NeuroImage 90 (2014) 84–92

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Association of hearing impairment with brain volume changes in older adults

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ARTICLE INFO

Article history:
Accepted 29 December 2013
Available online 9 January 2014

Keywords:
Hearing loss
Hearing impairment
MRI
Brain volume
Aging

ABSTRACT

Hearing impairment in older adults is independently associated in longitudinal studies with accelerated cognitive decline and incident dementia, and in cross-sectional studies, with reduced volumes in the auditory cortex. Whether peripheral hearing impairment is associated with accelerated rates of brain atrophy is unclear. We analyzed brain volume measurements from magnetic resonance brain scans of individuals with normal hearing versus hearing impairment (speech-frequency pure tone average > 25 dB) followed in the neuroimaging substudy of the Baltimore Longitudinal Study of Aging for a mean of 6.4 years after the baseline scan (n = 126, age 56–86 years). Brain volume measurements were performed with semi-automated region-of-interest (ROI) algorithms, and brain volume trajectories were analyzed with mixed-effect regression models adjusted for demographic and cardiovascular factors. We found that individuals with hearing impairment (n = 51) compared to those with normal hearing (n = 75) had accelerated volume declines in whole brain and regional volumes in the right temporal lobe (superior, middle, and inferior temporal gyri, parahippocampus, $p < .05$). These results were robust to adjustment for multiple confounders and were consistent with voxel-based analyses, which also implicated right greater than left temporal regions. These findings demonstrate that peripheral hearing impairment is independently associated with accelerated brain atrophy in whole brain and regional volumes concentrated in the right temporal lobe. Further studies investigating the mechanistic basis of the observed associations are needed.

Introduction

Two converging lines of evidence suggest that hearing impairment and alterations in peripheral auditory function could directly or indirectly lead to central effects on brain structure and function. Cross-sectional neuroimaging studies have demonstrated that peripheral hearing impairment is associated with reduced cortical volumes in the primary auditory cortex (Eckert, Cute et al., 2012; Husain, Medina et al., 2010; Peelle, Troiani et al., 2011) and variation in the integrity of central auditory white matter tracks (Chang, Lee et al., 2004; Lin, Wang et al., 2008). The basis of these associations remains unknown but may be related to alterations in the degree of neural activation provided by an impoverished auditory signal with subsequent structural changes in cortical reorganization and brain morphometry (Peelle, Troiani et al., 2011). Interestingly, degradation in the fidelity of peripheral encoding of sound likely results in recruitment and activation of broader neural networks needed for auditory processing (Davis and Johnsrude, 2007; Peelle, Johnsrude et al., 2010; Wingfield and Grossman, 2006), suggesting that peripheral hearing impairment may carry cascading consequences for other brain regions.

Broader functional implications of hearing impairment are suggested by epidemiologic studies investigating the association of hearing impairment with cognitive functioning. In these studies of older adults, peripheral hearing impairment was independently associated with poorer neurocognitive performance on both auditory and non-auditory tests (Gussekloo, de Craen et al., 2005; Lin, 2011; Lin, Ferrucci et al.,

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http://dx.doi.org/10.1016/j.neuroimage.2013.12.059

2011; Lindenberger and Baltes, 1994; Tay, Wang et al., 2006), accelerated rates of cognitive decline (Lin, Yaffe et al., 2013), and increased risk of incident all-cause dementia (Gallacher, Ilubaera et al., 2012; Lin, Metter et al., 2011). Hypothesized mechanisms to explain these associations include a shared neuropathologic etiology, cognitive load from the reallocation of brain resources for auditory processing (Tun, McCoy et al., 2009; Wingfield, Tun et al., 2005), and/or mediation through social isolation (Barnes, Mendes de Leon et al., 2004; Bennett, Schneider et al., 2006).

Whether peripheral hearing impairment is associated with regions outside the primary auditory cortex and with changes in brain volumes is unknown. A priori, we hypothesized that hearing impairment is associated with greater volume declines in regional brain volumes important for auditory and spoken language processing (superior, middle, and inferior temporal gyri) (Adank, 2012; Davis and Gaskell, 2009; Peelle, 2012). Understanding the association of hearing impairment with structural brain volumes may provide insights into mechanistic pathways through which peripheral impairments in sensory function could contribute to brain aging.

Methods

Study participants

Participants were followed in the neuroimaging substudy (Resnick, Goldszal et al., 2000) of the BLSA, an ongoing prospective study of the effects of aging that was initiated in 1958 and is conducted by the National Institute on Aging (Shock, Greulich et al., 1984). The present investigation is based on a longitudinal cohort of participants (n = 126, ages 56–86 at baseline) who were enrolled beginning in 1994 in the neuroimaging substudy of the BLSA and had audiometric assessments. Baseline was defined as the time at the first MRI scan. Individuals enrolled in the neuroimaging substudy were free of central nervous system disease (epilepsy, stroke, bipolar illness, prior diagnosis of dementia according to Diagnostic and Statistical Manual [DSM]-III-R criteria (Spitzer and Williams, 1987)), severe cardiac disease (myocardial infarction, coronary artery disease requiring angioplasty or bypass surgery), pulmonary disease, or metastatic cancer. Two participants were later diagnosed with having mild cognitive impairment at baseline based on retrospective review of their baseline neurocognitive and clinical data. Audiometric testing was performed concurrently or before enrollment in the neuroimaging substudy, and the mean time from hearing assessment to the baseline magnetic resonance (MR) scan was 1.7 years (range 0–5 years). Neuroimaging data gathered at and following dementia diagnosis were excluded in 13 participants who developed incident dementia during follow-up. All longitudinal MR scans prior to dementia diagnosis were included in analyses, for a total of 872 imaging observations from 126 participants. The mean number of scans obtained on participants was 6 (range 1–10). The NIA and the Johns Hopkins School of Medicine Institutional Review Boards approved this study, and all participants gave informed consent.

Audiometry

Pure-tone audiometric testing is a measure of the sensitivity of the peripheral auditory system (Pickles, 2008) and was performed using a semi-automated testing device (Virtual Equipment Co., Audiometer Model 320) in a sound-attenuating booth. A speech-frequency pure tone average (PTA) of air-conduction thresholds at 0.5, 1, 2, and 4 kHz was calculated for each ear. Hearing impairment was defined as a PTA > 25 dB in the better-hearing ear per the World Health Organization's definition of hearing impairment (WHO) (the level at which hearing impairment begins to impair daily communication) (WHO World Health Organization Prevention of Blindness and Deafness (PBD) Program, n.d). All thresholds are expressed in dB HL (ANSI, 1989).

MRI acquisition

MR imaging was performed annually on a GE Signa 1.5 T scanner (Milwaukee, WI) using a high-resolution volumetric spoiled-grass axial series (repetition time = 35 msec, echo time = 5 msec, field of view = 24 cm, flip angle = 45°, matrix = 256 × 256, number of excitations = 1, voxel dimensions 0.94 × 0.94 × 1.5 mm).

MRI analysis

Image processing procedures have been previously validated and described (Davatzikos, Genc et al., 2001; Goldszal, Davatzikos et al., 1998; Resnick, Pham et al., 2003). Briefly, images are corrected for head tilt and rotation, and reformatted parallel to the anterior–posterior intercommissural plane. Extracranial tissue is removed using a semiautomated procedure followed by manual editing. Next, images are segmented into white matter (WM), gray matter (GM), and CSF. The final step involves stereotaxic normalization and tissue quantitation for specific regions of interest (ROI). A template-based deformation approach is employed, using the ICBM standard MRI (Montreal Neurologic Institute) as the template and a hierarchical elastic matching algorithm for ROI determination (Shen and Davatzikos, 2002) (see Fig. 1 for ROI locations used in this study). Voxel-based analysis utilizes our RAVENS approach (regional analysis of volumes examined in normalized space) (Goldszal, Davatzikos et al., 1998), whereby local values of tissue density maps (GM, WM, and CSF) reflect the amount of respective tissue in the vicinity of a voxel. Tissue densities are mathematical quantities measuring local tissue volumes and do not reflect any microstructural physical density of brain tissue. Intracranial volume (ICV) is determined using the template warping algorithm modified for head image registration. First, the ICV in the template is manually delineated by an expert. Then, the template with its ICV mask is warped to the space of each individual head to extract the ICV of the individual.

Other covariates

We adjusted for covariates such as cardiovascular (hypertension, smoking) and demographic risk factors (age, sex) that are known to be associated with hearing impairment (Lin, Thorpe et al., 2011) and that could potentially confound the association of hearing impairment with structural brain volumes. The diagnosis of hypertension

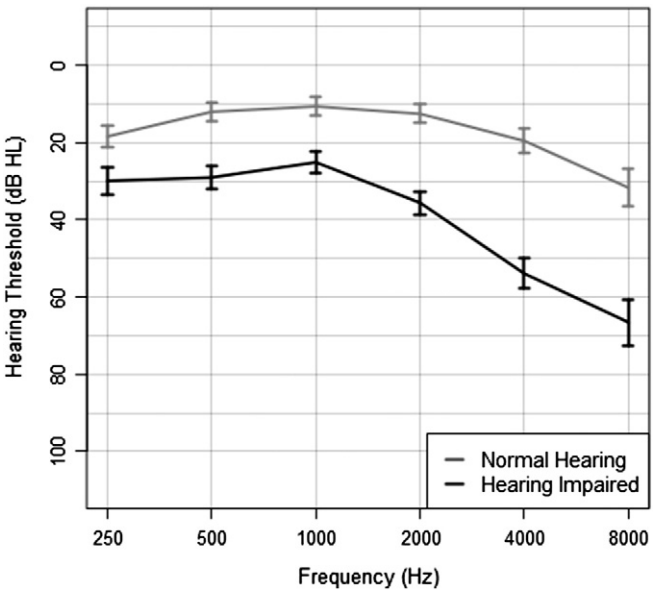

Fig. 1. Mean audiograms of individuals with normal hearing (n = 75) and hearing impairment (n = 51). Error bars denote 95% confidence intervals of the mean.