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Research paper

Brain structural and functional alterations in patients with unilateral hearing loss

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ABSTRACT

Alterations of brain structure and functional connectivity have been described in patients with hearing impairments due to distinct pathogenesis; however, the influence of unilateral hearing loss (UHL) on brain morphology and regional brain activity is still not completely understood. In this study, we aim to investigate regional brain structural and functional alterations in patients with UHL. T1-weighted volumetric images and task-free fMRIs were acquired from 14 patients with right-sided UHL (pure tone average $\geq$ 40 dB HL) and 19 healthy controls. Hearing ability was assessed by pure tone audiometry. Voxel-based morphometry (VBM) was performed to detect brain regions with changed gray matter volume or white matter volume in UHL. The amplitude of low-frequency fluctuation (ALFF) was calculated to analyze brain activity at the baseline and was compared between two groups. Compared with controls, UHL patients showed decreased gray matter volume in bilateral posterior cingulate gyrus and precuneus, left superior/middle/inferior temporal gyrus, and right parahippocampal gyrus and lingual gyrus. Meanwhile, patients showed significantly decreased ALFF in bilateral precuneus, left inferior parietal lobule, and right inferior frontal gyrus and insula and increased ALFF in right inferior and middle temporal gyrus. These findings suggest that chronic UHL could induce brain morphological changes and is associated with aberrant baseline brain activity.

1. Introduction

Sudden sensorineural hearing loss (SNHL) is a relatively common complaint in otologic and audiologic practices (Kuhn et al., 2011). The incidence of sudden SNHL is 5–20 per 100,000 (Fetterman et al., 1996). Of these patients, only approximately 2% have bilateral hearing impairments and most patients are diagnosed as unilateral hearing loss (UHL) (Fetterman et al., 1996). Interestingly, it is demonstrated that in addition to hearing impairments, patients with SNHL may show deficiency in other brain functions. For example, SNHL is found to be correlated with the cognitive, behavioral-emotional, and motor disorders (Chilosi et al., 2010). Additionally, Borton and Borton's colleagues (Borton et al., 2010) have found that UHL is associated with worse speech-language scores in children and may affect health-related quality of life. In fact, individuals with hearing deficits have been reported to have increased risk to develop cognitive and emotional processing impairments (Boi et al., 2012; Kiely et al., 2012; Lin, 2011; Lin et al., 2013, 2004). Moreover, it has been reported that in many SNHL cases, hearing will not be improved even after appropriate therapy and UHL persists (Kuhn et al., 2011), which may suggest the existence of irreversible impairments (e.g., brain structural change) in these patients.

Alterations in brain structure have been described in patients with hearing loss or deafness (Chang et al., 2004; Kim et al., 2009; Li et al., 2012; Lin et al., 2008; Shibata, 2007). Several brain areas, including both auditory and non-auditory areas (e.g., frontal and occipital cortex), frequently show abnormal cerebral gray matter and/or whiter matter structures. However, inconsistencies in cerebral structural changes can be found across previous studies. For example, Boyen et al. (Boyen et al., 2013) reported that patients

Abbreviations: SNHL, sensorineural hearing loss; UHL, unilateral hearing loss; HL, hearing loss; VBM, voxel-based morphometry; GMV, gray matter volume; WMV, white matter volume; ALFF, amplitude of low-frequency fluctuation; fMRI, functional magnetic resonance imaging; PTA, pure tone average; BOLD, blood oxygen level dependent

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with HL show decreased gray matter volume in the frontal area and increased gray matter volume in the temporal cortex. However, many other studies reveal brain atrophy and impaired microstructure induced by hearing loss. For example, cortical thinning and white matter atrophy are found in adolescents with prelingually profound SNHL (Li et al., 2012). Additionally, Shibata (Shibata, 2007) has emphasized the focal deficit of white matter in superior temporal gyrus in young prelingually deaf people. Meanwhile, decreased gray matter volume in the vicinity of the auditory cortex and impaired white matter microstructural integrity are reported in bilateral hearing-loss patients by Husain et al. (Husain et al., 2011). Taken together, given the inconsistent results in previous studies, a new study would provide additional insight into neuroanatomical changes in the presence of hearing impairments. In this study, we would like to investigate the influence of UHL on cerebral morphology, which has not been well revealed previously, especially in the adults. Given the reports of HL-related disuse-driven atrophy (Emmorey et al., 2003; Kim et al., 2009) and the fact that acoustic stimulations can contribute to larger auditory cortex (Schneider et al., 2002), we hypothesize that patients with UHL could develop atrophic brain structural changes.

Recently, the task-free (resting-state) functional magnetic resonance imaging (fMRI) has attracted attention in the study of spontaneous brain activity (Mantini et al., 2007) and has been used to reflect brain dysfunctions in various neuropsychological diseases, such as Alzheimer's disease, Parkinson's disease, and major depression. Based on the task-free fMRI method, the disruptions of intrinsic functional connectivity have been observed in patients with hearing impairments (Husain, 2014; Schmidt et al., 2013). In patients with hearing loss and/or tinnitus, disconnections are found in several brain networks, including default-mode, dorsal attention, and auditory networks (Schmidt et al., 2013). Moreover, abnormal brain interregional functional connections have been revealed in UHL children (Tibbetts et al., 2011). However, the existing studies only focused on the changes in the connectivity between disparate regions rather than regional brain activity. The patterns of intrinsic brain activity in patients with UHL across the whole brain are still poorly understood.

In this study, we aim to investigate the alterations in cerebral gray matter volume (GMV) and white matter volume (WMV) in patients with UHL, using the voxel-based morphometry (VBM) method. In addition, we will explore the aberrant regional brain activity at baseline by measuring the amplitude of low-frequency fluctuation (ALFF) of the fMRI signal. To our best knowledge, this is the first study about regional brain structural and functional changes in adult patients with acquired UHL.

2. Patients and methods

2.1. Patients

This study is comprised of 33 subjects: 14 patients with right-sided hearing loss and 19 healthy controls. The inclusion criterion was moderate-to-severe sudden sensorineural UHL. The patients included were right-handed and 41–60 years old. Pure tone audiometry with six different octave frequencies (0.25, 0.5, 1, 2, 4 and 8 kHz) was performed by a clinical audiometer to measure the pure tone average (PTA) and reflect hearing level. All patients in this study were diagnosed with right-sided hearing loss with hearing deficit in the right ear (PTA $\geq$ 40 dB HL) and normal hearing in the left ear (PTA $\leq$ 25 dB HL). The audiogram of the affected ear of each patient is shown in Fig. 1. For each patient, the hearing loss was sudden and persistent. None used a hearing aid on the impaired ear. The control group was well matched to the patient group in terms of age, sex, and education level (Table 1). Exclusion criteria

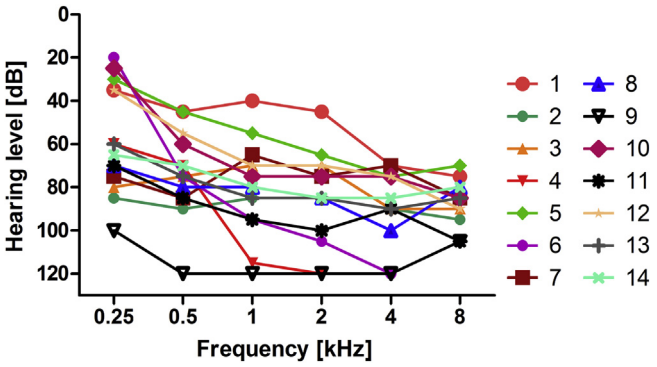

Fig. 1. The frequency-dependent hearing level of each subject in the affected ear.

for all participants were known neurological or psychiatric diseases, taking psychotropic medications, brain lesions such as tumors or strokes, and contraindications to MR imaging. This study was approved by the Ethics Committee of Southeast University, and a signed informed consent form was obtained from every subject prior to entering this study.

2.2. MRI acquisition

MR images were obtained using a Siemens Verio Tim 3.0 T MR scanner (Siemens Medical Solutions, Erlangen, Germany). All subjects were instructed to lie as still as possible with their eyes closed and not to fall asleep. For the task-free fMRI sequence, the echo-planar imaging sequence was used, with the following parameters: 36 slices, repetition time (TR) = 2000 ms, echo time (TE) = 25 ms, field of view (FOV) = 240 mm × 240 mm, matrix = 64 × 64, flip angle 90°, slice thickness = 4 mm, and a total of 240 volumes. We acquired 3D high-resolution brain structural images using a magnetization-prepared rapid acquisition gradient echo (MP-RAGE) sequence. The sequence parameters were: TR = 1900 ms, TE = 2.48 ms, inversion time (TI) = 900 ms, flip angle = 9°, FOV = 256 mm × 256 mm, matrix = 256 × 256, slice thickness = 1 mm, and 176 sagittal slices covering the whole brain.

2.3. Structural data processing

Image processing was performed using the VBM 8 toolbox (http://dbm.neuro.uni-jena.de/vbm/) that runs in Statistical Parametric Mapping software (SPM8) (http://www.fil.ion.ucl.ac.uk/spm/software/spm8/). In brief, T1-weighted images were corrected for bias-field inhomogeneity, registered using linear (12-parameter affine) and nonlinear transformations, and tissue-classified into gray matter, white matter, and cerebro-spinal fluid within the same generative model (Ashburner and Friston, 2005). The diffeomorphic non-linear registration tool (diffeomorphic anatomical registration through exponential lie algebra – DARTEL) was used to improve inter-subject registration (Ashburner, 2007). The resulting GM images were modulated to account for volume

Table 1
Clinical and demographic data of all subjects.

	Right UHL	Controls	*P* value
Age (year)	53.9 ± 7.6	53.6 ± 5.4	0.90
Male/female	5/9	8/11	0.50
Education level (year)	12.1 ± 2.4	11.5 ± 3.2	0.55
Disease duration (year)	14.2 ± 14.9	–	–
PTA of left ear (dB HL)	21.8 ± 3.2	22.2 ± 2.1	0.64
PTA of right ear (dB HL)	80.9 ± 17.4	21.3 ± 2.2	<0.001

Note: UHL – unilateral hearing loss; PTA – pure tone average.