Is anything known.....?

Dr. Rauschecker: I'm sorry to interrupt – I think it's one of the questions that you sent me: Are there sub-types of tinnitus? And I totally agree with that. I think there is and talking at the conferences and talking to other tinnitus patients I hear the same thing where somebody says: “I have had this since childhood. I had an injury and it has been there ever since and has not really changed.” This is maybe a different form of tinnitus which has nothing to do with what I have just talked about – emotional influences and so on. Sorry to interrupt.

Hazel: No, that's a good addition. So what factors do you think are involved when there is variation in someone's tinnitus; when it either fluctuates a lot or it gradually becomes worse or actually better over time. What factors do you think are involved in that?

Dr. Rauschecker: Well, with a gradual increase, like I said, that was predicted by someone who I talked to originally when I started having tinnitus. That is something I don't understand.

It's maybe just an ageing issue or it may be why tinnitus can be progressive in these kinds of cases and it's kind of similar in other disorders; so that is, I think, separate from the question why it fluctuates.

I think it fluctuates because – let's bring it down to the receptor level, or to the pharmacological level. Ultimately, this is I think what we need to understand, is that there are systems in the limbic system and in the gating system, in the nucleus accumbens; there are modulators like dopamine and serotonin which are not well understood neuromodulators so they're not part of the main transmitter systems like glutamate and GABA, the main excitatory transmitters. But dopamine plays a role in a lot of different disorders you know. The most famous one is Parkinson's Disease and once it was discovered that dopamine plays a role there – then we can also find treatments. L-Dopa came out of studies in non-human primates that isolated dopamine as one of the responsible transmitters in Parkinson's.

Since then we have learned that dopamine is involved in a lot of other mainly neuropsychiatric disorders. So, a lot of knowledge needs to be gained about these systems that do the modulation. I just bring that up as because when we want to understand the modulation and the fluctuations of tinnitus I think we really need to get down to that level. Also, if we want to, ultimately, find a cure, this is what we need, an understanding at that level. And this is what has been... I'm sort of jumping ahead now. But this is what has been frustrating, and I think people and funding agencies don't understand that and they are keeping to their old paradigms and are not willing to take the risk and take that jump into another domain where we have a much better chance of making huge progress and understanding with this disorder.

Hazel: Right, so we have to understand more about where tinnitus fluctuations come from and that could also lead potentially to a cure or treatment.

Dr. Rauschecker: I think it's crucial – I think this is absolutely crucial.

37:26 Sub-typing: Does it matter what caused one's tinnitus?

Hazel: Can we delve a bit more into this sub-typing issue? I am wondering, does it matter, in your view, at the level of the brain, what caused the tinnitus? For instance, does it make sense to distinguish between noise-induced or non-noise-induced tinnitus? There is also somatic and non-somatic tinnitus; some people who have problems in their neck or jaw; there is this theory that that could either trigger or contribute to the tinnitus. But do those things matter?

Dr. Rauschecker: Not in the sense of what I just talked about in terms of modulation. I may be wrong about this, but those forms like **somatic tinnitus**... which is, of course, a fact; people can modulate their tinnitus with jaw movements or neck movements and some people go as far as saying this is the whole part. I don't believe that. I don't believe that is the whole cause, but just one sub-type, and I may be wrong, but those people are maybe less prone to the fluctuations in terms of emotional co-morbidity and so on. But this is something we should look into, I think; isolating different sub-types where we can say... Your tinnitus, as you said, is constant; this may be a whole different ball game. And somatic tinnitus may be a whole different ball game. So, if we talk about those forms of tinnitus we may not have a lot to say in terms of emotional co-modulation. We may not have such a good chance actually in treating it. You know there may have to be other treatments, in the sense that we have to really get to the auditory system or some other sensory system in this case and fix what's broken there.

39:37 Comorbidities: How are depression and tinnitus interlinked?

Dr. Rauschecker: But I think that the majority of cases are the ones, and where people suffer most, are the ones where emotional involvement is there. This is where people get suicidal and want to kill themselves. They don't want to necessarily kill themselves because the tinnitus is there when they move their jaws. They have a problem in their nucleus accumbens and in their ventromedial pre-frontal cortex. You know they have a form of depression. Often it is not a major depression; in some people it is, but in the majority of cases it's mild

depression. It is sort of a mood disorder that gets to them and it is something that can be understood.

I think we have to be much more biological about understanding these mood disorders. You know, there is nothing really mysterious about them. It is something that we work on, on a daily basis. We ignore things and we... If we were to think about our own situation – that one day we are going to die, and all of the diseases in the world, and all of the suffering that we see, we might actually all be depressed. But the reason we are not is that we are ignoring these kinds of terrible things and are able to sort of blend them out with our gating system. This is part of the function of that gating system, which ignores a lot of bad things, and only if you are unable to ignore them then you become depressed. And if you are unable to ignore or take out your tinnitus perception, then you have that co-morbidity. There's more to be said, but I'm starting to ramble.

Hazel: No, that's fine. I am interested in exploring more the connection between tinnitus and mood disorders, depression, anxiety. We do see it a lot on the Tinnitus Talk Support Forum that people deal with these co-morbidities – many of them. Would you say that people who experience depression and anxiety before getting tinnitus are also more at risk to develop tinnitus?

Dr. Rauschecker: I think that would be the logical consequence. I don't have any data to support that, but it is, of course, what you would predict. I often get that question: How do you explain that somebody suddenly gets tinnitus without [something like] a gunshot near their head? How can you explain that with your gating theory? And my answer is: Their gate has already been broken by that time, so they can immediately see the onset of tinnitus, because then the two causes are there. And so equally I would expect that somebody – and that is the answer basically to your question – that somebody who has a problem in their ventromedial pre-frontal cortex, which is responsible also for depression – it's the same region that **Helen Mayberg** and others have identified or Wayne Drevets at NIH had an early PET study where he identified that same region that we found has a causal involvement in tinnitus is also a cause for depression. It is the same exact region, so I would expect the answer to your question is yes. They [people with depression] should be at a higher risk when they get hearing loss.

Hazel: So, in that example you mentioned someone being exposed to a loud sound. The sound is really just the trigger, but not the root cause?

Dr. Rauschecker: Well, not quite, it's one of the causes. Like I said, it's like an end, a logical and gate where you have to have two things happen either at the same time or staggered in time. You have hearing loss; you are at a higher risk of getting tinnitus because your gate might break, and then you have tinnitus. Or if you have a broken gate, you are prone to depression, then if you get hearing loss and you will develop tinnitus. So, both of these things have to happen either at the same time or one after another.

I have met people at talks that I gave. I remember one talk in Montreal and somebody came up to me afterwards from the audience and said: "Well, I think you are right. My brother died last year and since then I've had tinnitus." I said: "You probably already had some hearing loss, but it didn't cause tinnitus, but the emotional breakdown that you had after your loss then probably led to the tinnitus."

And we hear that all the time that people go through divorces and then suddenly develop tinnitus, which means they must have already had hearing loss, but it was hearing loss that didn't lead to tinnitus because their emotional regulation was still intact.

45:26 The role of stress in triggering tinnitus

Hazel: Thank you for that clarification, that helps. But I also want to get to your own current research. But maybe one last question on this topic: Apart from depression and anxiety, what do you think is the role of stress and what is the pathology of that? I heard something about

glutamate in the brain increasing the chances of tinnitus developing. Can you tell us more about that?

Dr. Rauschecker: Yes, I was getting to the stress earlier and then I thought this is really another topic, and I am glad you bring that up. I think stress is a major risk factor for tinnitus and we don't understand enough about the effects of stress on the brain. There is a selective area of research – and I have been talking to people in that field, because I am hoping that this will be another avenue towards solving the puzzle of tinnitus, and maybe come up with a cure.

If we understand how stress can damage our brains... There is no question about this. Stress can damage your brain and tinnitus could be one symptom of that damage, or ... I wouldn't call it a side effect, because it's a major effect, and it is certainly one of the consequences of stress. I can see that on myself: Usually on weekends my tinnitus is less than during the week, when I have a lot of stress in my job and often I get little sleep. And you know, sleep deprivation is a form of stress of course. So, understanding how stress can actually affect your brain would be major progress. Whether glutamate is involved or not I don't know, but there are definitely effects that have been measured.

Stress can have degenerative effects, can really kill cells, brain cells. The question is the same as for tinnitus. Why are some people more prone to the effects of stress than others? So, in that field – as in depression research – the question now circulates about vulnerability, or the opposite is resilience. Those two terms have now become very, very important terms in neuropsychiatric research. Why are some people getting depressed over a loss of a family member or any other adverse events in their lives and others are not? Others are sad for a while when something like this happens but then they develop defence mechanisms, and after some time of grieving, they get out of this phase and they can lead normal lives again. Whereas the same event might affect somebody else very differently and they might get into deep depression, and it might take them years to get out of this or never get out of this. I think it is the same kind of vulnerability or resilience – depending on your point of view – that is involved in something like tinnitus. And tinnitus is actually just a small example of that. There are many, many more examples of this in our whole brain health.

Hazel: I would love to delve into this further, but I do also want to touch on your own current research. But before we do that, was there anything else you wanted to bring up? Or discuss?

Dr. Rauschecker: I am sure I have forgotten a lot of important details, but people should feel free to contact me if they want to know more about it and I would be happy to answer questions at some point.

Hazel: Great. That is good to know.

49:44 Lack of funding for (cure focused) tinnitus research

Hazel: On your own research, can you describe for the listeners, what is the status quo of your research? What are you currently working on in regard to tinnitus?

Dr. Rauschecker: There are thousands of things I would like to work on and I think we could make progress on in tinnitus. Unfortunately, funding levels of funding agencies are frighteningly low. I don't think they understand the importance of that disorder and how widespread it is and how many people it affects.

I am always shocked how little, for example, the **Department of Defence** or the **Department of Veteran Affairs** here in the United States is doing. Their veterans are the group in society that is most affected by this. They all come back from these armed conflicts that the United States is partly responsible for, in Iraq, Afghanistan. You know that lots of veterans come back and have damaged ears, not only hearing loss but also tinnitus. The VA actually shows in their statistics that tinnitus is the biggest problem, and the number two is hearing loss. According to that they should spend millions and millions and millions on funding research on these disorders, but they don't.

It's very difficult to get funding, and I think it is a fact that everybody in the field feels, that we're not getting noticed enough, that we are not taken seriously enough. And people should complain about this, because we can't pursue our ideas and we can't do the research that we need to do in order to find solutions and ultimately come to a cure. I think it is possible to get to that point and we have clear objectives of what we want to do, and we want to do more, so we can finally get to a cure of this disorder.

51:52 Dr. Rauschecker's current and planned research – the importance of animal models

Dr. Rauschecker: Having said that, the highest priority that we give is two-fold: 1) I think there is more imaging studies we can do in humans, and connectivity studies is what everybody is doing now, and it is easy to do now, and what this reveals is that there are connectivity changes in the auditory system and the limbic system. That is not so surprising after all we know and what I said. 2) But I think the real breakthrough will come from animal models. I talked about the various transmitters, dopamine, serotonin, I mentioned glutamate and GABA may also play a role. All these things can only be revealed in animal studies. We can't open a human skull and look for these transmitters. There is a little bit of imaging we can do to identify transmitter systems, but actual work has to be done in animal studies.

And the only [relevant] thing I've seen in my whole career is these rodent studies – and they are fighting over what paradigm is better than the other. I think the rodent model is not sufficient in this case, as I described from my own studies, and I think this is where everybody would agree: There are higher brain structures involved – whether you call them gating structures or something else – there is no question that the pre-frontal cortex and the striatum are involved in tinnitus. And rodents don't have much of a pre-frontal cortex. It's a cognitive disorder, in our definition, so the little bit of cognition that rats have is not a good model for these kinds of higher human cognitive disorders like tinnitus or depression.

I think a paradigm shift has to happen, where we use non-human primates, because they are like us in that they have these gating systems, where they can use their pre-frontal cortexes for executive cognitive control of sensory perception etc. So this is the other thing where we are trying to make progress: We have now a small number of non-human primates that are used for experimental purposes, and approved protocols where we can initially induce tinnitus in these monkeys, like it is done in the rodents.

But ultimately, I think we can even use non-human primates that are sitting around in colonies. There are colonies of non-human primates centres in the United States and elsewhere where monkeys are used for other experimental purposes and they are getting old and my colleague and friend **Gregg Recanzone** reckons one of these primate centres in California, UC Davies, came to me one day and said: "You know, I have all these geriatric monkeys and they are developing hearing loss and I am sure a lot of them have tinnitus too." And so we are planning a study together where we are getting at the transmitter basis and morphological basis of tinnitus, and this will be a whole line of research that I personally find very, very promising. Because it will lead much further than these conventional neural rodent studies that have been done over-and-over again and don't really lead to anything.

55:45 The trouble with raising funds for studies involving primates

Hazel: So, the study you just mentioned, is this the one you are currently fund-raising for?

Dr. Rauschecker: Exactly right. It is especially difficult to get funding for that, because some of the foundations that are funding tinnitus explicitly say they are not funding non-human primate studies. And this is, of course, because they are afraid of animal rights groups that might attack them, which is totally without base. You know, we have to be courageous enough to defend our research if it is done correctly and if it is approved by the **Animal Care and Use Committees**, as in our case there are heroes out there in the field. My colleague and

friend **Nikos Logothetis** in Germany who was a pioneer in doing functional imaging in monkeys has been attacked by animal rights groups for years. He had to go to court and he won in court just a few months ago. The highest court in Germany ruled that he was right and that these animal rights groups have to shut up and give up their resistance, because it is important for our health research to use the correct species which, in this case, and in the case of tinnitus, is also a higher mammal. And if we want to understand the basis of cognitive brain disorders you have to use non-human primates – there is just no way around it.

Hazel: Yes, I would personally agree. I think many tinnitus sufferers would agree.

57:18 How will Dr. Rauschecker's research contribute to a cure?

Hazel: I know many tinnitus sufferers want a cure, but I don't think many of them have yet donated to your fundraiser. Maybe it would help if you could make clearer how this study could potentially lead to a cure.

Dr. Rauschecker: Yes, I would be happy to get into that. I am glad you are raising that sore point, that we need money for this. Like I said, tinnitus in our view is a cognitive brain disorder that needs specific treatment of a brain region that is – for whatever reason, and this is what we want to find out – is damaged or that is underperforming. Let's put it that way. It is therefore unable to keep tinnitus at bay. I think if we are able to understand that mechanism, we are able to cure tinnitus. In order to do that we need to... I think we would start with imaging of non-human primate brains and would ultimately study monkeys that are naturally ageing.

And we are right now, we are working on a diagnosis behavioural study where we can diagnose tinnitus in monkeys. It is partly based on these startle paradigms that have been used in many, many studies in rodents, but there are certain provisions that one has to take in monkeys because they are higher cognitive animals. So we are basing our startle responses on an eye blink response which has been used in humans as a measurement technique, and so far we are making progress. We have one monkey that is successfully responding to this test and we are using aspirin in one of these studies to induce temporary tinnitus. Again, something that has been done in rodents, but I think it is important to, as I said, to do this in a primate, and then ultimately, we will research the transmitter systems in these animals and find what's wrong in a geriatric monkey that is naturally diagnosed as having tinnitus. And then, you know, slowly, step-by-step we will get to the causes of tinnitus and will be able to hopefully reverse this. And once we have a diagnosis, and we have a system how we can diagnose tinnitus at this level, we will also be able to find a treatment and, ultimately, a cure.

1:00:31 Next steps: clinical trials, deep brain stimulation, pharmaceuticals

Hazel: Right, so, if you would successfully complete this study what would be the next steps? Would there be clinical trials for instance?

Dr. Rauschecker: Yes, of course, that would be the next step. Using Parkinson's as a model system, as I described earlier. This was the breakthrough. Once people had these results in non-human primates they were able to do the same thing in humans. You know, then you start a clinical trial based on these experimental data on the non-human primates; then you have justification for starting a clinical trial.

And certainly, there are a few clinical trials out there, **UCSF** has one, **Steven Cheung** and his colleagues in neurosurgery have been doing a clinical trial partly based on our results where they do deep brain stimulation of the striatum, and they have had some success. I talked to Steve just the other day and he said yes, they are enrolling more patients now and they are having encouraging signs. **Deep brain stimulation** is what I also mentioned in my TED Talk and it is one of the promising techniques that is now being used routinely for the treatment of Parkinson's, for example, and now being used more and more for other cognitive brain

disorders. Not everybody will be a candidate for that obviously, you know. We will start with the most severe cases, people who are really desperate about their situation. We would need volunteers for these kinds of treatments but then hopefully, once you understand this system in more detail, drug companies might become interested as well and help us develop drug treatments.

This is what happened in Parkinson's. Now, when we talk to drug companies we usually don't get much interest. This is a field that has become notorious in most drug companies as a huge field where no good theories are prevalent and therefore they don't want to invest. You know, drug companies want to make money, so they first need a good foundation, with a good basis for pharmacological work where they can enter and say: "Well, we will put some money into this clinical trial and see whether this drug might actually work or not."

I think this is what patients want to see, ultimately, is a pill that they can take. You know, it's not quite as easy but I think they want drug treatment for this, like migraine, which often has this similarity being talked about between migraine and tinnitus. It is not exactly the same. It is actually quite different, but there are now migraine treatments that are successful and that are promising so I think we have to get to that stage where we develop some treatments that work even if they are not perfect. And then ultimately, maybe ten years down the road, we might then have a cure. I am really hopeful about this.

1:04:00 Timeframe: When will we have a cure?

Hazel: I am glad you mentioned a time frame, because I was going to ask you: It all does sound very hopeful and promising. But also, still quite a long road ahead?

Dr. Rauschecker: I want to tell an anecdote. You know, when I started to do this research, the TRI (Tinnitus Research Initiative) was founded by a very generous donor. The donor came to one of our first meetings and interviewed each of us one-on-one and asked the crucial question: "How long do you think it will take you to find a cure?" And this was about, I think it was about ten years ago. And I said: "You know, it will take us at least five to ten years." And he said: "Well, you are the only one who is honest with me. The others all told me a couple of years and we will have a cure."

It's not that easy and even I underestimated the complexity when I said this ten years ago. Ten years is up, you know, time is up, and we still haven't found a cure. So, if I now say another ten years it might still be overly optimistic, but we'll see. We will see. I hope we will get there someday.

Hazel: Yeah, yeah, it is speculative but hopeful.

1:05:31 New treatments and lack of collaboration in the research community

Hazel: So, on the topic of cures and treatments: There are currently new treatments actually coming out. One that is very much hyped, I would say – at least within the tinnitus patient community – is this concept of **bi-modal neuromodulation**. What is your view on that as a potential treatment?

Dr. Rauschecker: Can you tell me what that is?

Hazel: Let's see if I can explain this well or not. The idea is to combine an audio stimulus through headphones with a stimulus to, in one case to the trigeminal nerve. There is a company called Neuromod Devices releasing a device that stimulates the trigeminal nerve through the tongue whilst at the same time playing some audio signals. And there is some other research going on, I think by Susan Shore, where it's the same concept but they are stimulating the vagus nerve. And the idea is that somehow this combination of stimulating the auditory pathways through two different channels could induce the right kind of neuroplasticity, and it has shown promising results at least in reducing tinnitus.

Dr. Rauschecker: Well, if it reduces the tinnitus for some people then it's worth pursuing, I think. I don't know much about this. I would rather abstain from voting yes or no on this. It is certainly not anything that would test the gating theory I don't think.

Hazel: I see, so you can't see how that relates to your model?

Dr. Rauschecker: This is another thing that I am a little disappointed about. When we came out with our two neuron papers in 2010/2011 they made a lot of noise. Everybody noticed these papers, and everybody was excited about them, but nobody did anything about them. There are some studies that picked up on that and certainly we continued our work, but people don't listen to each other in the field. Everybody does their own pursuit, and everybody thinks they're right and everybody thinks: "Let's just continue what we've been doing for the last fifty years."

And the fact that we are not making progress shows that we are on the wrong pathway. I think people should listen to each other more, and I would have thought that somebody would have picked this up and run with it, but this hasn't happened. And maybe the same is true for these other approaches that people are making. And the bottom line is that there is not enough funding. If we all had enough money for our research, then we wouldn't have to compete, and we wouldn't have to... If there was a whole institute for tinnitus research, let's say, with tens of millions of dollars of support, then I think we would have a cure in five years, not even just ten years. This would be easy to do but since the funding agencies have other priorities it doesn't happen.

1:08:56 Mobilizing patient communities to advocate for cure research

Hazel: What do you think the patient community could do to help out here?

Dr. Rauschecker: They should make more noise, you know. They should write to the **NIH** and funding agencies and let them know that here is this obvious cross-talk between deafness and mental health. There are these institutes in the United States. I'm not talking about Europe because I am less familiar with the various agencies there. But here, everything gets done within the limits of one discipline. So, deafness has an institute, the **NIDCD**, which does deafness research. And the **Mental Health Institute** does mental health research.

So I went to Deafness and said: "OK let's get this funded." I got one grant from them, but then when I asked to pursue this more mental health related approach that comes out of my gating theory, they said: "That's the domain of the Mental Health Institute." So, I went to the Mental Health Institute and said: "Here I have a paradigm in tinnitus that works, can we get this funded?" And they said: "No, no, tinnitus is the domain of the Deafness Institute."

So, you get the run-around and nobody feels responsible for picking up on a new idea that is inter-disciplinary. This is part of the problem that people are too narrow minded. They do not look beyond their coffee cups, and they do not easily cross boundaries, and I think even within the community this is what happens, that people don't see far enough beyond their own horizons, and that's part of the problem why we don't make enough progress.

Hazel: Yeah, I do recognise that. I think we as a patient community also have to put some real thought into how to overcome these barriers. I don't have any immediate answers, but we should think about it.

Dr. Rauschecker: Hazel, patient communities have a lot of responsibility here, and I think if there was more noise coming from the patient communities, I think it can only help. Because... You know one reaction that I often get right now... Here at my university neuroscience is very strong, and we are trying to set priorities, and I brought up tinnitus as an example disorder multiple times. And they say: "It is not as important as, let's say, Parkinson's or Alzheimer's. You can't die from it, right?" And I say: "Well, you can. You can commit suicide and then you can die from it." But it is always considered a minor disorder that doesn't get the attention that it deserves. So, I think if patients pointed out how they suffer and how they really are fed up with the lack of funding, it would really help to get their attention.

Hazel: Yeah, that's a really good point, and I recognise that as a big frustration in the tinnitus community; this lack of recognition and the sense that tinnitus is not being taken seriously enough. And, as you said, some people take their lives over tinnitus, so I think that is serious enough. But, at the same time, working as a volunteer for Tinnitus Hub, we are always trying to get patients engaged and taking part in campaigns and it is so hard to mobilise the community itself.

Dr. Rauschecker: I think that is part of the disorder.

Hazel: We'll keep trying and trying and pushing.....

Dr. Rauschecker: You know that people get depressed about it, and depression is the opposite of what you need. You need revolts and not resigning. People resign over it and say: "Well that's how it is." And this is actually what doctors tell them.

Hazel: Yeah....

Dr. Rauschecker: You know, this is the common response of the ENT doctor you go to as a tinnitus patient. They say: "Oh well, you just have to get used to it, get over it. It's ok, it isn't going to kill you." Isn't that what you've been told?

Hazel: Absolutely, yes. That is what almost everyone hears from their doctors. And even when people are not able to accept or resign to it, there is still, as I said, this kind of apathy, this lack of... People like to complain of course on Tinnitus Talk or other online forums, but not beyond. Just to each other, but that doesn't achieve anything, right? So, there is this sense of apathy that can be quite frustrating sometimes. But it is interesting to hear from you that this may be part of the condition.

Dr. Rauschecker: Yes, I just realised that myself.

Hazel: I never really thought of it that way, but of course it makes total sense.

1:14:30 Ideas for public awareness raising

Hazel: About awareness raising: Do you have any plans to raise more awareness, as you did with your TED Talk for instance? This was a great move and got nearly half a million views, so that's not nothing. Do you have any plans like that, or is there anything we can help you with in that department?

Dr. Rauschecker: I don't think there's another TED Talk on the horizon, although it was very well received, and the organisers were extremely interested and all that. But other venues like this might be appropriate.

The TRI is a good conference and they do invite, as far as I know, lay people and funding agencies. And there have been other conferences that I have been to where I have had interactions with patients at least, and this is always very fruitful, I find, where patients come to me and say: "You hit the nail on the head. This is exactly how I feel about tinnitus." And of course, this is where my own [tinnitus] experience comes in.

But to get this out and make it more public is a different job. I think if you want to try this and organise specific lectures it might be a great idea. I don't have any specific suggestions how to tackle it. I mean, there is the AAAS Meeting. These are broadly-based meetings – Are you familiar with AAAS? The **American Association of Advancement of Sciences**, basically the same organisation that runs the journal Science.

Hazel: No, actually.

Dr. Rauschecker: They have these lecture societies for neurosciences and have public lectures once a year. Venues like this might be interested in raising awareness. I think you are doing such a great job with your program, and I will leave that domain up to you, to find other organisations that team up with you and...

Hazel: Yeah thanks! That's a good tip, we'll follow up on that one.

1:17:00 Dr. Rauschecker's fundraiser: How will he keep donors updated?

Hazel: So, to start to wrap up, obviously you are raising funding for the animal study you described. I would encourage any listener to check it out and if they can, to donate. Can you tell us how you plan to keep donors updated on your research progress along the way?

Dr. Rauschecker: Our philanthropy department, **Fiona Zhu**, she is certainly planning to do that and keep the donors updated on what happens. We keep books on what comes in and we also keep books on what goes out and what it is used for. Right now, this is a very modest amount that is on the account and we haven't even started spending the money yet, as we are waiting for bigger donations. Every dollar does count of course, and we are writing grants to other agencies. Something will go out next week, in fact. The **Hearing Health Foundation** is definitely interested in tinnitus and there are other organisations that I have been funded by before (e.g. the **American Tinnitus Association**) and which we will go back to. If the expectation is for us to write an annual report, as one does for every other funding agency, we can do that as well.

I have to say; non-human primate research is usually slow. You only have a small number of animals available that you can work with. You have to train them. That's why the rat work is so much easier to do because you can use hundreds of animals at a time, which you can't in our field. But I think once we have access to these primate centres as we are planning to...

And **Gregg Recanzone** is maybe someone you should ask to interview at some point; he can certainly add another angle. He has done other work, you know measuring brain stem potential in other primates and is very knowledgeable and very interested in tinnitus as well. He is not as explicitly visible in the tinnitus field, but I think we need to bring other auditory researchers into the field, as well as people from mood disorder fields.

I think we need to create a new field for ourselves. The **TRI** was attempting to do that, but I think we need to go further. I think maybe these fundraising campaigns are a good way to do that. We should not only bring patients to the table, which is important of course, but we should also bring this to the awareness of the agencies and I see that as a central problem there.

1:20:19 Closing remarks and answering follow-up questions

Hazel: I think that is a great call to action and a good note to end on. Unless there was anything else maybe, Josef, that you wanted to convey?

Dr. Rauschecker: Well I think we've covered a lot of topics, Hazel, and I can't think of anything right now.

Hazel: Indeed.

Dr. Rauschecker: I would be happy, as I said at the beginning, to answer questions. I do get a lot of emails, especially after the TED Talk I got thousands of emails, and they are still coming in. I can't answer every one of them, but I have a whole archive of these emails and I am trying to be as diligent as possible in answering specific questions, and I am also certainly glad to give encouragement to say to tinnitus sufferers that we are on the right track.

Hazel: Well, what we can do for you is centralise and collect questions for you and send them to you all at once so that you are not bombarded by emails.

So, Josef, I would like to thank you so much for your time. This has been certainly very enlightening and inspiring for me personally, and I am sure for the listeners as well, and I also want to thank you for your passion and dedication for tinnitus research. It is very much appreciated by the patient community.

Dr. Rauschecker: This is certainly one of the most complex problems I have ever been working on in my life, and I am not going to give up looking for a cure and we are hoping to bring this to a successful conclusion.

Thank you very much.

1:22:27 Outro by Jack Straw

Sean, aka Jack Straw: And there we go everyone, a fantastic interview with Dr. Rauschecker by Hazel. I just want to thank Dr. Rauschecker again for giving his time to do this interview. I know that he's a very busy guy, and trust me, we are the last people that want to slow him down in his research! So, I just want to thank him again for being so generous.

That's about going to conclude it for this episode of **Tinnitus Talk**, but we got a lot of stuff coming up in future that we know you guys will enjoy; we've got interviews, a lot of things that we're excited about to present to you. So please stay tuned and join us on the next episode of **Tinnitus Talk**.