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DIFFUSION TENSOR IMAGING AND MR MORPHOMETRY OF THE CENTRAL AUDITORY PATHWAY AND AUDITORY CORTEX IN AGING

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Abstract—Age-related hearing loss (presbycusis) is caused mainly by the hypofunction of the inner ear, but recent findings point also toward a central component of presbycusis. We used MR morphometry and diffusion tensor imaging (DTI) with a 3 T MR system with the aim to study the state of the central auditory system in a group of elderly subjects (>65 years) with mild presbycusis, in a group of elderly subjects with expressed presbycusis and in young controls. Cortical reconstruction, volumetric segmentation and auditory pathway tractography were performed. Three parameters were evaluated by morphometry: the volume of the gray matter, the surface area of the gyrus and the thickness of the cortex. In all experimental groups the surface area and gray matter volume were larger on the left side in Heschl's gyrus and planum temporale and slightly larger in the gyrus frontalis superior, whereas they were larger on the right side in the primary visual cortex. Almost all of the measured parameters were significantly smaller in the elderly subjects in Heschl's gyrus, planum temporale and gyrus frontalis superior. Aging did not change the side asymmetry (laterality) of the gyri. In the central part of the auditory pathway above the inferior colliculus, a trend toward an effect of aging was present in the axial vector of the diffusion (L1) variable of DTI, with increased values observed in elderly subjects. A trend toward a decrease of L1 on the left side, which was more pronounced in the elderly groups, was observed. The effect of hearing loss was present in subjects with expressed presbycusis as a trend toward an increase of the radial vectors (L2L3) in the white matter under Heschl's gyrus. These results suggest that in addition to peripheral changes, changes in the central part of the auditory system in elderly subjects are also present; however, the extent of hearing loss does not play a significant role in the central changes.

Key words: presbycusis, aging, auditory cortex, auditory pathway, MR morphometry, diffusion tensor imaging.

INTRODUCTION

Hearing loss accompanying aging, called presbycusis, is one of the prominent sensory deficits in the elderly. Presbycusis is regularly diagnosed by audiometric methods, which in general comprise pure tone and speech audiometry. Since a major component of presbycusis is the loss of hair cells (Schuknecht and Gacek, 1993), the results of pure tone audiometry mostly reflect the deteriorated function of the auditory periphery, whereas speech audiometry also informs about the changes in the function of the central parts of the auditory system. Recent results of animal experiments point toward an important central component of presbycusis, which is evident mainly from the pathological processing of the temporal parameters of a sound (Eggermont, 1993; Walton et al., 1998; Mendelson and Ricketts, 2001; Caspary et al., 2008; Recanzone et al., 2011; Suta et al., 2011) and on the cellular level, on the dysfunction of a specific population of interneurons containing calcium binding proteins, particularly parvalbumin (Ling et al., 2005; Ouda et al., 2008, 2012). Both of these facts, accompanied by decreases of inhibitory neurotransmitters (Caspary et al., 1990; Burianova et al., 2009; Syka, 2010), point toward altered inhibition in the auditory cortex during aging. The results of many audiological studies (Mazelová et al., 2003; Hwang et al., 2007; Gates et al., 2008; Anderson et al., 2011; Humes et al., 2012) support the existence of a central component of presbycusis, yet direct proof is still missing.

Recent developments in magnetic resonance imaging (MRI), which enable the detection of changes in brain structure and function on a detailed level, promise to give insight into the mechanisms underlying the central

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Abbreviations: AC, auditory cortex; AP, auditory pathway above IC; DTI, diffusion tensor imaging; EP, elderly subjects with expressed presbycusis; FA, fractional anisotropy; GFS, gyrus frontalis superior; GM, gray matter; HG, Heschl's gyrus; IC, inferior colliculus; MD, mean diffusivity; MP, elderly subjects with mild presbycusis; PT, planum temporale; ROI, region of interest; SNHL, sensorineural hearing loss; V1, visual cortex; WM, white matter; WM_HG, white matter under Heschl's gyrus; YC, young subjects with physiologic hearing/young controls.

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component of presbycusis. MRI experiments are focused either on changes in the functional activity of the cortex examined by functional MRI (fMRI) or on morphological changes in the gray and white matter. MRI morphometry provides high resolution structural images focused on measuring the thickness, the overall volume as well as the surface area of the gray matter. One of the most commonly used techniques is voxel based morphometry (VBM) the main advantage of which is the possibility to compare anatomical differences throughout the whole brain with minimal subjective manual evaluation (Ashburner and Friston, 2000).

Similar methods might also be used for evaluating the state of the white matter, but diffusion tensor imaging (DTI) is generally considered as the most suitable examination technique. DTI uses water solubility, especially its isotropic diffusion properties, to evaluate microscopic tissue changes (Beaulieu, 2002). These changes are expressed by fractional anisotropy (FA; normalized value representing the degree of anisotropy of diffusion), mean diffusivity (MD; average rate of diffusion independent of direction) and axial (L1) and radial (L2L3) diffusivity (average rate of diffusion independent of direction represented by eigenvalues of the diffusion tensor) (Basser and Jones, 2002).

MR morphometry and DTI are ideal for detecting structural changes in the human brain. They have been previously used especially in research into several disorders of the central nervous system, such as cognitive decline, Alzheimer's disease, epilepsy, multiple sclerosis, schizophrenia and also hearing loss (Stebbins and Murphy, 2009; Madden et al., 2012). Several recent publications have described morphometric changes in the auditory cortex and in other parts of the cortex accompanying hearing loss. Decreases in the gray matter volume of the superior temporal gyrus (STG) and superior and medial frontal gyri were found in subjects with hearing loss; however, they were not present in subjects with hearing loss and tinnitus (Husain et al., 2011). In contrast to this, (Boyen et al., 2013) reported increases in gray matter volume in the superior and middle temporal gyri both in hearing impaired subjects and also in hearing impaired subjects with tinnitus in comparison with controls. Decreases were found in their study in both impaired groups in the superior frontal gyrus and occipital lobe. Congenital deafness affected predominantly the white matter and caused a decrease in its volume in the left posterior STG without any significant effect on the gray matter in this area (Shibata, 2007). Gray matter asymmetries in deaf persons were found to be similar overall to those in hearing persons with a larger planum temporale and HG in the left hemisphere (Emmorey et al., 2003; Penhune et al., 2003; Shibata, 2007). Previous DTI analysis of the auditory tract and AC showed changes in the auditory pathway associated with sensorineural hearing loss (SNHL) (Chang et al., 2004; Lin et al., 2008).

The aim of this study was to evaluate age-related as well as hearing-related changes in the acoustic pathway and auditory cortex and in related areas by measuring the DTI parameters of the white matter and changes in MR morphometric parameters such as the thickness, overall volume and surface area of the gray matter. The experiments were performed in two groups of aged subjects (one with mild presbycusis and one with expressed presbycusis) and in a control group of young subjects.

EXPERIMENTAL PROCEDURES

Subjects

Fifty-four volunteers were examined in this study: 20 young subjects with physiological hearing (YC) (n = 20 for morphometry, mean age ± SEM 24.34 ± 0.51, 11 men and nine women; n = 12 for DTI; 25.3 ± 0.72; four men and eight women), 17 elderly subjects with mild presbycusis (MP) (n = 17 for morphometry, mean age ± SEM 67.9 ± 0.45; five men and 12 women; n = 12 for DTI, 68.04 ± 0.6; five men and seven women) and 17 elderly subjects with expressed presbycusis (EP) (n = 17 for morphometry, mean age ± SEM 70.38 ± 1.18; five men and 12 women; n = 15 for DTI, 70.43 ± 1.34; nine men and six women). There was no significant difference in age between the two elderly groups (unpaired *t*-test, GraphPad Prism). All subjects were right handed according to the adapted Edinburgh handedness inventory. All subjects denied any previous otologic surgery, vestibular lesion, tinnitus, severe head trauma, lesion of the facial nerve, disorder of the cervical spine, self-reported central nervous system disorder or any contraindication for safe MRI scanning. None of the subjects was a musical professional, but several in both elderly groups played musical instruments regularly during their youth. Otoscopic examination with removal of cerumen and confirmation of an intact tympanic membrane were performed in all examined subjects. The examination procedures were approved by the Ethics Committee of the University Hospital Motol, Prague.

Assesment of auditory function

For assessing the hearing abilities of all subjects, the following procedures were used: tympanometry, pure tone audiometry in an extended frequency range and speech audiometry. Audiometric investigations were performed in a sound attenuated chamber; all measurements were performed monaurally, and the ears of each subject were tested successively.

Tympanometry was performed with an Interacoustics AZ26 tympanometer to confirm optimal middle ear conditions and an intact tympanic membrane. For pure tone audiometry over an extended frequency range from 125 Hz to 16 kHz, a Madsen Orbiter 922, Version 2, audiometer was used, calibrated by the Czech Institute of Metrology according to the Czech State Norm and the European Standards EN ISO 389-1and EN ISO 389-5. Acoustical signals were delivered monaurally via Sennheiser HAD 200 high-frequency headphones. Audiograms were measured in one-octave steps at frequencies ranging from 125 Hz to 8 kHz and then at