HHF Research Webinar Transcript
Auditory Gating in Tinnitus | Monday, June 26, 2023, 5pm ET
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ANIL K. LALWANI - Hello, and welcome to our Hearing Health Foundation Research Webinar. I'm Dr. Anil Lalwani, and I appreciate you joining us today. This evening has a live captioner and is being recorded. You can enable closed captions by clicking the CC button in the toolbar at the bottom of your screen. Now, if you need any other assistance using Zoom, please follow the link to the technical guide shared in the chat. Now, today's topic is an interesting one. It is auditory gating in tinnitus. As you know, tinnitus is hearing a sound without an external source. Now, although the exact underlying causes of tinnitus are debated, one mechanism may be decreased central inhibition. Now, our presenter, Dr. Julia Campbell, will explain more shortly.

By way of introduction, my name is Dr. Anil Lalwani. I'm a professor and vice chairman for research in the Department of Otolaryngology Head and Neck Surgery, or ENT, as well as the Associate Dean for Student Research at the Columbia University Vagelos College of Physicians and Surgeons in New York. I'm also a board member at Hearing Health Foundation, where I oversee the Emerging Research Grants program, affectionately known as ERG.

The ERG is a competitive program that awards funds to researchers conducting cutting edge hearing and balanced research. These grants supported many leaders in our field to become successful scientists, including our illustrious speaker today. I, too, benefited from this grant and it was really crucial in my career.

Dr. Julia Campbell, who's our speaker, is an Assistant Professor of Communication Sciences and Disorders in the Central Sensory Processes Laboratory at the University of Texas at Austin, where it is 108 degrees today. And she's a 2016 ERG scientist. Starting with this grant, which was generously funded by the Les Paul Foundation, she has been investigating the role of auditory gating in tinnitus patients. In both those with typical hearing and also those with typical hearing, but difficulty hearing speech and noise. She will share her team's research, including the goal of evaluating the clinical utility of gating as a measure of tentative dose in patients with varying degree of hearing loss.

Now that may sound Greek to you, but I'm sure Dr. Campbell is going to explain everything to us in just a moment. Now, the ERG program that provides seed money to scientists such as Dr. Campbell, myself, and others who are just starting who are just starting out in the field of research, is only possible through the generosity of supporters like you. If you'd like to support our work on hearing loss, tinnitus, and related conditions, you can do so today at hhf.org/donate. Now, we'll move to Dr. Campbell's presentation. Please ask any questions to the Question and Answers box linked at the bottom of the screen, and then we'll try to answer following the presentation. Thank you again for joining us, Dr. Campbell.

JULIA CAMPBELL - Just sharing. All right, can you see my screen? Great. Okay, so as previously said, I'm Dr. Julia Campbell. I'm very excited to be here and thankful for you all having me. And I'm going to be presenting on auditory gating in tinnitus. I thought I would start off with some basic statistics. Tinnitus afflicts about 30% of adults with hearing loss. However, it's also present in about 15 to 25% of adults with normal hearing. So that might be a large number to a few of you.

And anecdotally, the clinicians I've spoken with at different meetings have said that this is a growing population they're seeing in their clinics is adults with great hearing, but really struggling with tinnitus. And they really have their hands tied in terms of patient care because we usually just manage straight hearing loss, and we can help tinnitus sometimes with hearing aids. We'll get to this a little bit later in the talk, but we definitely were interested in looking at this population. We know very well that tinnitus

has no objective clinical measure. This means that we have no test that we can give that tells us somebody has tinnitus or how severe it is or how loud it is without the patient themselves telling us.

Now, this can be a problem for a few reasons. It can be a big problem in guiding targeted research and intervention. For example, one patient with tinnitus might have a deficit in the central nervous system, say in the brainstem, but another patient with tinnitus might have a deficit related to their tinnitus in higher order areas of the brain. And we have no way clinically of looking at where in the central nervous system this tinnitus is arising. So we can't target our treatment, and that's a big reason why there's no cure. We have no information to help us give an appropriate management or intervention plan.

This is also related to the heterogeneity of tinnitus, meaning that there's different types of tinnitus and different cortical or brain networks have been shown to be related to different aspects of tinnitus as well. Many, many different mechanisms have been proposed to underlie tinnitus. A very popular hypothesis is that tinnitus occurs because there's decreased central inhibition, and that is arising from a peripheral injury. What do I mean by that? There's hearing loss, there's damage to the cochlea or the inner ear due to noise, trauma, or ototoxic medications, or just genetics.

That injury causes a cascade that affects inhibition. What is inhibition? Inhibition is the ability of the central nervous system to suppress information that it doesn't want to get through or interfere with conscious perception. Let's take a quick look at a visual that describes this mechanism or why inhibition might be decreased when you have a hearing loss.

Here, we have our little visual. I want you to imagine that this black arrow represents the cochlea or the inner ear. At the base of the inner ear, we encode high frequencies. As we move up to the apex, we encode low frequencies. And then on the vertical axis here, I'm showing you the peripheral hearing system or the cochlea, the inner ear, all the way up through the central or higher orders of the nervous system. These circles represent neurons. And then these arrows are connections between neurons. We have red arrows that represent excitation. That just means that when one neuron is activated, it's going to get excited and send a signal up to the next, that says, "Fire," okay? Then we have our blue arrows, which represent inhibition. And you'll notice that these arrows are going laterally or to neighboring neurons.

This is a really cool aspect of the nervous system, and it's called lateral inhibition. And it's that when one neuron or group of neurons gets excited, they're going to send suppression or inhibition to neighboring neurons saying, "Don't fire." And you can imagine that this will boost that excitatory signal.

Let's imagine that there's hearing loss present. Let's say there's a high frequency hearing loss for many reasons that could occur. Due to this high frequency hearing loss our high frequency neurons are not getting incoming auditory signals. What that's going to result in, according to this model, is a decrease in activation of the neurons in this relay. So decreased activation, we don't have an incoming signal that's excitatory.

However, at the same time, these lateral inhibitory connections are also knocked out. That's going to result in overexcitation of neurons and neuronal networks that are still intact, because now we're not suppressing our neighbors, as well as sending excitatory information. And this overexcitation can then later influence gating areas in the cortex or higher areas of the brain and cause deficits in those areas, meaning we're not filtering out signals that we should be, and that might then be perceived as tinnitus.

What if you have normal hearing? We don't have a cochlear injury that we know about. There are subclinical types of hearing loss that audiologists are not currently capable of measuring in the clinic. But let's say for all intents and purposes, this person has normal hearing. Well, one hypothesized mechanism is that there could still be decreased central inhibition, but now it's due entirely to central dysfunction and not a peripheral injury.

Let's take a look at what that might look like. This area of the brain in blue is called the ventromedial prefrontal cortex, and it's basically right here, and it's an executive center that's involved with gating. So again, a filter. Are we allowing information or are we suppressing it? And several studies in tinnitus have shown that activation of this area is decreased, and that, or deactivation, is related to tinnitus.

Similarly, we have the pregenual anterior cingulate right here, and it is another gating region, again, prefrontal cortex. And we see that deactivation in this area is also related to tinnitus.

Essentially, deactivation of these gating regions results in overactivation of auditory cortex. These areas that are going to send inhibitory signals back down are not doing that inhibitory modulating. And this overexcitation or activation of auditory cortex could result in tinnitus. Because gating, at least in higher order areas of the brain, has been related to tinnitus and found to be related to tinnitus severity, we decided to look or use a measure called sensory gating to look at a very early stage of inhibition. the theory being there are many levels of inhibition in the central system.

Typically, I used to think of inhibition as ignoring information that I didn't want to pay attention to or process. I would only focus on information that I wanted to and ignore the rest, and that's how I thought of inhibition. And that is a type of inhibition, but that involves attention, executive function, your conscious perception. There's a very early stage of inhibition that we do not consciously control. It's automatic. If this really early stage of inhibition is dysfunctional, could it be possible that signals or input are getting in and up to these higher order areas that are then unable to filter out these extraneous signals? And that could be related to tinnitus.

Gating is how we measure this early stage of inhibition, or I should say sensory gating is how we measure it. We measure this function or process by recording cortical auditory evoked potentials, or CAEPs. This is a great measure because you don't need the patient to be involved. It's obligatory or automatic. Basically, we have the patient sit and watch a movie with subtitles, and it's muted, and then we play sounds for them, and that's it. We play sensors on the head and we're able to record electrical activity in the brain arising in response to all these sounds that are being presented. And we average that electrical activity over time, and we get a nice peak response of different levels of the central auditory system. I'll show you what that looks like in the next slide.

The advantages of sensory gating are, again, that it's tapping into this inhibition at a low, low level. This would be a great starting point of many studies, assessing levels of the central auditory system to see how these areas relate to tinnitus and how they interact and how it's going to be individualized. Again, one deficit related to tinnitus in one person might not be the same in another. And so we can't throw the same treatment at all of them. It's just not, it doesn't make sense.

The advantages of this measure are that it's noninvasive. We're just recording electrical activity through sensors on the head. We don't present electrical stimuli. It's very comfortable, it's cost-effective. In other words, it's cheap. We don't have to, all we have to pay for are sensors or electrodes.

It's very nice in comparison to things like fMRI. It has, or could have, a very fast clinical trajectory. What does that mean? There is a huge lag between clinical research findings and those evidence-based practices being implemented in the clinic. Big problem. If gating were to be shown to be a useful measure of tinnitus, our audiologists already have equipment that can measure this. They already have the expertise to do so. They're trained to measure CAEP in graduate school, or should be. And really, it could possibly just take a week of training to implement this in a clinic, and there's a billing code. Great trajectory there.

Let’s start off by looking at what a cortical auditory evoked potential is. This would be an average of electrical activity recorded in response to one sound presented over and over. On the vertical axis, we have amplitude in microvolts. On the horizontal axis, we have time in milliseconds. This line at zero represents when our auditory stimulus is presented. You'll hear me use the term latency, and that's simply the amount of time it takes for a peak to appear after the stimulus is presented. In a cortical auditory evoked potential, sometimes not guaranteed, you'll see a Pa peak. This represents subcortical activity, mainly in the thalamic, thalamus region.

Then, we will have the P50, and this is going to represent activity between the thalamus and the cortex and primary auditory cortex specifically. So neural connections between those areas. We have a third peak that's negative, the N1. This represents connections between primary auditory cortex in the brain and secondary auditory cortex, so, important for relaying sound into meaningful language. It's also been shown to represent auditory attention. It's going to have activation in areas like frontal cortex, which we just looked at.

Then finally, we have the P2 peak, which is not as well understood. It's considered to be the last precognitive peak or the last peak you would see before you have your participant engage in a task or respond to a stimulus. This is going to activate or show activation in auditory cortex, but it's also going to have connections outside of auditory cortex to areas like frontal cortex. This is your basic CAEP.

Now, let's talk about auditory gating specifically. This paradigm is what we use in the lab and could easily be used clinically. It's not that challenging to develop. And instead of just playing one sound at the same rate over and over, we're presenting tonal pairs at a specified rate. Let me explain that. We use a tone, a 250 hertz tone, so low frequency, and it plays for 50 milliseconds, so that's S1, the first tone. Then we have silence for 500 milliseconds, and then we repeat the same tone a second time for 50 milliseconds, and that is S2. This is our tonal pair. We wait then 7,000 milliseconds or seven seconds, and we repeat that tonal pair, and we just do that over and over.

What that results in, and you'll see this looks quite familiar from our CAEP slide, is not one CAEP, but two. We get a CAEP response to the first tone in the pair, and that is this solid black line. And then, we get a CAEP response to the second tone in the pair, and that is this dotted or dashed line. And I hope what you can kind of see right off the bat is that there is a difference in amplitude of the peak responses between the brain's response to the first tone and the brain's response to the second tone. This is an automatic suppression of that second brain response.

What's happening is the brain, without you even being involved, is saying, "Oh, I've already heard this tone. It's not important. I'm going to suppress it or suppress my response to it." And we really see that decrease in amplitude for the P50 peak and the P2 peak. Now, we can quantify this suppression by calculating an amplitude difference index or amplitude ratio. The difference would be taking the amplitude point of the P50 peak here at about, let's say it's 1.75, minus the peak amplitude of the second P50, which is maybe 1.25. Our difference would be 0.5 microvolts.

We could also take a ratio, we could take the amplitude of the second response and divide it by the amplitude of the first. In the literature, both measures or approaches to quantification have been used. The difference measure has been shown to be more sensitive or reflective of robust gating. But traditionally, everyone uses the amplitude ratio. In our lab, we always calculate both.

Let's get to the nitty-gritty. We did this study as an accident. We had a large population of young adults with clinically normal hearing and minimal tinnitus. What do I mean by minimal tinnitus? Very, very low level, not bothersome, but they could tell you if it was one ear or both ears, they could tell you what the pitch was. There was definitely something going on there. We decided to see, "All right, maybe there could be an issue in the gating mechanism. Let's take a look at this population first." It was helpful because we didn't have to control for hearing loss, we didn't have to control for age, and we were really able to look at this physiologic mechanism.

What I'm showing you right now are audiograms, and these are just clinical measures of hearing. On the vertical axis, you have intensity. It's kind of backwards, but very soft sounds are presented first, moving to louder levels. And then we test tones. So low frequency tones to high frequency. Down here, I'm showing you extended high frequencies because we're able to hear up to 20,000 hertz as humans. But in the clinic, we only test up to 8,000 hertz for reasons I won't get into right now.

It's good practice, especially with individuals with normal hearing, to test these extended high frequencies to see if there's a hearing loss there. However, there is no normative data for the extended high frequencies. We just decided to extrapolate from clinical knowledge and say that normal hearing would be designated as hearing below 15 dB HL, and we did that for the high frequencies as well. As you can see, the individuals without tinnitus in the black had great hearing even in these really high frequencies. And the individuals in the red who had tinnitus had almost identical hearing. That group, as a whole, at 16,000 hertz does look to differ a bit, but there was so much variability this difference was not significant.

What did we see between these two groups? Here’s what we got for the no tinnitus group. We did indeed see a significant P50 amplitude suppression of that second brain response. And we also saw a decrease in the latency of the second brain response. Basically, the second brain's response was inhibited, but it was occurring earlier than the first, which makes sense because it had already heard

that stimulus. We also saw a decrease in the N1 latency as well. Again, makes sense because the stimulus had already been processed once.

Now, let's look at our tinnitus group to see what gating differences we might see. Well, it looks to be pretty much the same. We do see significant gating reflected by the P50 peak. We don't see any latency differences, though. This was interesting because this was not what we expected to see. We expected to see more gating in, or no gating in the tinnitus group. On a whim, we ran a correlation to see if there was a relationship between any of these gating indices and tinnitus. And lo and behold, we saw some significant correlations. We saw two of note.

This is showing the tinnitus handicap inventory, which was the clinical measure that we used to document tinnitus severity. You can see that our scores range from zero to 14, which is very minimal. They call this stage one or level one tinnitus severity. And for that Pa peak, we see that as your amplitude difference increases, your tinnitus severity decreases. So as the amplitude difference gets larger, tinnitus severity is less. As the amplitude difference gets smaller or more similar, tinnitus severity is worse. This fit our hypothesis of: All right, as gating gets worse, we see worse tinnitus.

But then, as always happens in my research, we find this unexpected significant correlation showing that as N1, that N1 peak amplitude difference gets larger, so more gating, tinnitus severity increases. And as N1 amplitude difference gets smaller, less gating, tinnitus severity decreases. We're seeing two very different relationships. Now, if you'll remember, the Pa peak comes first. It's very, very low level of auditory processing for us who talk about these cortical areas. And the N1 comes from higher cortical centers. Keep that in the back of your mind as we progress.

Because of these correlations, we decided to do kind of an exploratory analysis and create subgroups. What we did was we calculated the median THI tinnitus severity score for the tinnitus group, and it happened to be six. A score of six. And we separated the tinnitus group and the individuals who had a severity below six and a severity higher than six.

We then looked at the gating responses in these subgroups, and this is really interesting. For our low tinnitus subgroup, we see the same finding that I showed you was present in the entire tinnitus group, typical gating suppression in that P50 peak. But when we look at tinnitus sufferers with a THI above six, we see something very different. We see that the Pa, the second brain response, has increased amplitude above that of the first. So that's what that correlation was telling us was that as Pa gating gets worse, tinnitus is worse. We see no gating through that P50 peak. And here is where we see that N1 peak gating improve. If you can look at the first group again, our N1 amplitude is larger in the second brain response. There wasn't really any gating happening here, but it was fine. It wasn't needed because there was gating happening earlier. As this gating starts to go out, the N1 starts to step in and try to gate as a compensatory function.

Essentially, that was explaining the N1 correlation of gating improving but tinnitus getting worse, right? Let's say, "Why is this interesting?" We've found that sensory inhibition changes after a THI of six. So we have a point of tinnitus severity at which we're starting to see brain changes.

The second really interesting point is that we found that a higher level in the gating system is trying to compensate for deficit early on. We did a statistical model also including extended high frequency thresholds of these gating functions, and found that together, thresholds N1 and Pa gating accounted for close to 50% of the variance in the tinnitus severity for the young adult, which is pretty significant. This could be a mechanism in this population, again, not for everybody, but for maybe a majority of telling us where the dysfunction in the system is happening, and can we target that dysfunction.

Waves are great, but we want to know what's happening in the brain. What's the brain doing? We actually just submitted this study last week. It took way too long to finish. But we did some brain modeling using our EEG information or data to estimate where in the brain these gating responses are occurring. Let's look at our control group first. Normal hearing young adults without tinnitus.

Let me orient you. These are sagittal MRI slices, so this is the model that our responses are constrained to. And these bits of color are showing the estimated areas of activation. So you can see the eye orbits here. This is the front of the head, and this is the back of the head, and then this is the side. All right, so when we did cortical sources for that Pa gating network, we saw activation of

temporal cortex, including auditory cortex, as well as frontal cortex. And this is, nobody's modeled the Pa gating peak before. We didn't have anything to compare it to, but this is consistent with the following peak, what we see. We think it's pretty accurate. That P50 peak, we see a very large continuous gating network with auditory cortex extending all the way to frontal and prefrontal cortex. The P50 gating peak has been modeled by many different groups. We've modeled it in a few different studies, and this is a very typical response, very consistent with the literature. In the N1 peak, we see some temporal activation, some frontal activation, and then we see a lot of prefrontal activation here. Then the P2 peak, very similar to the Pa, we see auditory activation and frontal activation. These are our control networks, all right? We have networks that are associated with inhibiting auditory information that is deemed extraneous. And these networks, again, consistent with the literature, include temporal areas, frontal areas, and prefrontal areas. That's a typical gating network.

Let's look at what's going on in our young adults with tinnitus. All right, so that Pa peak, we do see typical gating regions in frontal and temporal areas. We also see this little guy out here. This is a parietal source, a multisensory area. So just keep that in mind. If we move to the P50, even though the group waveforms were not significantly different, we see a difference in network activation. The tinnitus group is lacking significant frontal and prefrontal gating networks. So that's of interest as well. That N1, we're not seeing that large prefrontal activation that we saw for the control group, but we are seeing these guys, temporal and frontal. And then for the P2, we're seeing very comparable gating networks, which makes sense because the P2 didn't show us anything.

Let's go to those subgroups because I think they're a little more interesting. The tinnitus low group. This is where we still saw normal, or I should say typical gating function, but we do see a decrease in prefrontal or frontal activity. And again, that little parietal source is popping up. This is for the tinnitus low group, less than a THI of six. For the P50, even though we saw the waveforms telling us gating was typical, we see a very different gating network. We do see our typical gating network of temporal and frontal, but then we see this huge extraneous network. We have auditory areas here, and then we even have some visual areas thrown in.

We're seeing some plasticity. This network is changing, it's still working, it's still providing the inhibition necessary, but it's changing. Our N1 looks pretty typical, but remember our control group had a really large activation up here, prefrontal areas, and we don't see that in the tinnitus low group. And then our P2 is boring. It's showing us what our control group showed. This is really interesting because the tinnitus low group is not really significantly different from our control group waveform-wise, but we're seeing these networks change. So the networks are still working, but they're changing.

Let's compare it to our tinnitus high group. Our Pa was that really different gating peak where we saw a huge second brain response that we shouldn't have seen. And now, we can see that the gating network that's showing up is spurious. It's diffused, not connected, and it's showing us, again, that parietal area, all right? For the P50, we don't even see temporal activation or auditory areas at all involved in the network. Instead, we have entirely frontal and parietal areas, and even in the occipital regions. Now, the N1, remember that was our waveform that showed an improvement in gating. And lo and behold, it has the prefrontal region that we saw in the control group. What we're essentially seeing here are changes in gating networks that are maladaptive. They're not helping support gating function, but then we're seeing a compensatory gating response where this network is being pulled in that wasn't needed or wasn't implemented for the low group.

This is maladaptive and this is compensatory. And we see that in the waveform showing us stronger gating. And our P2, I don't even, I shouldn't have even showed it, it's boring. So that was all done in normal hearing, young adults, not much variability there. But what does gating look like in hearing loss? From that model I showed you at the beginning of the talk, we know that inhibition is decreased in hearing loss. It's just a bottom up repercussion of cochlear injury. Would gating pick up on this and would it look the same or different to what we saw in the normal hearing group?

Here, we have audiograms again with 15 dB HL being our cutoff for normal hearing thresholds. Soft sounds up here, louder sounds down here. Our normal hearing adults responded in this range in black is what what they're represented as. And then our hearing loss adults have a high frequency loss that ranges from mild to moderate-severe. This high frequency loss is very typical of individuals you would see in the clinic who were unaware of their hearing loss. Maybe their spouse or their

partner made them come in to get their hearing tested. But it's a very typical early type of hearing loss, not really considered to be severe. And some audiologists might not even aid this type of loss. So let's look at gating in these folks. All right, for our normal hearing group, we see something interesting. We don't see our Pa peak that we saw in the young adult group. There could be many different explanations for that, but we can talk about that after the talk if you all are interested. So here, we see for the P50 peak, there isn't a significant amount of inhibition. It doesn't look like there's gating really present, which was surprising. We didn't expect to see that. Could be a function of age. Everything decreases with age as I'm finding out. So that could be a reason for this. I think it's due to the filter settings we used, but I won't go into that.

So we don't really see any significant gating here, which isn't great. But, it's our control group, so we'll compare to it. Our hearing loss group does look quite a bit different. We see our second brain response for this P50 peak to be quite increased amplitude over the initial brain response. We also see a decrease in gating as compared to the control group for the P2. Now, none of this was statistically significant. It's just a visual trend. When we did correlations, we found that high frequency hearing loss, so this is your vertical axis, the worse that high frequency hearing loss gets compared to the P2 amplitude gating difference. We see that the P2 amplitude gating difference gets larger with less hearing loss. Better gating, less hearing loss. Amplitude gating difference decreases with more hearing loss. Gating gets worse as hearing loss increases. And that same trend was, significant trend was noted for the gating ratio quantification of that P2 peak as well.

Before I go into generators, why is that relationship interesting? There's a couple of reasons. The P2 peak is a very much higher order peak, and we've seen in previous research that that particular peak is related to hearing loss and compensation for hearing loss in brain processing. We start to process things reflected by the P2 in frontal regions of the brain that we normally wouldn't, we start using areas to listen. It might be a reason for listening fatigue. We see this in the P2. We also don't see a relationship between any of the earlier stages of sensory gating: the Pa, the P50, the N1, with this type of decreased inhibition related just to hearing loss. These guys don't have tinnitus. So, that's interesting. Could it be that gating might differentially be able to separate out hearing loss and tinnitus, which we know commonly co-occur? Could you test somebody with hearing loss and tinnitus, and the N1 peak be related to the tinnitus and the P2 peak be related to the hearing loss? A thought.

Let's look at the generators for these gating networks. Now, remember, these folks do not have tinnitus. This is just looking at hearing loss effects. All right, for the normal hearing, we didn't have a Pa peak. We looked at the P50. We see great typical gating network, temporal, frontal, prefrontal. N1, great gating network. We don't see the large prefrontal that we saw in our young adults, but these guys are a little bit older. We see frontal cortex, temporal and auditory areas. P2, remarkably similar to our young adults with auditory and frontal regions.

Let's look at our hearing loss group. Okay, so now for the P50, even though our waveform, our gating indices were not significantly different between groups, we do see a different network being active. We see a temporal network without any frontal or prefrontal activation. So again, some brain plasticity there, even though we didn't see it reflected in the waveforms. Our N1s are pretty similar in terms of networks, a little less frontal activity for the hearing loss group. Remember, our old boring P2 from our young adults didn't show us anything, but here's where it shines. So compared to our control group that had a great temporal and frontal gating network, we barely see, well, we have some auditory here, and then we have fusiform gyrus mainly responding. This, again, would be an example of a maladaptive gating network. It's not supporting the gating function.

What are the summaries of these studies? In subclinical tinnitus, aka tinnitus in normal hearing, there is decreased gating function at an initial early stage, which is then compensated for at a higher stage. And this is supported by a change or plasticity in gating networks that are maladaptive versus compensatory. So maladaptive, they don't support gating function. Compensatory, they do. In hearing loss, gating is also deficient, which we would expect, but at a much later stage, that P2 stage. And this is only supported by similar maladaptive gating networks, all right? so what are the next steps? We want to look and see if gating in tinnitus and hearing loss could be measured or quantified differently. I said it earlier, but I'm wondering if the Pa and N1 peaks might be more useful diagnostically for tinnitus deficits and the P2 peak would be related to hearing loss. If that's the case, these earlier

gating peaks could provide a biomarker for tinnitus severity despite hearing loss. ATA, the American Tinnitus Association, has graciously agreed to support this research study looking at the gating measure in individuals with both tinnitus and hearing loss to see if this could be a biomarker, but also if we could locate an earlier sites of dysfunction related to tinnitus severity that might be helpful for guided intervention.

I just want to thank a few people. I, first of all, want to thank Hearing Health Foundation. This grant was the first grant I got as an Assistant Professor, and none of these studies would've happened without that grant. It was very meaningful to me and my two graduate students, Connor Bean and Ali LaBrec, who are both distinguished audiologists now in Texas and Colorado. It really was the foundation that I could not have done without. And now, our work has been supported by the American Tinnitus Association as an extension of what we've done. We couldn't be more thrilled. And I was so excited that the Les Paul Foundation was the group under Hearing Health Foundation to support us. And I also have to recognize the Texas Speech-Language- Hearing Foundation that has supported this work. These are my undergrads in the CSP lab. Love them so much. This is my PhD student, Dr. Lauren Ralston, who submitted that gating network paper that you'll be seeing soon. And with that, I'm finished.

LALWANI - Well, Dr. Campbell, thank you so much for that engaging talk and a possible new mechanism for both tinnitus-induced gating. We have time for one or two questions that I'm going to ask you now. There are even more specific questions, and I would encourage those attendees, with very specific experimental questions to reach out directly to Dr. Campbell. We're going to take some general questions. The first one is you've sort of introduced a new concept which may be playing a role in tinnitus. How will this research inform and help the development of future tinnitus treatments? Many of our in audience suffer from tinnitus and they're wondering, "Will this have an impact for the patients who are suffering?"

CAMPBELL - Yes, that's the ultimate goal is to help people. We need to better understand what's going on to do that. I'm hoping that we, eventually, will be able to look at different plasticity-inducing therapies to see how that might affect gating. So things like vagal nerve stimulation, pairing that with sound therapy, and seeing if that can affect gating. In the gating literature, there's been some pharmacology showing that different drugs can improve gating because gating is a function of nicotine receptors. I know that some studies have looked at the use of nicotine to improve gating. I think there's a lot of different ways to go with intervention and pairing it. I'd also like to see how our adults with hearing loss, I would like to test them pre-hearing aid fitting and post to see how that might improve gating as well.

LALWANI - And there's a sort very broad and general question. What did you think this changes in gating function may play a role in other disorders, such as hyperacusis, misophonia? Your thoughts about that?

CAMPBELL - I absolutely think it might. It seems to be very related to auditory-specific disorders. There's gating in different modalities, excuse me. There's visual gating, there's somatosensory or touch gating. And we have found worse gating in hearing loss, worse gating in adults with speech perception and noise difficulty. I wouldn't be surprised if it was worse in hyperacusis or misophonia, but I do think there's some nuances of how the gating response will look or be affected, as well as the networks in each of those disorders.

LALWANI - Yeah, I think our last question really, it follows just this comment you made. You noticed that there were gating function changes even prior to measurable hearing loss, though tinnitus was present. Of course, there were changes that were slightly different when hearing loss was present. Do

you think the first group with normal hearing still has peripheral damage? Or do you think central changes can occur in absence of peripheral damage?

CAMPBELL - That's such a good question. I believe you're referring to the phenomenon of hidden hearing loss, which is also called cochlear synaptopathy. But that is where there are deficits in the cochlea or the peripheral nervous system that are underlying auditory processing issues. And currently, clinics don't have a way to measure those deficits. So that's why it's called hidden hearing loss a lot. We did test extended high frequencies, as well as speech perception in noise for that control group in the first study to see if there might be subclinical peripheral issues going on.

I know that speech perception in noise has been shown by several researchers to be indicative of subclinical peripheral injury, excuse me, injury. We didn't see that. We saw varying, within normal limits, function for that group. I wish we had done OAEs [otoacoustic emissions]. We had, Connor Bean, one of my graduate students, did a study in this group that wasn't published looking at OAEs, distortion product OAEs, and found that they had very low or atypical OAEs in the range of 6,000 hertz for the tinnitus group. So I do think OAEs would be very useful as well. And any clinicians working with normal hearing patients should use speech perception and noise, extended high frequencies, and OAEs to really get an idea of what the cochlea is functioning like.

LALWANI - Well, I think with that, we must come to the end because though you didn't hear it, there was a bell at my end that sounds like this and telling me that we must end this wonderful session. I think you have many years of research ahead of you that can be well funded, which is terrific. And we also thank all of you for attendance, and of course Dr. Campbell for this informative presentation. We're so grateful to you, our community, for your support of our Emerging Research Grants program that funds research like Dr. Campbell's. Remember that you can donate to our efforts to advance better treatments and cures or hearing and balance conditions by going to hhf.org/donate. Thank you, and please do enjoy the rest of the day. Good night.