Neuroscience 285 (2015) 333–342

CHANGES IN THE DEFAULT MODE NETWORKS OF INDIVIDUALS WITH LONG-TERM UNILATERAL SENSORINEURAL HEARING LOSS

G.-Y. ZHANG,[a,c*] M. YANG,[a] B. LIU,[a] Z.-C. HUANG,[b] H. CHEN,[b] P.-P. ZHANG,[b] J. LI,[a] J.-Y. CHEN,[a] L.-J. LIU,[d] J. WANG[d,e] AND G.-J. TENG[a]

[a] *Department of Radiology, Jiangsu Key Laboratory of Molecule Imaging and Functional Imaging, Medical School of Southeast University, 87 Dingjiaqiao Road, Nanjing 210009, China*

[b] *Department of Otorhinolaryngology and Head-neck Surgery, Zhong-Da Hospital, Medical School of Southeast University, 87 Dingjiaqiao Road, Nanjing 210009, China*

[c] *Department of Radiology, Taishan Medical University, Chang Cheng Road, Hi-Tech Development Zone, Taian 271016, Shandong Province, China*

[d] *Department of Physiology and Pharmacology, Medical School of Southeast University, 87 Dingjiaqiao Road, Nanjing 210009, China*

[e] *School of Human Communication Disorder, Dalhousie University, 1256 Barrington St, Halifax B3J1Y6, Canada*

Abstract—Hearing impairment contributes to cognitive dysfunction. Previous studies have found changes of functional connectivity in the default mode network (DMN) associated with cognitive processing in individuals with sensorineural hearing loss (SNHL). Whereas the changes in the DMN in patients with long-term unilateral SNHL (USNHL) is still not entirely clear. In this work, we analyzed resting-state functional magnetic resonance imaging (fMRI) data and neuropsychological test scores from normal hearing subjects ($n = 11$) and patients ($n = 21$) with long-term USNHL. Functional connectivity and nodal topological properties were computed for every brain region in the DMN. Analysis of covariance (ANCOVA) and post hoc analyses were conducted to identify differences between normal controls and patients for each measure. Results indicated that the left USNHL presented enhanced connectivity ($p < 0.05$, false discovery rate (FDR) corrected), and significant changes ($p < 0.05$, Bonferroni corrected) of the nodal topological properties in the DMN compared with the control. More changes in the DMN have been found in the left than right long-term USNHL (RUSNHL). However, the neuropsychological tests did not show significant differences between the USNHL and the control. These findings suggest that long-term USNHL contributes to changes in the DMN, and these changes might affect cognitive abilities in patients with long-term USNHL. Left hearing loss affects the DMN more than the right hearing loss does. The fMRI measures might be more sensitive for observing cognitive changes in patients with hearing loss than clinical neuropsychological tests. This study provides some insights into the mechanisms of the association between hearing loss and cognitive function.

Key words: unilateral sensorineural hearing loss, default mode network, functional connectivity, nodal topological property, cognitive function.

INTRODUCTION

Hearing loss and cognitive dysfunction commonly occur in adults over the age of 60 (Gennis et al., 1991). Several investigations on bilateral hearing loss have found an association between hearing and cognitive dysfunction, these studies suggest that hearing impairment contributes to cognitive dysfunction (Tay et al., 2006; Lin, 2011; Lin et al., 2011, 2013). However, it remains unclear whether partial hearing deprivation would similarly affect cognitive processing in patients with unilateral sensorineural hearing loss (USNHL).

The default mode network (DMN) (Raichle et al., 2001) is associated with cognitive processes—for example, emotional processing and self-referential mental activity (Lane et al., 1997; Gusnard et al., 2001), conflict monitoring (Kerns et al., 2004), memory retrieval (Wheeler et al., 2006) and cognitive control (Leech et al., 2011). Functional magnetic resonance imaging (fMRI) investigations have found enhanced functional connectivity (Husain et al., 2014; Wang et al., 2014) in the DMN in patients with sensorineural hearing loss (SNHL). Whereas task-based fMRI study reported an opposite result that children with USNHL displayed reduced deactivation of anterior and posterior regions of the DMN (Schmithorst et al., 2014). The former focuses on children, while the latter focuses on an adult population, which perhaps makes the difference. However, to update, the changes in the DMN in patients with long-term USNHL is still not entirely clear, and whether these

*Correspondence to: G.-Y. Zhang, Department of Radiology, Taishan Medical University, Chang Cheng Road, Hi-Tech Development Zone, Taian 271016, Shandong Province, China. Tel: +86-05386222723. E-mail address: gyuzhn@163.com (G.-Y. Zhang).

Abbreviations: ANCOVA, analysis of covariance; AVM, auditory verbal memory; AVMTR, auditory verbal memory test-delayed recall; BAs, Brodmann's areas; BDS, backward digit spans; DMN, default mode network; DSST, digit symbol substitution test; FDR, false discovery rate; FDS, forward digit spans; fMRI, functional magnetic resonance imaging; HL, hearing level; LUSNHL, left long-term USNHL; MMSE, mini-mental state examination; MNI, Montreal Neurological Institute; MPFC, medial prefrontal cortex; ROI, region of interest; RUSNHL, right long-term USNHL; SCWA, Stroop color–word test A; SCWB, Stroop color–word test B; SCWC, Stroop color–word test C; SNHL, sensorineural hearing loss; SS, semantic similarity; TMTA, trail making test part A; TMTB, trail making test part B; USNHL, unilateral SNHL; VF, verbal fluency.

http://dx.doi.org/10.1016/j.neuroscience.2014.11.034
0306-4522/

changes impact the cognitive abilities of patients is also unclear.

Mathematical models for computational network analysis based on graph theory have been applied to brain connectivity, in which the brain network is modeled as a graph with the nodes representing different brain regions, and the edges representing interregional connectivity (Whitlow et al., 2011). The topological properties of the entire brain network reflect the entire performance of the network, whereas the nodal topological properties of the brain regions reflect local performance of the network. Graph theory network analyses have demonstrated that patients with central nervous systemic dysfunction showed changes in the topological properties of the brain network (He et al., 2009; Bai et al., 2012). A recent study on nodal topological properties found that more topological clustering was associated with impaired cognitive performance (Giessing et al., 2013).

Therefore, we presume that long-term USNHL contributes to changes of functional connectivity in the DMN of patients, and further affects the nodal topological properties of the brain network. These changes impact cognitive processing. We expect that investigation on changes in the DMN can provide some insights into the mechanisms of the association between hearing loss and cognitive function.

EXPERIMENTAL PROCEDURES

Subjects

The protocol of this prospective study was approved by the institutional Ethics Committee of Southeast University, Nanjing, China, and all participants or their guardians signed informed consent forms prior to the experiment. A total of 32 subjects were recruited from Nanjing. Specifically, 11 patients (age, 27–60 years; mean = 47.2 ± 10.8 years; duration of the hearing loss, 2–50 years; mean = 14.9 ± 17.9 years; age at onset of unilateral hearing loss, 5–58 years, mean = 32.27 ± 19.42 years) had left long-term USNHL (LUSNHL) without tinnitus, 10 patients (age, 42–66 years; mean = 55.2 ± 6.8 years; duration of the hearing loss, 2–50 years; mean = 13.3 ± 14.6 years, age at onset of unilateral hearing loss, 16–55 years, mean = 41.90 ± 12.80 years) had right long-term USNHL (RUSNHL) without tinnitus, and 11 (age, 27–67 years; mean = 51.7 ± 12.4 years) were normal hearing volunteers. Hearing loss was acquired due to right acoustic neuroma in one patient, deafness was caused by infection in two patients, and hearing loss in others was unknown cause. All were right-handed and none of them had a history of medical, psychiatric disorders, strokes/cerebrovascular ischemia, head trauma/fractures. The frequency-averaged speech-frequency thresholds (0.25, 0.5, 1.0 and 2 kHz) of every individual was measured by pure tone audiometry. For the USNHL groups, the average hearing level (HL) was at least 70 dB in the deaf ear and less than 25 dB in the better hearing ear. All unilaterally deaf subjects had post-lingual deafness. Eleven control subjects were healthy volunteers with pure tone average below 25 dB HL for both ears. Cognitive abilities of participants were measured by the neuropsychological tests.

No subjects were excluded because of excessive head movement (greater than 2.5 mm or 2.5°) during imaging.

MR imaging

All imaging was performed on a SIEMENS Verio 3-T scanner. Each subject underwent an 8.06-min scan during a conscious resting-state. Functional images were collected axially using an echo-planar imaging sequence sensitive to blood oxygen level dependent (BOLD) contrast. The following parameters were used: 2000/25 ms (repetition time/echo time), 36 slices, 64×64 (matrix size), $3.75 \times 3.75 \times 4$ mm (voxel size), 1 mm (gap), 240×240 mm (field of view), 90° (flip angle). A high-resolution, three-dimensional T1-weighted structural image was also acquired for each subject using a magnetization prepared gradient echo sequence [repetition time (TR) = 1900 ms, echo time (TE) = 2.48 ms, flip angle = 9°, 176 slices with $0.975 \times 0.975 \times 1$ mm voxels].

During the resting-state scanning, the light was switched off. The subjects wore earplugs and headphones to reduce noise, and were instructed to keep still with their eyes closed, as motionless as possible and not to think about anything in particular. Head movement was minimized by placing soft pads at the sides of the head. All subjects did not fall asleep, as confirmed by the subjects after completion of the experiment.

Neuropsychological tests

Mini-mental state examination (MMSE) and Wechsler adult intelligence test (Wechsler, 1997) were used to assess the cognitive abilities of the participants. Tests were administered in a quiet setting with minimal distractions. Experienced examiners who were accustomed to working with deaf patients verbally gave all instructions in a face-to-face manner. All of the neuropsychological tests were provided in Mandarin. Participants were tested on (a) MMSE, (b) digit symbol substitution test (DSST), (c) forward digit spans (FDS) and backward digit spans (BDS), (d) verbal fluency (VF), (e) semantic similarity (SS), (f) trail making test part A (TMTA), (g) trail making test part B (TMTB), (h) Stroop color–word test A (SCWA), (i) Stroop color–word test B (SCWB), (j) Stroop color–word test C (SCWC), (k) auditory verbal memory (AVM), and (l) auditory verbal memory test-delayed recall (AVMTR). MMSE was performed for likely cognitive impairment, with test components covering concentration, language, and memory (Tay et al., 2006). DSST performance recruited different interrelated abilities such as perceptual speed, motor speed, response selection, and shifting of attention, as well as working memory (Fratiglioni et al., 2000). FDS was thought to measure the storage and maintenance components of working memory, and BDS was a complex task that relies heavily on working memory processing because it requires information storage as well as concurrent processing essential