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00:00:00,000 --> 00:00:27,000
I would like to talk with you about a medical disorder that is incredibly common and yet it gets often underestimated,

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00:00:27,000 --> 00:00:36,000
as one of our former presidents would have said, in its impact on our psychology of the patients.

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00:00:36,000 --> 00:00:41,000
The patients really suffer from it and it's very pervasive.

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00:00:41,000 --> 00:00:44,000
About 50 million Americans suffer from it.

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00:00:44,000 --> 00:00:50,000
I bet many of you in the audience will have friends or family that suffer from it.

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00:00:50,000 --> 00:00:55,000
What I'm talking about is tinnitus or tinnitus, the ringing in the ears.

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00:00:55,000 --> 00:01:04,000
It's often depicted in this painting by Edvard Munch, although we don't know for sure whether he actually had tinnitus himself.

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00:01:04,000 --> 00:01:16,000
But the person in the painting is sort of covering his or her ears and it doesn't help because the ringing is actually generated in the brain.

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00:01:16,000 --> 00:01:20,000
It's not a real sound that is there that the person hears. It's a phantom sound.

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00:01:20,000 --> 00:01:25,000
So we often talk about it as ringing in the brain rather than ringing in the ears.

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00:01:25,000 --> 00:01:33,000
And of those 50 million Americans that suffer from it, about 10 million of them really suffer very badly.

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00:01:33,000 --> 00:01:39,000
They go to the extent that they have depression and suicidal thoughts.

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00:01:39,000 --> 00:01:45,000
And I get emails every day from patients that are asking, is there not a cure?

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00:01:45,000 --> 00:01:48,000
And there is no cure, unfortunately, at this point.

00:01:48,000 --> 00:01:55,000
And part of our research is aiming for that, of course, that we're trying to find ways to help these patients.

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00:01:55,000 --> 00:02:02,000
And I can play some examples for you of what this sounds like.

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00:02:02,000 --> 00:02:05,000
This is just a pure tone of single frequency. It's relatively rare.

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00:02:05,000 --> 00:02:08,000
Usually tinnitus sounds more like the next one.

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00:02:08,000 --> 00:02:19,000
You can imagine how annoying that is if you hear that all the time in one of your ears or both of your ears.

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00:02:19,000 --> 00:02:23,000
You can't turn it off. You can't run away from it. It's always there.

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00:02:23,000 --> 00:02:29,000
Sometimes you get this more sophisticated cricket sound that you hear.

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00:02:29,000 --> 00:02:31,000
So people suffer from it.

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00:02:31,000 --> 00:02:36,000
The groups that are more affected or at risk than others.

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00:02:36,000 --> 00:02:42,000
Musicians get it surprisingly often because they are exposed to louder sounds that they realize.

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00:02:42,000 --> 00:02:46,000
I once remember being at the Kennedy Center in Washington DC, where we live,

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00:02:46,000 --> 00:02:54,000
and went to a concert there, an orchestra symphony concert by the National Symphony.

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00:02:54,000 --> 00:02:58,000
They played Shostakovich's War Symphony, very loud, of course.

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00:02:58,000 --> 00:03:05,000
And one of the violinists in the first or second row was sitting right in front of the trombones behind her.

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00:03:05,000 --> 00:03:09,000
And the trombone was sort of blowing right into her ear.

00:03:09,000 --> 00:03:13,000
And she was reflexively covering her ears to protect herself.

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00:03:13,000 --> 00:03:15,000
This is actually the right reaction.

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00:03:15,000 --> 00:03:26,000
You have to avoid loud noises in order to avoid getting hair cell damage and then hearing loss and ultimately tinnitus.

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00:03:26,000 --> 00:03:30,000
So loud noise exposure is certainly one of the biggest risks.

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00:03:30,000 --> 00:03:32,000
And then you take a group like construction workers.

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00:03:32,000 --> 00:03:36,000
If they don't wear hearing protection, that can be very risky.

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00:03:36,000 --> 00:03:41,000
And the group most at risk are our war veterans, of course.

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00:03:41,000 --> 00:03:49,000
They are constantly exposed to artillery fire, to bomb explosives, and so on.

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00:03:49,000 --> 00:03:54,000
In addition, this is a very important factor, which I want to stress in this presentation.

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00:03:54,000 --> 00:03:57,000
Stress is a very important factor.

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00:03:57,000 --> 00:04:00,000
So it's not just the loud noise exposure that can give you tinnitus.

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00:04:00,000 --> 00:04:03,000
It actually doesn't always do that.

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00:04:03,000 --> 00:04:10,000
But if it combines with a stressful situation, this is the most likely scenario where you end up getting tinnitus.

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00:04:10,000 --> 00:04:18,000
So our veterans are much more likely to come home from the battlefield with tinnitus.

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00:04:18,000 --> 00:04:27,000

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00:04:27,000 --> 00:04:30,000
Hearing loss is the second most frequent one.

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00:04:30,000 --> 00:04:36,000
Tinnitus has often been compared with other phantom sensations like phantom limb pain, which you might have heard about.

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00:04:36,000 --> 00:04:46,000
In this case, somebody misses a limb because of an accident or an explosion that damaged his arm or her leg.

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00:04:46,000 --> 00:04:48,000
And it's a very similar thing.

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00:04:48,000 --> 00:04:51,000
In this case, again, the brain is the cause for this.

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00:04:51,000 --> 00:04:58,000
Even though the leg may be missing, the neurons in the brain that represent the brain are still there and are firing along.

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00:04:58,000 --> 00:05:05,000
And on occasions, the person might get the impression that his leg is still there and you can actually feel pain in that leg.

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00:05:05,000 --> 00:05:13,000
And animal experiments have shown, that's shown on the right of that slide here, that this is in fact what's happening.

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00:05:13,000 --> 00:05:24,000
In monkeys that have lost a hand, for example, the hand representation gets filled in with input from the face representation, which is right next to it.

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00:05:24,000 --> 00:05:40,000
And Ramachandran, then a neuroscientist in California, did studies on amputees where he showed that if you touch the face of an amputee, they actually feel their phantom hand in this case more frequently than not.

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So there's a profound reorganization going on in the brain, both in phantom limb and in tinnitus, which is the equivalent in the auditory domain.

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And people have referred to this often as maladaptive plasticity.

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We are learning, this is plasticity.

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00:06:01,000 --> 00:06:04,000
Memory is kind of a form of plasticity.

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00:06:04,000 --> 00:06:07,000
So we associate this with an adaptive function.

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00:06:07,000 --> 00:06:10,000
But in this case, is it really adaptive?

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I would think so.

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00:06:11,000 --> 00:06:18,000
It's not necessarily maladaptive because the brain has set out a plan how to deal with these kinds of situations.

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00:06:18,000 --> 00:06:25,000
So if you have loud noise exposure, you lose, you kill some of your hair cells in the inner ear and they can't be replaced.

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00:06:25,000 --> 00:06:26,000
They don't grow back.

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00:06:26,000 --> 00:06:30,000
So what the brain does, it kind of fills in that gap.

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00:06:30,000 --> 00:06:33,000
Nature doesn't like gaps.

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00:06:33,000 --> 00:06:44,000
So the gap is filled in with neurons that normally respond to other frequencies, like on the left or right of that gap.

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00:06:44,000 --> 00:06:46,000
Another example is the blind spot in your eye.

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You all know we have a blind spot in our retina where there are no photoreceptors.

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00:06:57,000 --> 00:07:03,000
We don't see but we don't notice that hole because of the same mechanism, the brain fills in that hole.

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00:07:03,000 --> 00:07:09,000
And the same thing happens, we call this lesion-induced plasticity, the same thing happens in tinnitus.

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00:07:09,000 --> 00:07:11,000
So it is per se an adaptive mechanism.

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00:07:11,000 --> 00:07:20,000
But it has an unintended side effect, this hyperactivity that I've been talking about that we can actually visualize with fMRI, for example.

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00:07:20,000 --> 00:07:25,000
And then the next step is missing in tinnitus patients.

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00:07:25,000 --> 00:07:27,000
Normally the brain is even more clever.

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00:07:27,000 --> 00:07:30,000
It realizes there is this internal noise being generated.

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00:07:30,000 --> 00:07:36,000
So it puts its executive sentence in play and they suppress that noise.

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00:07:36,000 --> 00:07:41,000
So most people actually, even after extensive loud noise exposure, don't get tinnitus.

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00:07:41,000 --> 00:07:44,000
You might have hearing loss but you don't end up with tinnitus.

82
00:07:44,000 --> 00:07:49,000
You go to a loud noise concert, for example, a loud rock concert, and you have tinnitus maybe the next day.

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00:07:49,000 --> 00:07:51,000
But then it goes away after a few days.

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00:07:51,000 --> 00:07:55,000
So many people have just temporary tinnitus which gets repaired by the brain.

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00:07:55,000 --> 00:07:57,000
There are mechanisms for that.

86

chronic tinnitus patients.

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00:08:04,000 --> 00:08:14,000
So in the next few slides I'll show you the brain and how it is organized, how it reacts to these events and these situations.

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00:08:14,000 --> 00:08:20,000
Here is the brain as a whole and you see the auditory cortex somewhere in the middle there.

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00:08:20,000 --> 00:08:22,000
It's been exposed.

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00:08:22,000 --> 00:08:24,000
And this is just a drawing.

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00:08:24,000 --> 00:08:30,000
You see the tonotopic map, how the different frequencies are laid out along the auditory cortex.

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And you see how normally this is pretty regular.

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00:08:34,000 --> 00:08:36,000
All the frequencies are equally spaced.

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00:08:36,000 --> 00:08:42,000
But after you lose that yellow region there, then the green and the orange region move in.

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00:08:42,000 --> 00:08:49,000
And they are the ones that are over-represented and give you the tinnitus noise, the tinnitus signal.

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00:08:49,000 --> 00:08:51,000
So now we have a real picture.

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00:08:51,000 --> 00:08:59,000
This is an old research scanner at NIH where some of these techniques have actually been established.

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00:08:59,000 --> 00:09:06,000
Now you can do this with any MRI scanner that you've probably seen and been in yourself.

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00:09:06,000 --> 00:09:12,000
And we can visualize the auditory cortex in normal controls without tinnitus.

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00:09:12,000 --> 00:09:15,000
You see a nice activation in the auditory cortex.

00:09:15,000 --> 00:09:20,000
And in patients that constantly have tinnitus, this activation is doubled or tripled.

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00:09:20,000 --> 00:09:22,000
It's very significant to increase.

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00:09:22,000 --> 00:09:26,000
So this is the physical realization of what people actually perceive.

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And, but this is not the whole story.

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00:09:30,000 --> 00:09:38,000
The rest of the talk will try to convince you that this is not, tinnitus is not just an auditory disorder.

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00:09:38,000 --> 00:09:40,000
It is more than that.

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00:09:40,000 --> 00:09:45,000
This has to do with the higher brain functions in the frontal cortex and the limbic system.

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And if you think about it, there's good reason to assume that it's more than an auditory disorder.

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Because not everyone, as I said, ends up getting tinnitus even if you have a hearing loss and have suffered from loud noise exposures many times.

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A lot of people only have intermittent tinnitus.

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If you're like me, you often have stressful situations like a deadline that you have to meet.

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You're working very hard.

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00:10:10,000 --> 00:10:13,000
You get less sleep during that period.

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00:10:13,000 --> 00:10:17,000
And then your tinnitus suddenly appears.

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00:10:17,000 --> 00:10:22,000

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00:10:22,000 --> 00:10:26,000
Then you submit the grant or the project that you've been working on.

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00:10:26,000 --> 00:10:27,000
You're finished.

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00:10:27,000 --> 00:10:28,000
You have a good feeling.

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00:10:28,000 --> 00:10:29,000
You get a good night's sleep.

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00:10:29,000 --> 00:10:31,000
Next day the tinnitus is gone.

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00:10:31,000 --> 00:10:33,000
So that shows you that it's not just auditory.

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There's something regulatory higher up in the brain that can normally take care of this.

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00:10:40,000 --> 00:10:45,000
And there's also comorbidity with depression.

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If you feel bad and you have sort of a...

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00:10:48,000 --> 00:10:55,000
If you're sad or if you're stressed out, then your tinnitus is much more likely to come up and get worse.

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So there's clear comorbidity with these kinds of mechanisms, which we refer to often as the limbic system.

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So on the left, the blue region is the auditory system.

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00:11:07,000 --> 00:11:11,000
Every sensory system has its representation in the brain.

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00:11:11,000 --> 00:11:17,000
And then in the frontal cortex, sort of in the front part of the brain, there's the screen system,

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00:11:22,000 --> 00:11:27,000
And it has some very well-defined building blocks in there, which I'll show you in a minute.

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The ventromedial prefrontal cortex, the nucleus accumbens, they all play their role.

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00:11:31,000 --> 00:11:39,000
And they interact with the sensory systems and kind of are able like an operating system in a way in a computer

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00:11:39,000 --> 00:11:50,000
to emphasize or deemphasize what you hear, what you see, and sort of give you the actual percept, experience of your daily lives.

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00:11:50,000 --> 00:11:58,000
So the upshot of all that is that tinnitus as a phantom sensation depends on three things.

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First of all, in most cases, there is a peripheral auditory lesion. There's no way around that.

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Some people say there is tinnitus without hearing loss, but it's very, very rare.

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00:12:09,000 --> 00:12:15,000
It may happen sometimes with accidents. But in regular cases, there's a lesion there.

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00:12:15,000 --> 00:12:20,000
Then there is central auditory reorganization, as I've shown you with the fMRI.

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00:12:20,000 --> 00:12:24,000
And then there's this non-auditory gating system. And the rest of the talk is only about this.

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So we found, about ten years ago, we had a crucial finding that was, again, a brain imaging study

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that we did in collaboration with the German MIT, as you just said in the introduction in Munich.

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And we found that in tinnitus patients, there's a very significant shrinkage in one region.

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We call it a volume decrease because the MRIs determine the volume of a part of the brain, of the brain tissue.

00:12:51,000 --> 00:13:00,000
And this was in the ventromedial prefrontal cortex, which normally is there for the perception of unpleasant sounds, say.

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There was a study before that that showed if we hear unpleasant sounds, the same region lights up.

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00:13:06,000 --> 00:13:13,000
So it makes sense that this region was affected, but we didn't know at the time how crucial it was.

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Another finding that helped us understand what was going on is that this region in the ventral striatum,

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00:13:21,000 --> 00:13:24,000
in the basal ganglia, right in the middle, you see this red spot there.

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00:13:24,000 --> 00:13:32,000
This is called the nucleus accumbens. It's a small center that regulates our emotions.

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00:13:32,000 --> 00:13:38,000
It's often been called the pleasure center. It's actually involved in giving you addictions.

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00:13:38,000 --> 00:13:43,000
It has all kinds of roles in terms of emotional regulation.

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And surprisingly, this region was highly hyperactive.

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00:13:47,000 --> 00:13:50,000
This was increased in its activity in tinnitus patients.

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A very, very significant effect, as you can see on the right, if you understand statistics.

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So those two regions together form an internal noise cancellation system, is what we figured.

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00:14:02,000 --> 00:14:07,000
You've all had noise cancellation headphones on the airplane.

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And what this does is it doesn't make the...

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00:14:15,000 --> 00:14:19,000
But the system adds another form of noise to that signal.

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And that's, you know, the negative form of the original noise.

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00:14:22,000 --> 00:14:24,000
And that cancels out the original noise.

163
00:14:24,000 --> 00:14:29,000
And therefore you don't hear anything or you get sort of much milder effect.

164
00:14:29,000 --> 00:14:35,000
And that system normally, with the red box there, inhibits the internal noise signal.

165
00:14:35,000 --> 00:14:37,000
And you don't have tinnitus.

166
00:14:37,000 --> 00:14:40,000
But if that system is broken, then you end up having tinnitus.

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00:14:40,000 --> 00:14:47,000
So here in the close-up, you see that the nucleus accumbens is part of that evaluation system.

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00:14:47,000 --> 00:14:50,000
And the medial prefrontal cortex does the volume control.

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00:14:50,000 --> 00:14:54,000
It turns down the gain when the nucleus accumbens tells it so.

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00:14:54,000 --> 00:14:57,000
And then together, this works or it doesn't work.

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00:14:57,000 --> 00:14:59,000
So where do we go from here?

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00:14:59,000 --> 00:15:02,000
We have hints from this last slide.

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00:15:02,000 --> 00:15:05,000
You see the boxes on the right. There's dopamine and serotonin.

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00:15:05,000 --> 00:15:11,000

175
00:15:11,000 --> 00:15:15,000
If they're low, then you get depression, for example, and you get tinnitus.

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00:15:15,000 --> 00:15:20,000
So this may be opening an avenue for drug treatment in the long term.

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00:15:20,000 --> 00:15:26,000
But there's another form of treatment that we might be able to use in the future.

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00:15:26,000 --> 00:15:28,000
This is called deep brain stimulation.

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00:15:28,000 --> 00:15:32,000
And it's been established for Parkinson's disease and major depression.

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00:15:32,000 --> 00:15:39,000
And I'll show you in a brief video the patient that actually undergoes this treatment.

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00:15:39,000 --> 00:15:41,000
It may be shocking for you at first.

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00:15:41,000 --> 00:15:46,000
But it's become routine in many disorders.

183
00:15:46,000 --> 00:15:48,000
And the patient actually lies there awake.

184
00:15:48,000 --> 00:15:50,000
She's slightly sedated.

185
00:15:50,000 --> 00:15:54,000
She's able to talk to the surgeon and report her feelings.

186
00:15:54,000 --> 00:15:58,000
Does it have any mental qualities to it or is it still mostly physical?

187
00:15:58,000 --> 00:16:09,000
Actually at that time it kind of was, there was a lighterness of my moods that went with the lighterness of my feeling.

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00:16:13,000 --> 00:16:15,000
The transformation was traumatic.

189

190
00:16:22,000 --> 00:16:26,000
Happiness felt like a possibility again.

191
00:16:26,000 --> 00:16:32,000
So I hope I've been able to tell you that we're getting closer to understanding what tinnitus is.

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00:16:32,000 --> 00:16:40,000
And with these considerations that I've just said, we may be able to ultimately find a cure.

193
00:16:40,000 --> 00:16:43,000
And I may be able to respond to these emails that I'm getting and saying,

194
00:16:43,000 --> 00:16:45,000
Well, help is on the way.

195
00:16:45,000 --> 00:16:47,000
We're not there yet, but help is on the way.

196
00:16:47,000 --> 00:16:49,000
We'll have something for you soon.

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00:16:49,000 --> 00:16:50,000
Thank you.

198
00:16:50,000 --> 00:16:51,000
Thank you.

199
00:16:51,000 --> 00:16:52,000
Thank you, Dr. Yusuf.

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00:16:52,000 --> 00:16:53,000
One quick question for you before you leave the stage.

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00:16:53,000 --> 00:17:11,000
So with the leaps and bounds of research in brain research, what do you see as the impact going forward for society?

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00:17:11,000 --> 00:17:15,000
Oh, I think it's immeasurable.

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00:17:15,000 --> 00:17:18,000
I think the impacts for society are incredible.

Because our brain is us.

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00:17:20,000 --> 00:17:25,000
You know, we have to realize that this is where we feel, where we dream, where we plan.

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00:17:25,000 --> 00:17:30,000
So the more we understand about the brain, we understand about human beings as such and about humanity.

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00:17:30,000 --> 00:17:32,000
And I think this is how I look at it.

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00:17:32,000 --> 00:17:33,000
Yeah.

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00:17:33,000 --> 00:17:34,000
Thank you.

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00:17:34,000 --> 00:17:42,000
And if we have disorders like this one, which seem so intractable, we first have to understand the brain and then we can maybe help people.

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00:17:42,000 --> 00:17:47,000
So I think it has a lot of deep impact for us as a society.

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00:17:47,000 --> 00:17:51,000
Well, thank you so much for sharing your knowledge with us today.

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00:17:51,000 --> 00:17:52,000
Thank you.