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The Interhemispheric Connectivity of the Auditory Cortices

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THE INTERHEMISPHERIC CONNECTIVITY OF THE AUDITORY CORTICES

by
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ABSTRACT

Objectives: The corpus callosum of the brain is an important and complex structure that allows communication between the two cerebral hemispheres. In the absence of knowledge about the relationship between the corpus callosum and the auditory cortices, this study aimed to investigate how the structure changes. Specifically, we explored the age associated changes of interhemispheric connectivity between left and right cortices through the corpus callosum.
Methods: Using Diffusion Tensor Imaging (DTI) data from enhanced Nathan Kline Institute-Rockland Sample (NKI-RS), we isolated the auditory corpus callosum, or the section of the corpus callosum that transfers auditory information, in each individual subject (N=466) using probabilistic tractography. As a measure of the white matter microstructure integrity, the mean fractional anisotropy (FA) of the whole auditory corpus callosum was examined and tested for an association with age.
Results: A significant association between age and the auditory corpus callosum was found. Age was associated with an increase in the integrity of the auditory corpus callosum, adjusted for sex.
Discussion: The current study does not prove a causal relationship between age and auditory corpus callosum integrity, but it is the first evidence of a relationship. This information provides new evidence on the hearing and neurological systems of the body, and how this relationship impacts our daily lives and audiological practice.

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Introduction

When studying split- brain patients who had their corpus callosum removed to treat their severe epilepsy, researchers and scientists first considered this structure's importance. The corpus callosum is the structure that physically and neurologically connects the left and right hemispheres of the brain, allowing for interhemispheric communication. Through studying the atypical split- brain patients, the significance of this ability of the brain to communicate with itself was revealed (Gazzaniga 2000). Today, researchers continue to study and observe a multitude of patients, typical and atypical, to examine the impact of the corpus callosum in many areas like behavior, language, hearing, and aging.

Regarding aging, this factor is shown to be correlated with diminished corpus callosum functioning, making further research on this topic important; studies on aging and this structure have clinical implications for audiologists and all other health care providers. For example, Water, Sawyer and Gansler (2016) showed that the white matter integrity of the corpus callosum can be used to distinguish normally aging patients from those with dementia. Similarly, research of this kind informs aural rehabilitation, counseling, and binaural hearing aid use in a clinical setting. Particularly, Bellis and Wilber (2001) concluded that individual differences in binaural processing in an aging individual influences the individual's ability to complete auditory tasks that require communication between hemispheres, like sound localization and speech-in-noise abilities. Further supporting this notion, Dias, McClaskey, Eckert, Jensen, and Harris (2020) determined that white matter tracts and proper auditory spatial processing, another ability that requires interhemispheric communication, are impacted by age.

Corpus callosum integrity can also be impacted by neurological conditions. Neurological conditions including schizophrenia, attention-deficit disorder, and autism spectrum disorder (ASD) are currently being explored to determine how interhemispheric functioning plays a role in these disorders. Linke, Keehn, Pueschel, Fishman, and Muller (2018) linked reduced interhemispheric connectivity between the auditory cortices to increased auditory thalamocortical connectivity, lower verbal IQs, and greater sensory deficits in children with ASD. For schizophrenia, it has been hypothesized that the mental disorder is impacted by an altered integrity of the interhemispheric auditory pathways and an asynchrony between left and right auditory cortices. Steinmann, Leicht, and Mulert (2019) examined how these factors regarding the corpus callosum contribute to auditory verbal hallucinations, a common symptom of schizophrenia. Last, Hinkley et al. (2012) studied patients with agenesis to provide evidence that diminished or no corpus callosum functioning, like in other disorders, decreases the patients' other abilities, including decision making, memory, and motor planning.

Studying the structure across the lifespan, researchers have gained knowledge on how the structure impacts the brain's functioning as a whole. Adibpour, Dubois, Moutard, and Dehaene-Lambertz (2018) examined infants with agenesis to determine when language lateralization and the left hemisphere advantage develops; their results indicated that this develops early along with an asymmetric transfer of auditory responses. How the brain, especially the corpus callosum, processes auditory signals is studied in geriatric patients as well. Dias, McClaskey, Eckert, Jensen, and Harris (2020) established that intrahemispheric and interhemispheric mechanisms are involved in skills that require both hemispheres to communicate, like auditory spatial processing, localization, and attention. Furthermore, Waters, Sawyer, and Gansler (2018) argue that these mechanisms are impacted differently by aging. Intrahemispheric tracts are not changed due to aging while interhemispheric tracts are mediated by age. These structures and auditory corpus callosum connectivity prove to be structurally significant as Seydell-Greenwald, Raven, Leaver, Turesky, and Rauschecker (2014) gained preliminary evidence that it could play a role in tinnitus.

Strides were also made to understand the workings of the corpus callosum by studying its physiology. Andoh, Matsushita, and Zatorre (2015) provided evidence that supports that the corpus callosum mediates functional asymmetry of the brain and uses a theoretical model to determine this. Dennis et al. (2015) also proposes ways to study the structure and factors that point to the validity of results; they recommended a multimodal approach as they used pediatric patients with traumatic brain injuries to link interhemispheric functioning to disrupted white matter. Lastly, Quigley et al. (2002) also studied how the corpus callosum mediates functional connectivity and concluded that this functional connectivity is diminished in the auditory cortices of patients with agenesis compared to healthy patients. In this case study of three subjects, they used fMRIs of different tasks to look at the synchrony of blood flow changes in the corpus callosum.

To examine the interhemispheric connectivity of the auditory corpus callosum, Diffusion Tensor Imaging (DTI) was utilized since it allows for examination of the axonal white matter integrity in the brain. Strong associations between white matter regions and factors such as age and gender have been found, like DTI studies that revealed these difference between childhood, early adulthood, and late adulthood (Peters et al. 2014). Although the relationship between the white matter integrity of the corpus callosum and sex is not well known or researched, we adjusted for this factor when examining the association between age and the auditory corpus callosum.

Methods

Imaging and Behavioral Data

DTI data were gathered from the Nathan Kline Institute- Rockland Sample (NKI-RS: http://fcon_1000.projects.nitrc.org/indi/enhaced/), which utilizes an open neuroscience model to provide a large neuroimaging dataset with deep and broad phenotypic measures (Nooner et al. 2012). Participants recruited from Rockland County, NY demographically represented the United States. Furthermore, the participants were screened for psychiatric, neurological, and chronic medical illnesses before being included. There are 502 samples that contained DTI data. This study and its analyses were approved by the Institutional Review Board of the University of Mississippi (14x-244).

The DTI series had 128 volumes of noncolinear directions along with 9 volumes without diffusion weighting (TR=2400ms, TE=85ms, matrix=128x128, FOV=256mm). Each of the volumes consisted of 64 contiguous 2-mm slices with 2mm^3 isotropic resolution.

Imaging Data Analysis

Imaging process took place through the use of the Functional Magnetic Resonance Imaging of the Brain Software Library (FSL version 4.1.8; Oxford, United Kingdom; http://fsl.fmrib.ox.ac.uk/fsl). Using FSL's eddy tool, eddy-current induced distortions and head-motion displacements in the 128 diffusion volumes (b=1500) were corrected to the first b=0 volume. The b-vector table (i.e., gradient directions) was also corrected according to the rotation parameters of this linear alteration for each participant. Non- brain tissue was displaced using FSL's Brain Extraction Tool. Fractional anisotrophy (FA), which measures the value of white matter integrity, was calculated at each voxel of the brain by fixing a diffusion tensor model to the raw diffusion data.

Tractography Analysis

Using Markov Chain Monte Carlo sampling in FSL's Bedpostx tool (Behrens et al. 2003, 2007), the local (i.e., within-voxel) probability density functions of the principal diffusion direction were approximated. Then, a spatial probability density function across voxels was estimated based on these local probability density functions using FSL's Probtrackx tool (Behrens et al. 2007). 5000 samples were taken for each input voxel with a 0.2 curvature threshold, 0.5 mm step length, and 2000 steps per sample. Using FSL's FMRIB58_FA template as a DTI specific reference, segmentation of the arcuate fasciculus was determined based on the MNI152 T1 brain provided in FSL.

The probabilistic tractography was conducted between white matter of bilateral Heschl's gyri, determined by Harvard- Oxford Cortical Atlas (Desikan et al. 2006). In order to avoid thalamic projections, a termination mask is placed at the thalamus, determined by Harvard-Oxford Subcortical Atlas (Desikan et al. 2006). These seed regions of interest and masks were linearly registered to the native diffusion space of each acquisition. The tract between bilateral heschl's gyri in each subject was given a threshold at a normalized probability value of 0.06.

Tractography outputs for each of the 466 individuals were visually examined using in-house script. This opens images by fslview, allowing for a comparison of the average tract. An image received a rating from 1 being the worst to 5 being the best. Images that were rated 2 and below were disqualified. Images that were rated 3 were re-examined by the second evaluator. All other images above a 3 were automatically included in the study. A multiple linear regression was tested to predict the FA of thee auditory corpus callosum based on sex and age.

Results

Using all the 466 individuals, males showed higher integrity of the auditory corpus callosum than females. A significant regression equation was found ($F(2, 464)=4.79$, $p=0.009$) with an R^2 of 0.016. The predicted FA of the auditory corpus callosum was equal to 0.40 - 0.014 (sex) + 0.00025 (age). The sex ($p=0.0072$) age ($p<0.040$) significantly predicted FA of the auditory corpus callosum.

There was an age associated increase in the integrity of the auditory corpus callosum, adjusted for sex. These results are expected to survive after quality control (p<0.001).

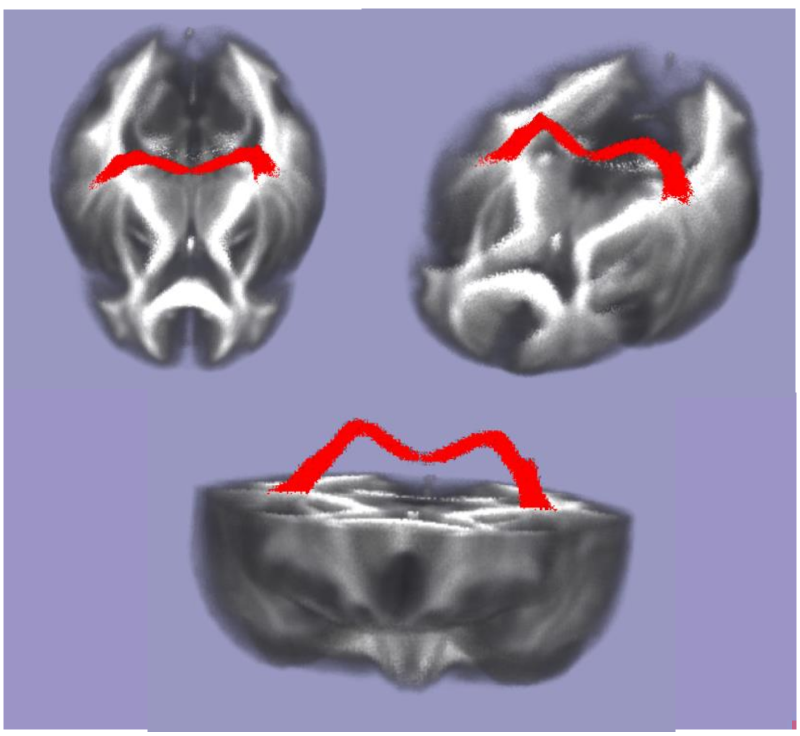

Figure 1-3. Average tractography of the auditory corpus callosum from multiple

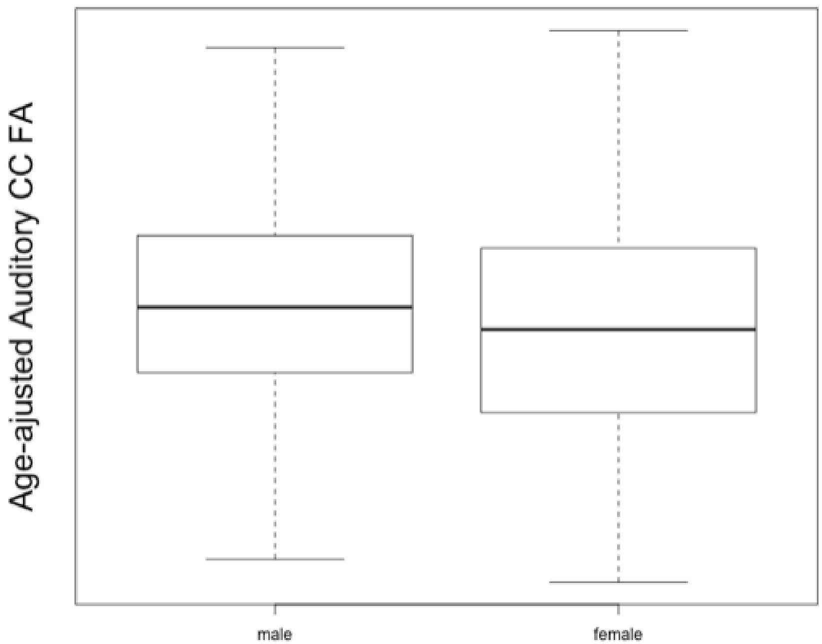

Figure 4. Age adjusted auditory corpus callosum fractional anisotropy measures.

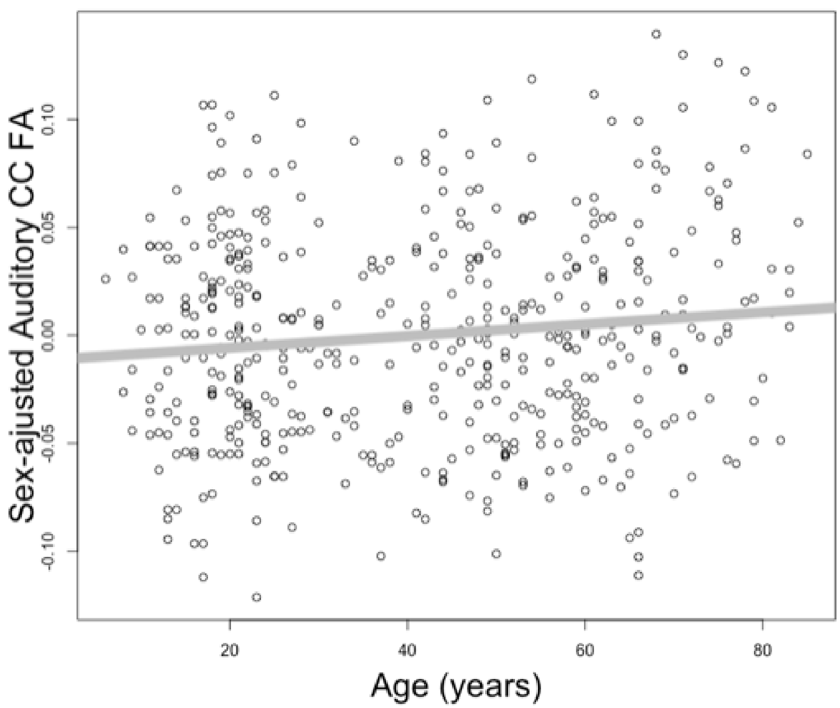

Figure 5. Sex adjusted auditory corpus callosum fractional anisotropy measures.

Discussion

This study sought to examine the age associated changes of interhemispheric connectivity between left and right cortices through the corpus callosum. The current results showed a significant association between interhemispheric connectivity of the auditory cortices and both age and gender. Although plenty of research over the years has studied how the corpus callosum varies between genders and changes due to age, to our best knowledge, this is the first study directly examining this structure related to the auditory cortices and hearing. Our results indicate that the relationship between these structures is associated with gender and age.

Specifically, the current study revealed higher FA in men than women, indicating higher white matter integrity. On the other hand, FA also increased with age, indicating that aging individuals have a higher white matter integrity. Different areas of the brain undergo aging, and therefore changes in white matter, differently. Specifically, Peters et al. (2014) concluded that corpus callosum, anterior thalamic radiation, and the corticospinal tract showed the lowest ages at peak FA while the association tracts and the cingulum showed higher ages at peak FA; researchers studied the corpus callosum spelenium and the corpus callosum genu, while the current study examines part of the corpus callosum body. Accordingly, it is proposed that the brain is strengthened in the areas examined because the hearing system, particularly the cochlear, becomes weaker. Otherwise, our results are consistent with previous studies of the auditory radiation that reported a similar increase in FA with aging (Ikuta, Stansberry, & Lowe 2020).

One limitation of this study is that we cannot determine the type of causal relationship between interhemispheric connectivity and the factors of gender and age. Other studies have implications of a correlative relationship between the corpus callosum and aging, proposing that this relationship can be used to distinguish normally aging individuals from those with dementia. Another limitation is that the hearing status of the subjects were not available. Research of this kind informs clinical practice for aural rehabilitation, binaural hearing aid use, and geriatric counseling, so hearing status could have impacted the results of the study. However, the impact of interhemispheric connectivity on hearing ability has not been directly established.

Nonetheless, the current results provide insight on the relationship between the brain and hearing. The interhemispheric connectivity of the auditory cortices is correlated to both factors of gender and age. Further research can be conducted to determine the type of causal relationship between these structures and factors. This research would further provide new insight and understanding of the relationship between the brain and hearing system, how this varies across genders and ages, and how this relationship impacts our daily lives and the audiological profession.

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