

# Unilateral hearing loss in children affects development of the default mode network

Vincent Schmithorst<sup>1,2</sup>, Scott Holland<sup>2</sup>, and Elena Plante<sup>3</sup>

<sup>1</sup>Radiology, Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA, United States, <sup>2</sup>Radiology, Children's Hospital Medical Center, Cincinnati, OH, United States,

<sup>3</sup>Speech, Language, and Hearing Sciences, University of Arizona - Tucson, Tucson, AZ, United States

## Target Audience

Researchers interested in the development of the default-mode network (DMN) and effects of mild sensory deprivation on development of the connectome.

## Purpose

There is currently a paucity of data on how higher-order cognitive processes may be affected by subtle sensory deficits such as experienced by children with unilateral hearing loss (UHL). UHL primarily affects sound localization abilities, as inter-ear differences in amplitude and phase used for sound localization in binaural-hearing individuals are unavailable. However, children with UHL also show difficulties in speech and language, and exhibit academic, behavioral, and psychosocial deficits<sup>1</sup>. The neurological underpinnings of these deficits are currently unknown. In this study we investigate the neural correlates of audio-visual association in children with UHL.

## Methods

Participants with UHL (N = 21) and normal-hearing controls (N = 23) between 7 and 12 years of age were either referred from the Audiology Clinic at Children's Hospital Medical Center (CCHMC), or were recruited via flyers placed at CCHMC main and satellite locations. All participants with USNHL had normal hearing ( $\leq 15$  dB HL) in the good ear and at least mild sensorineural hearing loss ( $> 40$  dB HL) in the impaired ear. Participants with mixed or conductive loss were excluded. All normal-hearing participants had  $\leq 15$  dB HL in both ears. Normal levels of cognitive function were verified via the Wechsler Full-Scale Intelligence Scale for Children (WISC-IV).

All scans were acquired either on a Siemens 3T Trio system or on a Philips 3T Achieva system. The fMRI paradigm consisted of a "modified token task" in which an orange arrow moves from one "token" (a completely filled-in shape) on the video screen to another token. Simultaneously, the participant hears a sentence such as "Touched the small green square and the large blue circle". The participant was instructed to respond by button press if the presented auditory sentence matched what was seen on the video screen. During the control trials, the visual stimulus was the same but the audio stimulus consisted of a continuous 440 Hz tone. Trials were either "simple" sentences, with "and" as the conjunction; or "complex" sentences, with either "before" or "after" as the conjunction. Stimuli were presented monaurally to the good ear for the UHL cohort; and monaurally to an ear selected at random for the normal-hearing cohort. A silent-gradient acquisition technique was employed to eliminate interference from the scanner gradients during stimulus presentation. Stimulus order was randomized at runtime.

Frames were grouped according to 1st, 2nd, or 3rd scan after the silent period and analyzed separately. After motion correction, frames were "scrubbed" from analysis if an intensity-based cost function exceeded a threshold determined via visual inspection. Datasets were transformed into stereotaxic space using landmarks from the T1-weighted anatomical images. A General Linear Model was performed for the contrasts of all speech vs. control, simple speech vs. control, complex speech vs. control, with a linear function added to the design matrix as a covariate of no interest to account for possible scanner drift. Magnitudes and variances of functional contrast were combined across frame groups to yield a total T-score.

In the second level analysis, one-sample T-tests were performed on the USNHL and normal-hearing cohorts separately. Results were spatially filtered with  $\sigma = 4$  mm. On the subset of voxels found from this analysis with either significant activation or de-activation, a GLM was performed with USNHL status as the variable of interest and age, sex, full-scale IQ, scanner, square root of the number of retained frames, and side of presentation as covariates of no interest. Results were spatially filtered with  $\sigma = 4$  mm. Using Monte Carlo simulation, intensity and spatial extent thresholds were chosen to correspond to a family-wise-error (FWE) corrected  $p < 0.05$ .

## Results

For the contrast of all sentences vs. control (Figure 1, top), activation was seen in the superior temporal gyrus bilaterally, Broca's area, and audio-visual association areas (BA 19/37/39), while deactivation was seen in medial and lateral DMN regions. Children with UHL displayed greater activation in the posterior aspect of the left superior temporal gyrus (Figure 1, bottom right) and smaller de-activation (Figure 1, bottom left) in the posterior cingulate/precuneus and medial orbitofrontal/prefrontal regions, the major posterior and anterior regions in the DMN. Differences related to UHL status were identical for the contrast of simple sentences vs. control, and complex sentences vs. control (data not shown). We did not find significant differences in regions typically recruited for audio-visual association (BA 19/37/39), although this might be due to insufficient power.

## Discussion

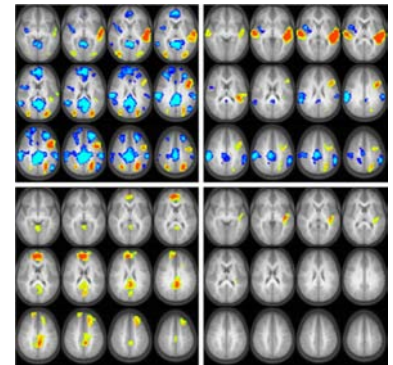
This study provides unique insights into the effects of mild sensory deprivation on brain development. The major finding of our study is deficiencies in DMN deactivation. Deficiencies in DMN deactivation during the performance of demanding cognitive tasks has been demonstrated in various other developmental neuropathologies, including math disability<sup>2</sup>, dyslexia, autism, schizophrenia, and ADHD<sup>3</sup>. Previously, academic and consequent behavioral and psychosocial difficulties by children with UHL have been thought to be the result of sensory difficulties in interpreting speech-in-noise (e.g. a teacher in a noisy classroom). However, attempted interventions such as contralateral routing of signal (CROS) hearing aids, preferential seating, or FM amplification systems have produced equivocal results.

## Conclusion

The evidence of altered physiology accompanying UHL strongly suggests that 'one good ear' is not enough to promote normal function. This physiologic signature may underlie the poor academic outcomes associated with UHL. An important question for future research is to investigate whether DMN deficiencies are a mere epiphenomenon of other, more fundamental neuropathologies; or whether, in fact, DMN deficiencies are themselves a fundamental neurobiological etiology of various disorders, which differ in both behavioral manifestations as well as regional brain function and structure.

## References

1. Lieu JE, Tye-Murray N, Fu Q. Longitudinal study of children with unilateral hearing loss. *Laryngoscope*. Sep 2012;122(9):2088-2095.
2. Davis N, Cannistraci CJ, Rogers BP, et al. Aberrant functional activation in school age children at-risk for mathematical disability: a functional imaging study of simple arithmetic skill. *Neuropsychologia*. Oct 2009;47(12):2470-2479.
3. Christakou A, Murphy CM, Chantiluke K, et al. Disorder-specific functional abnormalities during sustained attention in youth with Attention Deficit Hyperactivity Disorder (ADHD) and with Autism. *Mol Psychiatry*. Jan 31 2012.



**Figure 1.** Top row: regions with significant activation (hot colors) or deactivation (cold colors) from normal-hearing children (left) and children with UHL (right) performing an audio-visual "modified token" task.

Bottom row: regions with significantly greater deactivation in normal-hearing children (left) and significantly greater activation in children with UHL (right). Images in radiologic orientation.