HHF Research Webinar Transcript
Brain Structure Associations With Age-Related Hearing Loss | October 30, 2023, 5pm ET
Mark Eckert, Ph.D.

ANIL LALWANI - Well, hello and welcome, to our Hearing Health Foundation Research Webinar. I'm Dr. Anil Lalwani and I appreciate you joining us today. This event 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. If you need any other assistance using Zoom, follow the link to the technical guide shared in the chat.

Today's topic is a very interesting one, it's the changes in brain structure associated with age-related hearing loss. Now, age-related hearing loss appears to occur with changes in brain structures across multiple research studies, and this webinar presented by Dr. Mark Eckert will critically examine these correlational observations and address their functional significance.

By way of introduction, my name is Dr. Anil Lalwani, and I'm a professor and vice chair for research in the Department of Otolaryngology, Head and Neck Surgery, as well as the associate dean for student research at Columbia University Vagelos College of Physicians and Surgeons in New York.

I'm also a board member at Hearing Health Foundation and the head of Hearing Health Foundation's Council of Scientific Trustees, which oversees the Emerging Research Grants program affectionately known as ERG. So ERG is a competitive program that awards funds to researchers conducting cutting edge hearing and balance research. These grants supported many leaders in our field to become successful scientists, including our illustrious speaker today.

A 2009 ERG scientist, Dr. Eckert is professor in the Department of Otolaryngology, Head and Neck Surgery at the Medical University of South Carolina, where his research includes the study of communication problems using neuroimaging methods. Now, the ERG program that provides seed money to scientists just starting out in their field of research is only possible through the generosity of supporters like you. Now, if you'd like to support our work on hearing loss, tinnitus, and other related conditions, you can do so today at HHF, that's Hearing Health Foundation, hhf.org/donate. Now, without further ado, we'll move to Dr. Eckert's presentation. Please do ask your questions to the Q&A box linked at the bottom of the screen that we'll try to answer following the presentation. Dr. Eckert, welcome and thank you so much.

MARK ECKERT - Okay. Great, well, thanks again, Anil, for the introduction, and thank you to Hearing Health Foundation for inviting me. It's a really nice honor, and I'm excited to be able to share our work with you on brain structure associations with age-related hearing loss. But before I do, I have one more thank you, which is to thank Hearing Health Foundation for the Emerging Research Grant award that we received way back, way back in 2009 on neural changes underlying speech perception training in the aging brain.

I can't emphasize enough how important this kind of grant mechanism is for people starting off with a new laboratory like me where I was still trying to get my lab up and going at MUSC. And it was really helpful in showing that we could be productive and convincing future grant reviewers that we would be successful if they funded our application. It was really helpful for my laboratory, so I can't say thank you enough. But it was also helpful in really kind of unexpected ways.

And to explain that, I need to describe just one little result from this project where we examined physiological and neural changes that occur with about 8 to 12 weeks of speech training in people who were hearing aid candidates. And so this is a speech training program that Larry Humes developed to use orthography to remap phonological representations with the goal of improving word recognition so that when someone gets a hearing aid, they're going to benefit more from that aid than if they hadn't gone through the speech training. And the training program is pretty remarkable in terms of the word recognition improvement that people demonstrate, and we wanted to really understand some of the changes that occurred with those improvements.

One thing that we did was to look at the pupil response when people were recognizing words and noise. What I'm showing you here in this plot is, on the x-axis, the time from when we first presented a word, and then on the y-axis, a measure of pupil size or pupil diameter. And you can see that as people are starting to recognize the word, the pupil expands its size. And in the training group, you can see that response was a little bit bigger and happened a little bit earlier following training compared to the baseline assessment, and in comparison to controls.

So this is kind of a neat result because it tells us that not only were participants doing better in terms of recognizing words, they were recognizing them faster. So they became much more efficient at recognizing speech following the intervention. So kind of a neat, neat result in my view. This project involved the contributions from lots of people, but was really driven, especially the pupillometry work, by someone named Dr. Stefanie Kuchinsky who was a postdoctoral fellow in my lab at the time. And Stefanie has gone on to use pupillometry in her work at the University of Maryland, and now at Walter Reed, and really become a leader in this area. This is just one example of how the support from Hearing Health Foundation helped not just my lab, but really helped propel another career that I'm really excited about. So again, thank you very much.

I thought we should start the talk by asking a big question, which is, why should we examine hearing loss and brain structure associations in the first place? So there's kind of the obvious reasons. We want to characterize the pathophysiology of hearing loss, for example, but we think too that brain structure findings may be foundational for understanding a whole host of different kinds of questions, including listening effort and compensatory neural support, which we think related to that listening effort. And I'm going to come back to that idea towards the end of the talk. And then a number of other things, many topics that are kind of, we won't get into too much detail here, but are certainly relevant in terms of the brain structure and hearing loss findings that are important.

But I think probably the area where there's the most potential for significance is the knowledge that we get that I hope is going to motivate intervention maybe at an earlier time point in life because we know from Annie Simpson and Judy Dubno's work that it's about nine years from hearing aid candidacy to adopting a hearing aid. So if the knowledge that we get from these kinds of basic science studies can motivate someone to get a hearing aid a little bit earlier in life, when their brains are a little more ready to deal with the aid and benefit more, then I'll be really excited about having been involved in this area of research.

In terms of an overview for the talk, I'm going to give you a kind of a big picture, historical and conceptual framework for why we would study brain structure and function associations with MRI data. So it's amazing to me after all the years in the field that we see correlations between behavior and functional measures, and honestly, relatively gross MRI measures of brain morphology. So we're not measuring neuronal density necessarily, or the number of inhibitory neurons, we're measuring gross brain structure. And that's important to keep in mind. And I want to give you a little bit of a more detailed understanding of what we're going to talk about when I show you relationships between brain structure and hearing loss.

So we'll talk a little bit about methods that are used to collect volumetric, voxel-based, and cortical thickness kinds of measures, but I promise I won't go into too much detail about that. Then we'll get into what those brain structure findings are. And in the context of the auditory cortex findings, whether they're reliable or not, we'll come back to this idea about whether structural declines impact listening. And then we'll end with what we need to know as a way to transition the webinar into the question and answer section.

We're going to start with the understanding or the idea that our brains include maps of our specific sensory worlds. So you all are familiar with the fact that you have lots of sensory receptors on your hands, and the projections from those sensory receptors into your brain take up a lot of space in your brain, lots of neurons dedicated to fine touch and proprioception on your fingers in comparison to the small of your back. So there's a nice mapping between the number of receptors on your hand and in your brain, the neurons in your brain, rodents have a similar somatotopic organization, but they also have something really cool called barrel cortex.

There's a picture of a rodent brain. And so you're looking down on the top of the brain, and you can see that here is the barrel cortex in these blue ovals. So there's a lot of space in the rodent brain dedicated to these barrel cortex regions because these barrels represent what's happening out here in the periphery for these whiskers. So whiskers are really important for rodents. And so what Woolsey and Van der Loos showed many, many years ago was that the whiskers out here have an explicit mapping between the space of the whisker here and the barrel cortex here. And each whisker has its own barrel where there is a set of neurons that represent the experience from the whisker. So there's these projections into the barrel cortex, and the larger the whisker, the more important the whisker for exploring the world, the larger the barrel.

So what we have here is an example where the central nervous system has dedicated a lot of resources to processing information from these whiskers that are really important. So there's a relationship between the size of structure and perceptual or sensitivity. And so these kinds of observations were really critical for human imaging studies where the idea was that we could look at the size of brain structures like Heschl's gyrus and auditory cortex, and try to relate that to perceptual abilities with the idea that, the size of the structure reflects the size of the map in our brain.

We have maps of sound frequencies in our brain, or tonotopic maps. Here's an example from a mouse. So you can see that there's, across the space of the cortex, there's cortex that really likes high frequencies. And then you can see that there's a drop off or a gradient change from high to lower frequencies, down to the lowest frequencies that mice like. Humans have something very similar in our auditory cortex, and sitting right on Heschl's gyrus, Sandra Da Costa showed that we have low frequency representations on the crown of this gyrus.

This brain has kind of been flattened, or it's blown up a little bit, so the gyrus isn't really a bump. I'll show you the pictures of the gyrus in just a bit, but you can see again that there's a low frequency representation on the top of the gyrus, and then higher frequency representations on the side of the gyrus. So here we have a mapping of tonotopic space or sound frequency space across the surface of this structure. And interestingly, larger Heschl's gyri are found in musicians and people who have better, perfect, better, excuse me, better pitched learning. And we know from even earlier studies that children with language impairment and phonological processing problems tend to have smaller Heschl's gyri.

This supports the idea that the size of our auditory maps would relate to brain structure and therefore perceptual abilities. So the question for today is whether auditory cortex structure changes with changes in hearing sensitivity, and we know from animals that have been exposed to noise that they can exhibit atypical auditory cortex morphology and histology.

Before we get to those hearing loss and brain structure studies, we'll talk a little bit about the MRI measures we use in these studies. The kind of old school approach and still kind of the gold standard was to manually trace brain structure. So we would sit in dimly lit rooms for hours and get carpal tunnel syndrome as we traced around these Heschl's gyri here in the right hemisphere and the left hemisphere. And we could sum up the surface areas across these sections of the MRI scan to get a volume and compare, for example, like Peter Schneider did in 2002, the Heschl's gyri here that are rendered for non-musicians, professional musicians, and amateur musicians.

And you can see that the Heschl's gyri for the non-musicians kind of look like they're on a diet in comparison to the relatively plump Heschl's gyri for the professional and amateur musicians. So that's fine, it's a good approach, but it takes a long time. It requires lots of expert knowledge about so-called gyral variability of this Heschl's gyrus structure. And there can be measurement reliability challenges, so it can sometimes be hard to get reliability, and then you worry that results won't replicate in follow-up studies. So that led to automated measures including something called voxel-based morphometry, where you measure the amount of gray matter volume in each voxel or resolution element of an image that's representing the brain.

Here I'm showing you a section of a T1-weighted MRI scan of a 20-year-old, and you can see that the white matter where white matter fibers or pathways that are myelinated show up as white, and brain matter regions where there are neurons show up as gray, and areas where we have cerebral spinal fluid outside of the brain, and these ventricles are darker. And because there's this kind of difference in signal intensity distribution across these different tissue types, we can segment these images into gray matter and white matter images.

We can then compare this 20-year-old's image to a 71-year-old's image, and you can see that there's a little less gray matter here in the 71-year-old and a little less white matter and bigger spaces between the sulci here where there's cerebral spinal fluid. So the way we do the voxel-based analyses is we will go into each voxel and collect the value that represents the gray matter volume there. for the, for example, 20-year-old and the 71-year-old. And then we can compare those values across lots of subjects like this. So we can look at the distribution of gray matter volume across age, and you can see that we see the expected effect where there's a gradual decline in gray matter volume as we get into our 80s.

Cortical thickness is somewhat related measure, but it tells us something a little bit different. Here with cortical thickness, it's kind of an easy method to understand, a little harder to implement, but what we basically do is measure the distance from the surface of the brain down to the boundary between the brain matter and white matter. So you can do that again for the 20-year-old and the 71-year-old, and you can see there's a little bit of difference in cortical thickness for these two people. And we can analyze, again, the data across all of the participants and do something fancy like this where we look at every position in the brain to see if there's a relationship between age and cortical thickness. And what I'm showing you here are the relationships between decreasing cortical thickness and increasing age.

You'll note that one of the areas that exhibits the strongest change in cortical thickness with age is auditory cortex where we have our Heschl's gyrus. Note too that frontal cortex is also declining significantly with age, and that will come up at towards the end of this. So to do these voxel-based and cortical thickness kinds of analyses, we have to take big brains and little brains and squish them into a common coordinate space or common brain space. And so we warp these images, and the procedures for doing that are relatively well worked out, and they work very well if all the brains have similar shapes. But sometimes there are sulcal-gyral features that are qualitatively unique, and we have to be thoughtful about conditions where we may have a single Heschl's gyrus or have this kind of heart-shaped Heschl's gyrus here. And these things are here a little bit harder to warp into the space of this single gyrus, for example. So we do have to inspect our data to make sure that some of these factors don't influence the results.

And the other challenge that you should be aware of, and you may be aware of based on the the popular press, is that these kinds of voxel-based and cortical thickness analyses involve lots of comparisons. So we've gone from comparing a few brain regions or a few measurements with the manual approach to comparing tens of thousands of voxels across across the brain. And so again, we have to be careful about the statistical thresholding approaches that we're using to make sure that we don't have false positive results. And ideally we're able to replicate those findings in another study.

We are now going to transition into talking about some of the findings that are in the literature linking age-related hearing loss to brain structure. But one of the reasons before I show them to you, one of the reasons I talked about methods is not just to give you a good understanding of the different types of measures that I'll be showing you, but also to give you the impression that there are lots of different ways to analyze brain imaging data. Sampling approaches are different in terms of the subject population. There are differences in the, again, the type of measurement. There are differences in the types of statistical analysis people use.

If you look across all the studies I'm going to share with you today, unless the study was done in someone's lab as a replication, it's unlikely that the methods are exactly the same. So it is, I think, a little bit remarkable if there are any replications of studies at all. But there are some. So what we see in one of the first studies to report a relationship between hearing loss and brain morphology of auditory cortex was, again, a project done by Peter Schneider in 2009, where what they found was that a high frequency pure-tone threshold average measure was related to the volume of Heschl's gyrus.

In this scatterplot, what you're seeing is more hearing loss in the high frequencies as we're moving towards the left of the x-axis. And you can see that the amount of Heschl's gyrus gray matter volume decreases with increasing hearing loss. Fatima Husain showed something roughly similar with a voxel-based brain outer morphometry approach where she compared normal hearing participants to people with hearing loss. And you can see here in the red and yellow regions that the people with normal hearing had more gray matter in these regions compared to those with hearing loss. And then Jonathan Peelle also showed something similar in 2011 with a pure-tone threshold average measure where with more hearing loss, moving now to the right of the plot, there is lower gray matter volume in these red Heschl's gyrus or auditory cortex regions.

One of the things I'd like you to notice from these scatterplots is that these effects are relatively modest. They're significant, but you can see that there's a lot of error around the regression line. So hearing loss isn't perfectly related to the structural differences across participants in these studies. We showed similar results in 2012, and then again replicated these findings in 2019. And what you're seeing here are, there's the amount of gray matter volume in these three different auditory cortex regions with increasing high frequency hearing loss. So you can see again as high frequency loss increases over the thresholds rise for high frequency thresholds, there's a drop in the amount of brain matter volume for these participants. And the effects here are present across males and females, even though the males have a little bit more hearing loss in the high frequencies.

Now, we didn't see similar effects for the low frequency measure. There is maybe more laterally a low frequency effect, but for these more medial Heschl's gyrus regions, there was not a strong relationship between low frequency hearing loss and the amount of gray matter volume. And I'd note that Chan in 2017 reported something similar with a temporal lobe atrophy measurement where temporal lobe atrophy was observed more for people with higher frequency hearing loss. So that's exciting. We've got a bunch of studies that have replicated, and there's even more here that report associations between hearing loss and the morphology of auditory cortex.

And this is kind of generally consistent with the animal studies that I mentioned earlier, and some studies of prelingual deafness where there's atypical auditory cortex morphology, that area's a little messy, kind of like this area that I'm going to describe in just a bit. But in meta-analyses, there does seem to be a relationship between prelingual deafness and atypical auditory cortex morphology. So that is great, except there are studies that don't show a relationship between hearing loss and auditory cortex morphology.

These studies in red may have reported effects in other brain regions, just not in auditory cortex. And so that raised concerns for us. So why was there inconsistency in the studies? And we have spent a lot of time trying to figure this out, and we think we've solved in part, not fully, but in part. So one of the things that we've noticed is there are two kinds of approaches that people will take in designing their studies.

One is a hearing loss group difference design. So people will classify or group people into a normal hearing group and a hearing loss group, often based on a pure-tone threshold average, threshold cutoff, and then compare the groups for their auditory cortex morphology. And what you can see is that for these studies where there's a nonsignificant effect, these are group difference designs, and there are some studies that show significant effects, but not as many as we would like.

In comparison, when people use an individual difference design, where we're looking at correlations across participants, we see fairly consistent significant effects. So it seems like this individual difference design is an important feature for replicating findings of auditory cortex and hearing loss. So this is important in the context of the modest effect sizes that I was describing to you earlier. So we want an individual difference design that's going to be a little more sensitive to seeing those differences across people, especially when there are modest effects.

There's another, I think, valuable, there's additional value, excuse me, for using this individual difference design because it also reminds us that what we're doing here are correlational analyses, so for cross-sectional studies. So these studies don't tell us a whole lot about causation. And so one of the things that we've been very interested in is trying to move beyond these cross-sectional studies, and consider longitudinal changes in hearing that might be occurring with longitudinal changes in brain structure.

So we did this, we looked at this question in 2019 in 30 middle-aged to older adults, and we tracked other change in hearing thresholds and brain structure over two and a half years. And what we found was significant differences in thresholds or changes in thresholds and significant changes in brain structure. But that variance in change for those two sets of measurements was not strongly correlated. And so that was a little disappointing, it may have been due to the fact that we were just looking over two and a half years.

But there was something else that I think was important in this study, which is that the baseline hearing loss was predictive of future or the rate of longitudinal change in brain morphology. What I'm showing you here in red are all of the brain regions that contracted at a more rapid rate in people who had more baseline hearing loss. And the purple and blue regions represent the ventricular areas that were filling up with cerebral spinal fluid to accommodate the changes in the tissue over that time period, and especially in the people with more hearing loss at baseline. tTese kinds of whole brain results really need replication, and that's something we're working on. And I also want to note Frank Lin's work in 2014 where he observed that the baseline degree of hearing loss was related to again, or more baseline hearing loss was related to, more longitudinal change in the temporal lobe.

These results, assuming again we can replicate them, which I think is important to do, suggest that there are changes that are occurring across the brain with hearing loss, and not just in frontal regions, not just in auditory cortex regions, but also regions in the frontal cortex that help support speech recognition, for example, or listening in challenging conditions. We were interested in what is happening in our brains when we're listening to speech in noise, or in challenging listening conditions, and the degree to which brain structure might be important.

One of the things we did many years ago now was to ask participants younger and older to listen to words in noise and report what they heard to us when they were in the MRI scanner, so that we could measure their brain activity during this task. And interestingly, we didn't see pronounced differences in activity in auditory cortex during this task, but what we did see was pronounced differences in activity in these frontal cortical areas. And these are brain regions we now know are important for performance monitoring to help us track how well we're doing in an experiment or in a task.

And probably most importantly in the study, what we also found is that the amount of gray matter volume, auditory cortex, predicted the degree of activity in these frontal brain regions. So it appeared that a diminished auditory cortex structure, perhaps diminished central auditory system more broadly, increases a reliance on a frontal cortex that's important for performance monitoring. So the tasks got a little bit harder because of these auditory system declines, and that led to an increased reliance on these frontal regions.

So those frontal regions involved in performance monitoring aren't there just to tell us that we've made an error, or that the task is hard, they're there to try to help us optimize our performance during challenging tasks. And we wanted to ask the question as to whether activity in these regions could predict future performance in word recognition. Is there evidence of adaptive control based on activity in those brain regions? And what we found in young adults is that when activity in these cingulo-opercular regions was elevated, it predicted performance on the next trial. This elevated activity predicted word recognition, I should say, on the next trial. So that's pretty exciting because that word recognition trial was happening about eight seconds into the future. So pretty remarkable the fact that we've replicated it now a number of times.

And we've also seen this effect in older adults. However, the effects are a little bit smaller. And so what I'm showing you here in this scatterplot is the relationship between participant age on the x axis and this association between activity in frontal cortex and performance on the next trial. And you can see that this association of this effect that we described as adaptive control is kind of dropping or declining with increasing age. We think that's due in part to those changes in auditory system function, central auditory system structure and function.

Because if you have begun declines in your auditory system, you can try and try to optimize your behavior or modulate the function of your auditory cortex, but maybe that becomes a little more difficult with those declines. It's also possible, and we had some evidence of this in the study, that there are declines elsewhere in the brain that are contributing to this change in.

So at this point, my hope is that you're wondering, well, what are the mechanisms, what's happening to explain the changes in hearing and changes in brain structure that people are seeing? And one of the things that we are currently working on is to examine the degree to which there are distinct mechanisms of presbycusis or age-related hearing loss that can explain the auditory cortex effects, for example. So we're working on estimating the components of sensory presbycusis, metabolic presbycusis, and neural presbycusis to see which one of those types of presbycusis might relate to the auditory cortex effects that we're seeing.

Let me back up a little bit and say that when we talk about sensory presbycusis, I'm referring to what we think are declines in hair cells. Our measure of metabolic presbycusis, we think is a measure of a change in the cochlear amplifier. And for these two methods, two constructs, we are using audiometric data to estimate sensory and metabolic presbycusis. And then for neural presbycusis, we're working with Kelly Harris's group at MUSC to operationally define neural presbycusis with a auditory nerve phase locking measure. And that's shown here on the x axis of the scatterplot where Kelly and her group will place an electrode on the tympanic membrane, and then record the consistency of the response from the auditory nerve across repeated presentations of a quick stimulus. And so that provides a measure of phase locking or auditory nerve consistency and response.

What I hope you see here in this plot is that there's a nice relationship between the phase locking of the auditory in the gray matter volume in this auditory cortex region where I can outlined a region of interest over Heschl's gyrus. So this is ongoing work, and the goal here is to compare the relative contributions of these sensory, metabolic, and/or neural presbycusis components to the variation in auditory cortex and beyond. So stay tuned for that.

There's another mechanism that I think we should think about, or mechanisms, and that's that there may be common cause explanations for what we're seeing in some of our results, especially the results where we're seeing associations between hearing loss and brain structure outside of auditory equipments. And so one of the things that is very common with aging is small vessel disease and inflammation. And I say that it's common because in many of the adult participants who are relatively healthy coming to our studies, we often see this kind of feature in a type of T2 weighted MRI scan where these bright spots show areas of, or these, I guess we call them white matter hyperintensities, are areas of a limited of pathology that is thought to reflect small vessel disease and/or inflammation that's occurring.

And so we were interested in the degree to which this evidence of small vessel disease, is related to hearing loss. And so the idea was that the small vessels in your inner ear might be equivalently affected, like these small vessels that penetrate your brain because of a systemic change in vascular health. And so one of the things that we observed a number of years ago now is that the probability, the likelihood that you have small vessel disease, especially in these frontal regions here, was related to elevated thresholds in the low frequencies. And so a slightly different profile, audiometric profile, and we're continuing to follow up on this study for a finding too.

We can summarize now, and we can say that there are modest associations that are observed between the extent of hearing loss and brain structure, especially in auditory cortex. And this means that we can't tell you with a whole lot of confidence how much auditory cortex you have based on your pure-tone thresholds. We need lots of participants to see these relatively modest associations. And those associations that I described today are really only suggestive that hearing loss causes brain atrophy. We don't have good evidence of that yet.

We need to determine still whether peripheral losses have cascading effects throughout the auditory system, and/or there's a common cause underlying inner ear and brain declines. So I'm going to stop there, and thank you very much for attending. I want to thank the current and former members of our Hearing Research Program at MUSC that includes people like Kenny Vaden and Carolyn McClaskey, Judy Dubno, Lois Matthews, Kelly Harris, Jane Holstrom, and many former members, people like Stefanie Kuchinsky, Susan Turose, who I've had the pleasure to work with for a number of years now. So again, I can't name everybody, so I apologize if you're here, and I wasn't able to for this to, and I want to thank the NIDCD for very generous support over many years and, of course, Hearing Health Foundation.

And if you have any questions that are not addressed in the next section of the webinar, feel free to reach me at my email address here, or if you aren't happy with any of my answers, please feel free to reach out to me. I'm happy to talk with you and communicate about our work and hearing and brain function structure, more generally. So thanks again, and I'll stop sharing my screen.

LALWANI - Mark, that was just amazing, really, really exciting, fascinating work with a lot of implications and stuff. And we have some great questions for you. One of the listeners asks, so are you saying that the auditory cortex is more the problem with hearing loss as opposed to degradation of hair cells or something in the periphery?

ECKERT - A loss of hair cells or a change in the cochlear amplifier is certainly the primary problem here in terms of age-related hearing loss, but we're talking about with the changes in auditory cortex morphology is maybe a consequence of that hearing loss, or a common, as I mentioned, a common cause mechanism that's affecting both the inner ear and the brain. Where it's significant is in the degree to which your central auditory system is important for helping you recognize speech. So when we talk about interventions that focus just on the auditory periphery, we may not be fully accounting for some of the central auditory system mechanisms that are important for helping us understand, especially in challenging listening conditions, whether that's primary auditory cortex, auditory association cortex, or even frontal regions that help to modulate the responsiveness of auditory cortex.

LALWANI - Mark, you talked about changes in gray matter and white matter What's happening, are the cells shrinking? Are they dying or when you get them bigger and like the musicians, what's going on? What do you think is happening there?

ECKERT - A really important question, and it's hard to answer that question with the neuroimaging approaches. We can talk about, with neuroimaging, we can talk about white matter and the extent of myelination. We do think, especially in the musicians, that there is increased myelination, probably increased synaptic density in their cortex. So that is certainly the case. One of what we need to do really is postmortem studies to better understand how the cortex is changing with changes in the auditory periphery. If you have hair cell loss or you have stria loss or stria vascularis loss in your inner ear, what is the corresponding change in histology and genetic expression in the cortex? That's really the next step I think.

LALWANI - And I'm going to follow up with that. Another question along the same lines. So do you think wearing a hearing aid will lead to preservation of volume or alternatively, how can we keep our brain volumes in the hearing area, at least as large as it's always been?

ECKERT - We need to do that, those studies. So we need to understand the potential long-term benefit of wearing a hearing aid and whether it slows the rate of decline in auditory cortex , that's a really important question that I don't think we have a good answer to yet. Those are hard studies to do, and they take a long time. In terms of preventative perspective, in terms of making sure that we have great ear and brain health.

One of the things that is pretty clear from the literature is that vascular disease is a potential problem for both our brains and maybe our inner ear. There's some studies suggesting that if you have conditions like diabetes that occurs with vascular decline, you're at greater risk for hearing loss. So if you have a condition associated with vascular declines, then certainly, you want to be preventative with your physician, and making sure you're following up and well-controlled.

But more broadly, we also know that exercise is helpful. So in terms of brain health, and it looks like, a little bit with respect to our auditory thresholds, people who exercise a little bit more have slightly better thresholds, at least in one study. And we know from a mouse study, or I guess a mouse study, that mice that run on wheels a lot have better hearing as they get older, and they have not only better hearing, but their inner ear is much more healthy in terms of the histological features that are observed after their study. And that's in comparison to the couch potato mice that don't run on the wheel. So they lose hearing at a much more rapid rate, and they have a more atypical morphology in their inner ear.

LALWANI - Well, I can't say I like your last answer, Mark. Being a couch potato, now I'm going to have to get up and exercise all the time and be healthy. That's terrible.

ECKERT - We're all going to have to go exercise tonight.

LALWANI - So an anonymous attendee's asking, and he or she says, this is a cause and effect question, Do most, and this has to do with expansion in the musicians, in Heschl's gyrus, do most children prior to entering a musical field or training exhibit Heschl's gyri of similar size, which then expands among these children who enter a musical field, which comes first? The structure or the external stimuli over the years?

ECKERT - I said that that's a really interesting, great question. So the only study that I'm aware of on this topic involved string musicians. And so the people who played a string instrument had larger motor cortex and somatosensory cortex early in life, and there was a suggestion that playing a string instrument also led to an expansion of the cortex and increased myelination. So I would assume that something similar is happening in the auditory system for musicians.

LALWANI - A broad question, Kumar asked this question, Have you observed each of the changes in other structures, such as the cochlear nucleus, inferior colliculus, that are related to age-related hearing loss?

ECKERT - Great anticipatory question here. This is something that Carolyn McClaskey in our Hearing Research Program is working on. She's interested in the inferior colliculus, and how it's changing with age. So look for her work in the future. But the resolution for many of the neuroimaging studies that we have is a little too gross for some of these kind of smaller brainstem structures that you're mentioning. There are different kinds of studies that need to be done with that. The human imaging studies haven't been done, there's some, but not as, as many as we would like. There are studies of the auditory nerve, so people are collecting very high resolution images of 0.5 millimeters approximately and seeing differences in the auditory nerve. That relates, for example, to the the phase, auditory nerve phase locking measure that I mentioned earlier. There is some, some work in this topic, but not as much as the cortical work. And in my laboratory we've really focused on cortex.

LALWANI - Got it. So Catherine asks, and there's a follow-up question too. We're going to go in the area of sort of acoustic trauma or noise-induced hearing loss. What are your thoughts, do you have thoughts about if or how acoustic trauma may affect cortical structures? We know about its effect on the peripheral system. Are there either primary or secondary effects? Can you broadly expound on that for us?

ECKERT - So the animal study suggests that acoustic trauma does lead to changes throughout the central auditory system. And our findings with high frequency hearing loss suggested that it's a possibility that noise exposure was contributing to some of those findings as well. So yes, I think that's a possibility.

LALWANI - And so Dan asks, as a follow-up question to this, a number of studies show that age-related hearing loss is really noise induced hearing loss. Your comments about sensory, metabolic, and neural impact seems to indicate it's more complex, but might noise be the greatest contributor?

ECKERT - Sure, I just suggested that it could be a significant contributor, and I guess I'm starting to think about the accumulation of noise experiences across our lifetime as not just noise exposure, but in interaction with the aging process. So we are going to experience some trauma in our aging ears, and we may be less and less effective at dealing with that trauma. So there are many people, including Hainan Lang in our program, who are interested in inflammation. So the process of inflammation that is a normal response to an injury, but as we get older, it's hard to turn that off. And so that could further exacerbate an acoustic trauma, for example. So I think there's an interaction between experience and our aging ears and brains.

LALWANI - So multiple question-asking individuals have complimented you on your talk, so let me just repeat that again, thank you so much for your wonderful talk. But now the question Gavin asked is, and I think, you can take this any way you want to because I think a lot of people will be interested in your insights about this, hearing loss and cognitive decline. They're both common in aging. So to what degree are the changes in the auditory cortex the result of cognitive decline or driven by the prefrontal changes you see, or vice versa. This in the context of Lin's work suggesting hearing loss as a catalyst for cognitive decline. So you can take that any way you want to, give us your opinion, facts, whatever you want. Take it away, Mark.

ECKERT - Okay, you're giving me the impression, this is a bit of a loaded question, so no, I'm happy to answer this question. So we've begun to study this question about age-related hearing loss and cognition. And in our lab we've replicated, in our program, we've replicated some of the general cognitive function associations with hearing loss in about 350 participants. And we see that it can explain about 4% of the variance. So meaning that hearing loss can explain 4% of the variance in cognition. So some people report larger effects, but in our sample it's a modest, it's significant, but it's a modest effect. So in that situation, when we talk about small effect sizes, I usually think that there's an indirect relationship. So if the effect sizes are really big, then I think there's something causal about the two variables. But given that the effects are modest, I think of more common cause explanations like small vessel disease. And so I think that's one primary area of focus that's important.

LALWANI - Mark, somebody asked, I'm sorry I'm not going to be able to give credit to who asked this question, but they were asking in general imaging vascular insufficiency, whether it's in the brain, can you image it or can you image vascular supply to the cochlea or abnormality of the vascular supply to the cochlea? Any of those questions?

ECKERT - So we would love to image vascular supply in the cochlea for our magnetic resonance imaging, especially at a magnet strength of three Tesla. That's really hard, we can't get the resolution to image the cochlea very well.

We could try to image the vertebral arteries and supply of vessel or vascular blood to the inner ear, but that's a little indirect. For the brain, we can use something called profusion imaging and get a measurement of the flow of blood into the brain. And that is something that we're doing for some of our imaging studies where we want to control for... So let me back up. So in our functional imaging studies, what we're measuring is to a certain extent oxygenation, oxygenated blood. And so if we're worried that there's an alteration in blood flow, we want to measure the degree of perfusion in the brain as a control measure. And so we're collecting some of that data now, we can ask questions about whether profusion differs in people with varied hearing loss.

LALWANI - Janet asks, do you, and this is sort of a technical question, again, you can take it in, because we have really a mixed audience of both scientists like Janet is and other lay people. Do you think that perhaps examining speech understanding in everyday listening situations, which show a clearer relationship with changes in auditory cortex with age? That's the question. I think if you could ask why that's even important, whether you test with a noise or without noise, and how that might be important in imaging, if you could address that.

ECKERT - I think when we talk about hearing in noise versus in clear conditions, we might be able to differentiate the source of a problem. We might think that in noise there's greater contribution of central auditory systems relative to in quiet. I think that's what Janet is getting at maybe. And so, yes, I think, and there are people who are interested too in doing pure-tone testing in noise and demonstrating central effects there too.

LALWANI - I really like this question. I'm not sure if you're going to be able to answer it. Does hearing loss affect your spelling because you hear words differently?

ECKERT - Hmm, yeah, no, it's an interesting, it's an interesting question. I don't know. We were interested, so we were, I don't know, as someone who is very interested in reading disability, I think it's a neat question maybe certainly from a pediatric perspective, but in the context of age-related hearing loss, I think I wouldn't expect a phonological processing problem necessarily in an older adult, but you never know. I am interested in the degree to which having a reading disability later in life contributes to speech communication problems, especially in noise. So I think that's an important area of study.

LALWANI - When you want to be a better tennis player, the recommendation is go practice, practice, practice. So Judith asks, is there anything we can do to improve our ability to discern speech, or just hear better, in fact?

ECKERT - I think go out and be social and talk to people, that will certainly help in challenging conditions. But I don't know the status of Larry Hume's intervention or speech training program, that certainly helped people a lot in terms of improving their word recognition. So some kind of program like that might be helpful.

LALWANI - Would you recommend a glass of wine every night, Mark, now you've got us to exercise--

ECKERT - I think you're hoping, no, I think you're hoping. I'm not recommending alcohol necessarily, but if it's helpful to you, that's great.

LALWANI - And I think we're just let down to the last couple of question, consequences of, some of you talked about cutting the cochlear nerve, Eric did and his consequences. How about unilateral hearing loss or cutting a cochlear nerve, either one. What do you think will be the central consequences of those conditions?

ECKERT - So I'm thinking about unilateral hearing loss where someone had a virus and lost hearing in one ear, for example. And so I don't know the literature very well in that area. I would expect that in the contralateral pathway that there'd be some hypertrophy, some change related to the loss of input, and that there would be some compensation in the other ear and pathway. But that's me speculating a little bit.

LALWANI - Kumar has an excellent question. Can you comment on congenital deafness and AC morphology, the auditory cortex morphology, and maybe put it in a context of rehabilitation with either hearing aids or cochlear implants? Are we born with normal structures, and we lose them or? Take it away, Mark.

ECKERT - No, this is, I mentioned earlier that this literature is really complicated in terms of people who are prelingually deaf in terms of whether an auditory cortex morphology difference is observed or not. It seems like there are changes in white matter morphology that may reflect an experiential change. And so I would think, I think this is, again, not my area. I don't study cochlear implants and deafness, but I would think that it's an example of the value of earlier intervention in terms of having an intact structure that's not declining because of loss, lack of input. So it's too much speculation for me, I'm sorry.

LALWANI - Mark, I need a 30 second summary from you about what we want to walk away with, changes in the central cortex and how we can prevent them?

ECKERT - I'm going to have to, if you'd like, you could go for a walk tonight with a glass of wine. Maybe that would be helpful for you, maybe for me too.

LALWANI - So I guess in some ways we should walk away with that changes do occur and anything you can do to have auditory experience probably will help you. Would you agree with that, Mark?

ECKERT - Definitely agree with that. And I started the talk mentioning the potential importance of these kinds of studies, hearing loss and brain structure studies on motivating intervention. And I hope that's also a message from this that because of the changes that are occurring, regardless of whether they're due to hearing loss or because of just age in our brain, the earlier we get an intervention, I think the better.

LALWANI - Well, we are coming to the end of another wonderful webinar. Thank you all for your attendance and Dr. Mark Eckert for this very informative session, in his presentation, really a lot of things we have to think about. I recommend sitting on the couch and drinking, but I think he wants you to get up and walk around and be social. We're so grateful to you, our community, for your support of our Emerging Research Grants program. Remember that you can donate to our efforts to advance better treatments and cures for hearing and balance conditions at HHF. That's Hearing Health Foundation hhf.org/donate. Thank you, and please enjoy the rest of your day.