Unilateral Sensorineural Hearing Loss in Children is Predicted by Reduced Mean Diffusivity in the Sublenticular Region of the Left Internal Capsule

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Introduction

Prevalence of unilateral hearing loss (UHL) in school-aged children is around 0.4 – 0.5 % for moderate to profound (> 50 dB HL) and could be as high as 1 % for all severities (> 30 dB HL) [1,2]. Thus, in the U.S., approximately 400,000 children have some kind of unilateral hearing loss. Some research suggests that these children may be more at risk for communication, language, and educational problems [3,4]. In this study we use multi-voxel pattern analysis (MVPA) [5] on diffusion tensor imaging (DTI) data to attempt to predict UHL status in children. Knowledge of a neurophysiological marker for UHL may help in understanding its possible relationship to later communicative and language difficulties.

Materials and Methods

The study cohort consisted of 44 children ages 6 – 12 years. Hearing was verified via standard pure-tone audiometry, with normal hearing being < = 15 dB HL. There were 23 normal-hearing children (11 M, 12 F, age ± std. = 9.4 ± 1.37 yrs.), and 21 children with unilateral sensorineural hearing loss (USNHL; 9 M, 12 F, age ± std. = 9.24 ± 1.63 yrs.) Of the children with USNHL, 11 had right-sided and 10 had left-sided deafness, while 3 had mild-to-moderate hearing loss and 18 had severe-to-profound. All USNHL children had a confirmed diagnosis for at least 2 years. The Bamford-Kowal-Bench speech-in-noise (BKB-SIN) test [6] was used to gauge participants' ability to interpret speech in noise; results are the SNR level at which the participant interprets 50% of the words correctly. In addition, participants were tested for higher-order auditory processing ability using three tests: low-pass filtered words, a subtest of the SCAN-C test for auditory processing disorders [7]; and time-compressed sentences at 40% and 60% compression [8].

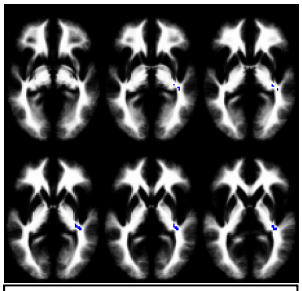

Figure 1. Region found to predict USNHL in children from MD. (Images in radiologic orientation: slice locations: Z = -4 mm to +6 mm, MNI coordinate system)

All DTI scans were acquired on a Siemens 3T Trio system or a Philips 3T Achieva system. Scans were visually inspected for gross motion artifacts, or slice dropouts due to motion during application of the diffusion sensitizing gradient. Fractional anisotropy (FA), mean diffusivity (MD), radial diffusivity (RD), and axial diffusivity (AD) maps were computed. Whole-brain T1-weighted anatomical images were segmented using SPM8 (Wellcome Dept. of Cognitive Neurology, London, UK). FA maps were co-registered to the white matter maps, and the white matter maps were then normalized to the white matter template in SPM8. The transformation was stored and applied to all DTI parameter maps. Analysis was restricted to voxels with FA > 0.25 and WM probability 0.9 in each subject.

The MVPA analysis was performed using in-house routines written in IDL (ENVI, Boulder, CO). A Gaussian Naïve Bayes (GNB) classifier with a 5-X-5-X-5 searchlight was used. Classifier accuracy was estimated using leave-one-out cross-validation (LOOCV). Voxels were selected from the training set by averaging values over the 5-X-5-X-5 cube centered over each voxel, ranking voxels based on performance of the GNB classifier (using LOOCV), and selecting the number of voxels (from the best-ranked) by again estimating performance of the GNB classifier using LOOCV. The GNB was then trained using the selected voxels, and these parameters were then used to classify the test subject.

Results

No classifier was successfully trained for FA, AD, or RD. However, a classifier was successfully trained for MD. Classifier accuracy was 68%, significantly different from chance ($p < 0.02$). The relevant region (Figure 1) was the sublenticular region of the left internal capsule. Children with USNHL show less MD in this region ($p < 0.001$, unpaired T-test). Children with USNHL also exhibit reduced RD ($p < 0.001$, unpaired T-test) but no significant change in AD ($p > 0.15$, unpaired T-test); hence, children with USNHL also show greater FA ($p < 0.02$, unpaired T-test), in this region. There was no difference in any DTI parameter between children with right and left USNHL ($p > 0.5$).

There was a main effect of USNHL status on BKBSIN performance ($F(1,41) = 7.88$, $p < 0.01$). However, neither a main effect of RD or MD, nor a DTI parameter-X-group interaction on BKBSIN performance was shown. There was no significant main effect of USNHL status, DTI parameter, or interaction on any of the other three auditory processing tests.

Discussion

Differences in RD, without differences in AD, are likely the result of activity-dependent changes in myelination [9,10], although differences in axonal caliber are also a possible explanation. The particular region implicated in this study, the sublenticular region of the left internal capsule, has connections to the thalamus and the auditory cortex through the auditory radiations. Thus, our results appear to indicate increased myelination and therefore improved connectivity in children with USNHL in the final part of the auditory pathway connecting the medial geniculate to the auditory cortex in the left hemisphere. In children with UHL, reorganization of auditory pathways [11] occurs such that ipsilateral pathways become as prominent as contralateral ones. In addition, due to the lack of binaural input, one would expect decreased use of the binaural pathway (comprising neurons in the ventral cochlear nucleus synapsing in the superior olivary complex), and concomitantly more use of the monaural pathway (comprising neurons in the dorsal cochlear nucleus directly connecting with the inferior colliculus). Our results show this experience-dependent plasticity to also affect the section of the auditory pathway above the inferior colliculus (the last point in the pathway where there is decussation).

However, the decreased RD and MD did not appear to be associated with performance on higher-order auditory processing tasks involving language. This may indicate a cortical etiology of the deficit seen in interpretation of speech-in-noise in children in USNHL. Future research will involve prediction of auditory processing and language performance from neuroimaging data, using classifiers able to predict continuous variables, such as Support Vector Regression [12].

Conclusion

Unilateral sensorineural hearing loss in children is predicted by decreased MD in the sublenticular portion of the left internal capsule, which connects the medial geniculate body to the auditory cortex. This difference is not associated with performance differences in higher-order auditory and language processing tasks, indicating a possible cortical etiology.

References

[1] Lee, D.J., et al., *Ear Hear*, 19, 329-332, 1998. [2] Peckham, C.S., et al., *Dev Med Child Neurol*, 14, 592-602, 1972. [3] Culbertson, J.L. & Gilbert, L.E., *Ear Hear*, 7, 38-42, 1986. [4] Downs, M.P. In: Roeser, R. & Downs, M.P. (Eds.), *Auditory disorders in school children*, 188-200, 1994. [5] Pereira F. et al., *Neuroimage*, 45(1 Suppl), S199-209, 2009. [6] Bench J., et al., *Br J Audiol*, 13, 108-112, 1979. [7] Keith, R.W., *J Am Acad Audiology*, 11, 438-445, 2000. [8] Keith R.W., *J Educational Audiology*, 10, 15-20, 2002. [9] Dubois, J., et al., *Hum Brain Mapp*, 29, 14-27, 2008. [10] Fields, D.R., *Neuroscientist*, 11, 528-531, 2005. [11] Vasama, J.P., et al., *Neuroreport*, 6, 961-964, 1995. [12] Vapnik, V., et al. In: Mozer, M., et al. (Eds.), *Neural Information Processing Systems*, Vol, 9, 1997.