Decreased auditory GABA+ concentrations in presbycusis demonstrated by edited magnetic resonance spectroscopy

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Target audience: This work will be of interest to clinicians and researchers studying presbycusis, as well as neuroscientists with an interest in dysfunctional GABAergic neurotransmission in the central auditory system.

Purpose: Gamma-aminobutyric acid (GABA) is the main inhibitory neurotransmitter in the central auditory system[1]. Altered GABAergic neurotransmission has been found in both the inferior colliculus and the auditory cortex in animal models of presbycusis[1-2]. Edited magnetic resonance spectroscopy (MRS), using the MEGA-PRESS sequence, is the most widely used technique for detecting GABA in the human brain. However, to date there has been a paucity of studies exploring changes to the GABA concentrations in the auditory region of patients with presbycusis. In this study, J-difference edited MRS was used to investigate GABA concentrations in the auditory region of patients with presbycusis and healthy controls and their relationship to audiological outcomes.

Methods: The study was approved by the local institutional review board and each participant provided informed consent. Sixteen patients with presbycusis (5 males/11 females, mean age 63.1 ± 2.6 years) and twenty healthy controls (6 males/14 females, mean age 62.5 ± 2.3 years) underwent audiological and MRS examinations. Pure tone audiometry from 0.125 to 8 KHz and tympanometry were used to assess the hearing abilities of all subjects. The pure tone average (PTA; the average of hearing thresholds at 0.5, 1, 2, and 4 kHz) was calculated. All subjects were scanned on a 3T scanner (Philips 'Achieva' TX, Best, The Netherlands) using an eight-channel phased-array head coil for receive. The MEGA-PRESS sequence was used to measure GABA+ concentrations in 4 x 3 x 3 cm^3 volumes centered on the left and right Heschl's gyri (Fig. 1). The following experimental parameters were used: TR 2000 ms; TE 68 ms; 320 averages; acquisition bandwidth 1000 Hz; and total acquisition time 11 minutes. The MEGA-PRESS data were analyzed using 'Gannet' (GABA-MRS Analysis Tool) in Matlab 2010b (Mathworks) with Gaussian curve fitting to the GABA+ peaks[3]. 3 Hz exponential line broadening was applied. The ratios of the integrals of the GABA+ and water signals, making corrections for T1 and T2 relaxation times and partial volume effects, were used to calculate water-scaled GABA+ concentration in mmol/L (mM) using a formula[4-5].

Results: Edited spectra were successfully collected from all 36 subjects, and the fitting error of GABA+ in all spectra was below 10%. GABA+ concentrations were significantly lower in the presbycusis group compared to the control group (left auditory regions: 1.25mM ± 0.40mM vs. 1.65mM ± 0.29mM, p = 0.002; right auditory regions: 1.01mM ± 0.26mM vs. 1.28mM ± 0.31mM, p = 0.008). Significant negative correlations were observed between PTA and GABA+ concentrations in the presbycusis group (r = −0.57, p = 0.02), while a similar trend was found in the control group (r = −0.40, p = 0.08). Significant negative correlations were also observed between PTA and GABA+ concentrations in all subjects (r = −0.72, p < 0.001) (Fig. 2).

Discussion: Our study demonstrates that GABA+ concentrations were reduced in auditory regions of patients with presbycusis, as compared to age- and gender-matched healthy controls. Significant negative correlations between GABA+ concentrations and PTA were also observed in patients with presbycusis. PTA is often used to calculate the degree of hearing loss in speech frequency. The results might demonstrate a mechanistic connection between the GABAergic neurotransmission and hearing function.

Conclusion: These results are consistent with a hypothesis of dysfunctional GABAergic neurotransmission in the central auditory system in presbycusis, and suggest a potential treatment target for presbycusis.

References: [1] Caspary et al., 1995, Exp Gerontol 30, 349-360. [2] Syka, 2010, Hear Res 264, 70-78. [3] Edden et al., 2013, J Magn Reson Imaging, doi: 10.1002/jmri.24478. [4] Gasparovic et al., 2006, Magn Reson Med 55, 1219-1226. [5] Mullins et al., 2014, Neuroimage 86, 43-52. Sponsored by NIH: P41 EB015909, R01 EB016089 and National Natural Science Foundation of China (Grant No. 81171380).

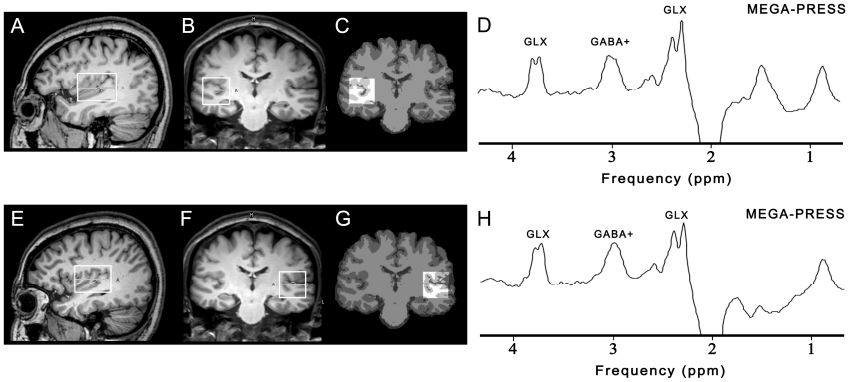

Figure 1. The position of volumes of interest (4 x 3 x 3 cm3) in the right (above) and left auditory region (below) on sagittal (A, E) and coronal (B, F) T1-weighted images. The corresponding results of brain segmentation are shown for the right (C) and left auditory region (G). Representative GABA+-edited MEGA-PRESS spectra from the right auditory region (D) and the left auditory region (H) are shown.

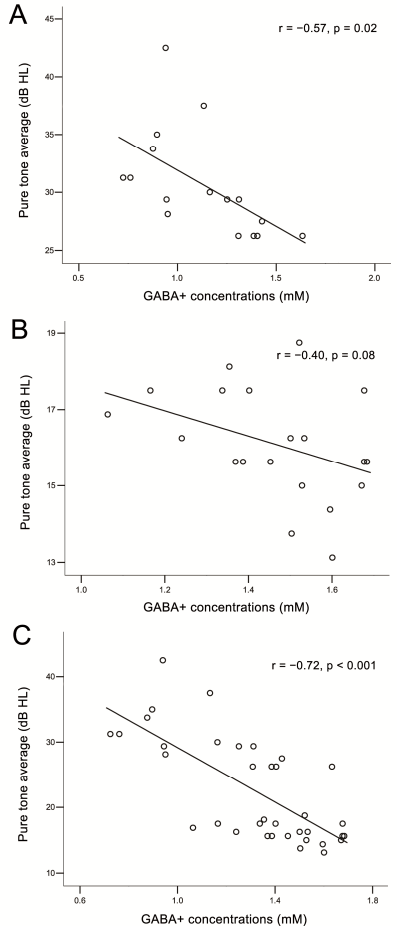

Figure 2. Correlations between pure tone average (PTA) and GABA+ concentrations in the presbycusis group (A), normal control group (B) and all subjects (C). A significant negative correlation was observed between PTA and GABA+ concentrations in the presbycusis group (r = -0.57, p = 0.02). A trend toward correlation was seen in the normal control group (r = -0.40, p = 0.08). A significant negative correlation was also observed between PTA and GABA+ concentrations in all subjects (r = -0.72, p < 0.001)