GABA and Glutamate/Glutamine Concentration in Auditory Cortex Correlate with Hearing Loss in Older Participants

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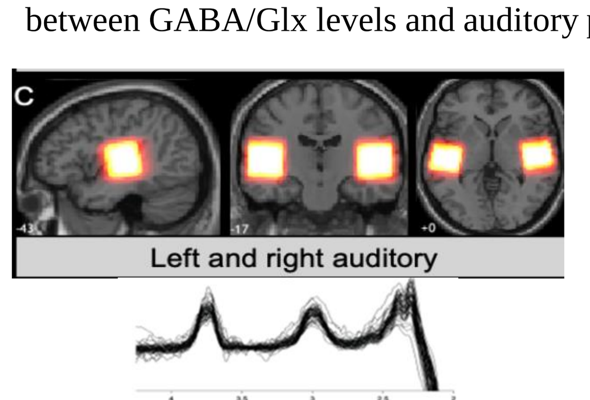
Introduction

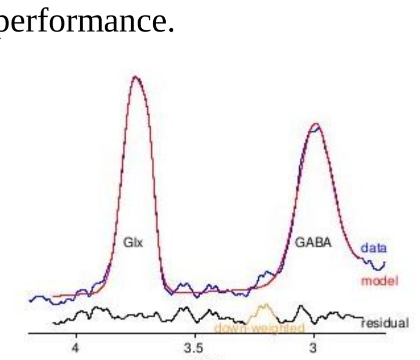
Background:

- Aging is associated with deterioration of hearing function (Profant et al., 2013).
- Previous aging studies report a relationship between auditory performance and excitatory and inhibitory neurotransmitters, GABA and Glx (Dobri & Ross, 2020, Huang et. al, 2016).
- GABA levels in the auditory cortex were found lower in older compared to younger adults, and that these GABA levels were correlated with auditory performance (Dobri & Ross, 2020).
- Glx was also lower in auditory cortical levels cross-sectionally, which potentially accounts for presbycusis hearing threshold changes (Profant et al., 2013).
- The importance of the ratio of glutamate to GABA (excitatory and inhibitory) on auditory function remains unclear.
- The purpose of this study is to replicate previous GABA findings and to further explore the role of excitatory neurotransmitters (glutamine/glutamate), EI ratio on age-related auditory performance decline.

Methods:

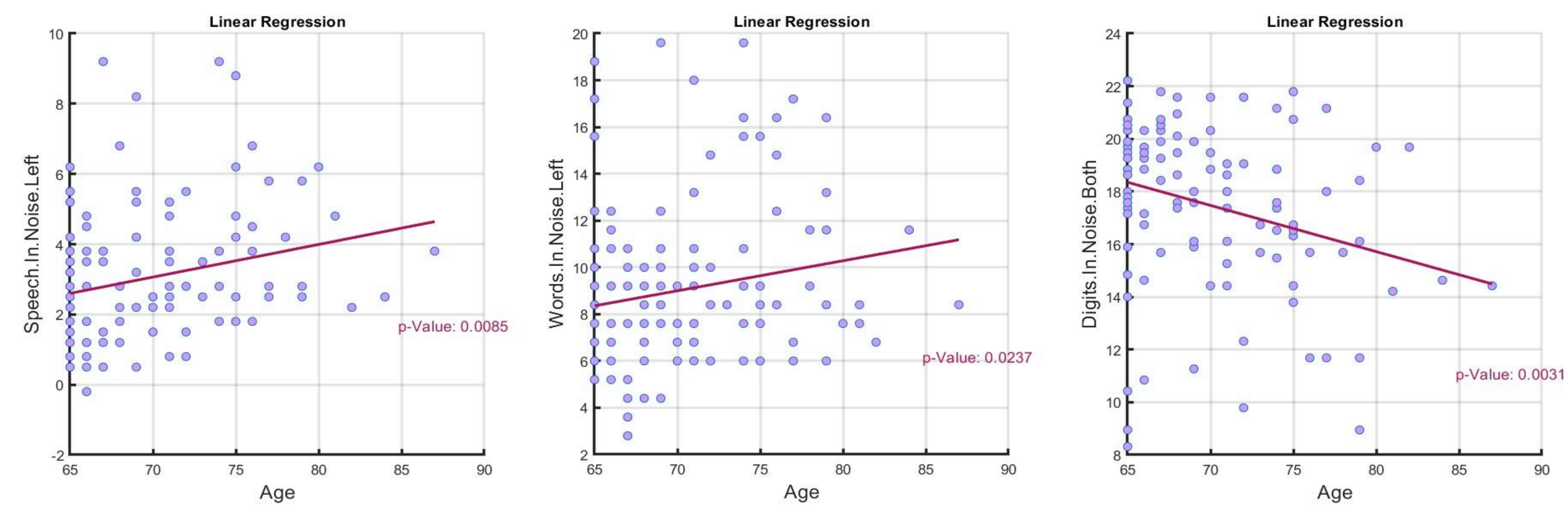
- 144 healthy old adults (54 males, 90 females, average age = 70.0) and 60 young adults (31 males, 29 females, average age = 22.7) were recruited as a part of the Michigan Neural Distinctiveness (MiND) study. Each participant completed 3 sessions that collected the behavioral, fMRI, and MRS data.
- The auditory behavioral performance was measured by using the Speech-in-Noise (QuickSIN) test (Killion et al., 2004), Words-in-Noise test (Wilson et al., 2007), and in-house Digits-in-Noise test. Acoustic stimuli were presented in different signal-to-noise ratios of multitalker babble to evaluate the ability of individuals to understand speech in background noise.
- A 30 × 30 × 30 mm^3 voxel of interest (VOI) was placed in order to maximize overlap with fMRI activation from auditory tasks assessed individually for each participant.
- Magnetic Resonance Spectroscopy (MEGA-PRESS, 1H-MRS at 3 Tesla, TR = 1800 ms, TE = 68 ms) was used to collect GABA-edited MR spectra data in both left and right auditory cortices.
- GABA and glutamate-plus-glutamine (Glx) levels were estimated using Gannet 3.3.1 MATLAB toolbox (Edden et al., 2014). A Gaussian-Lorentzian model was used to fit the 3-ppm peak and 3.74-ppm peak in the difference spectra to quantify the GABA and Glx concentration separately.
- To ensure the MRS data quality, we used Gannet 3.3.1 to calculate model fit error, signal-to-noise ratio, and full width half maximum (FWHM) measure. If a participant's data was outside 3 standard deviations in the FWHM measure, they were excluded from further analysis.
- Linear regression analysis was applied to examine the association between GABA/Glx levels and auditory performance.





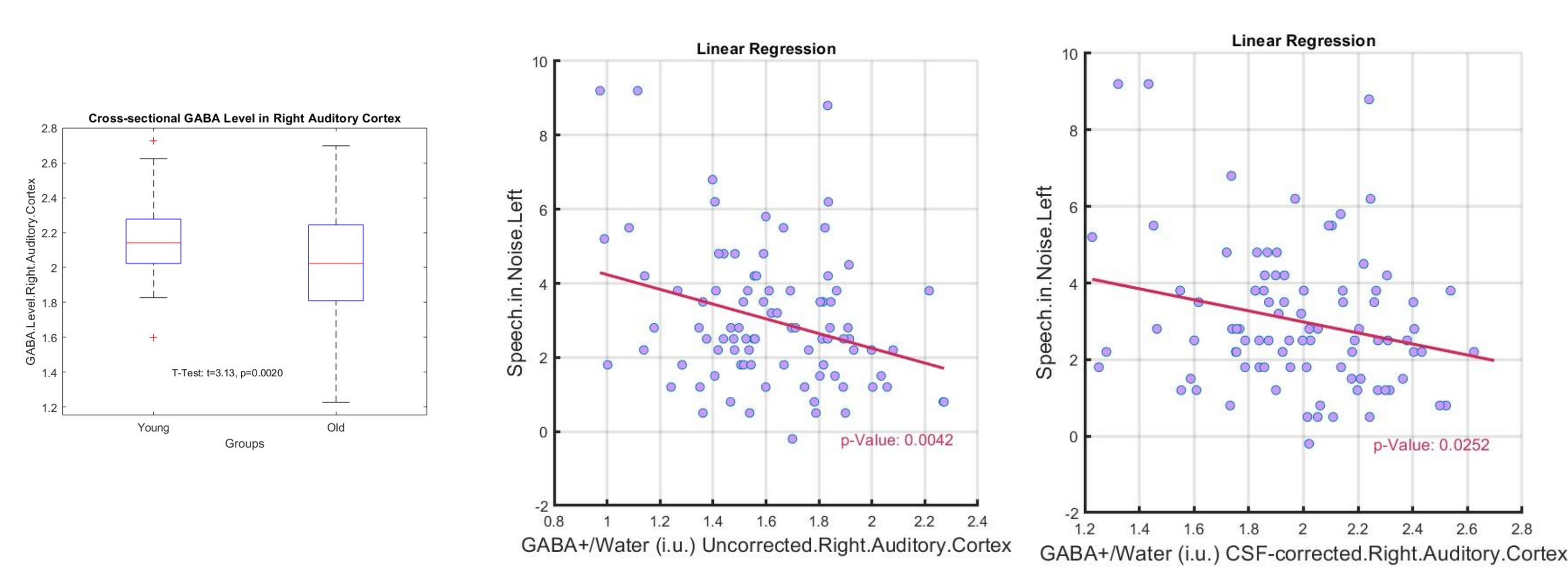
Results

1. Age Effect on Auditory Performance in Older Adults

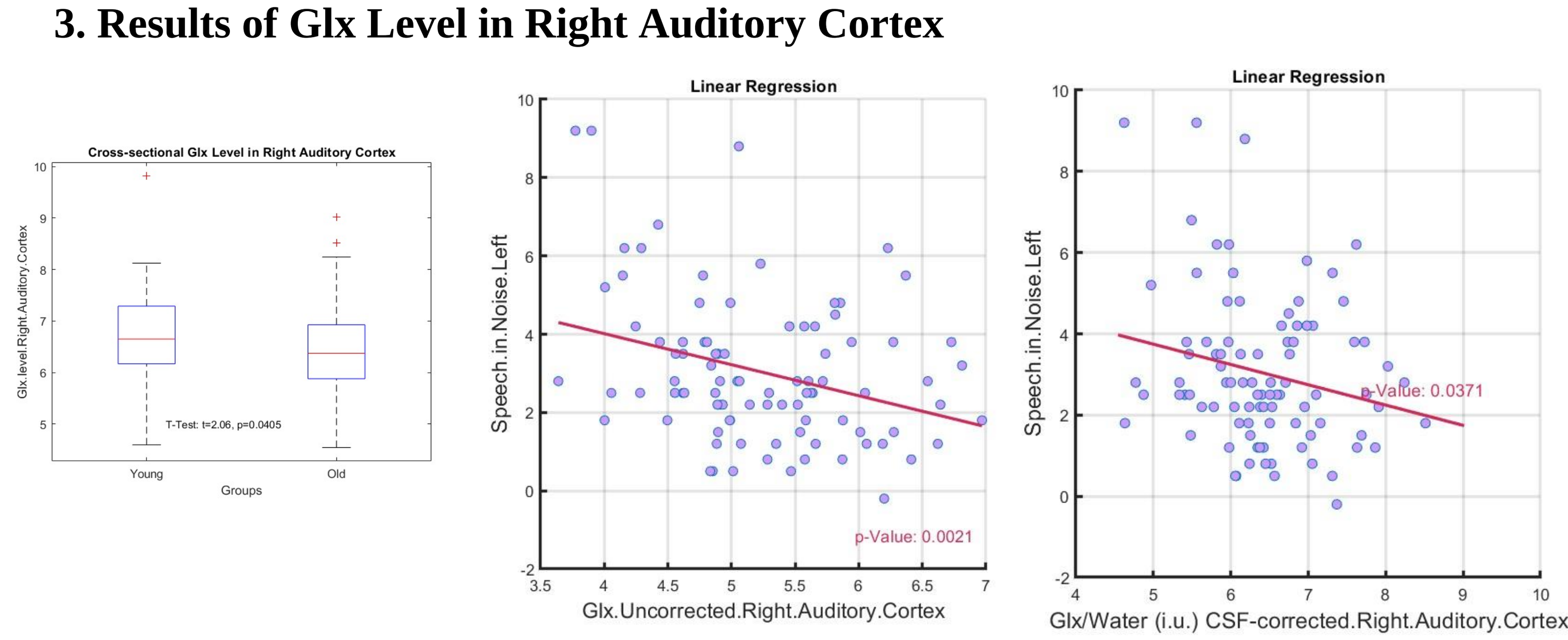


Model		Estimated Coefficient	SE	T value	P value
1 AudioSINLeft ~ Age	Intercept	-3.438	2.433	-1.413	0.160
	Age	0.093	0.035	2.679	0.008 *
2 WINLeft ~ Age	Intercept	0.010	3.938	0.003	0.998
	Age	0.128	0.056	2.287	0.02 *
3 DINBoth ~ Age	Intercept	29.758	4.067	7.317	<0.001
	Age	-0.175	0.058	-3.025	0.003 *

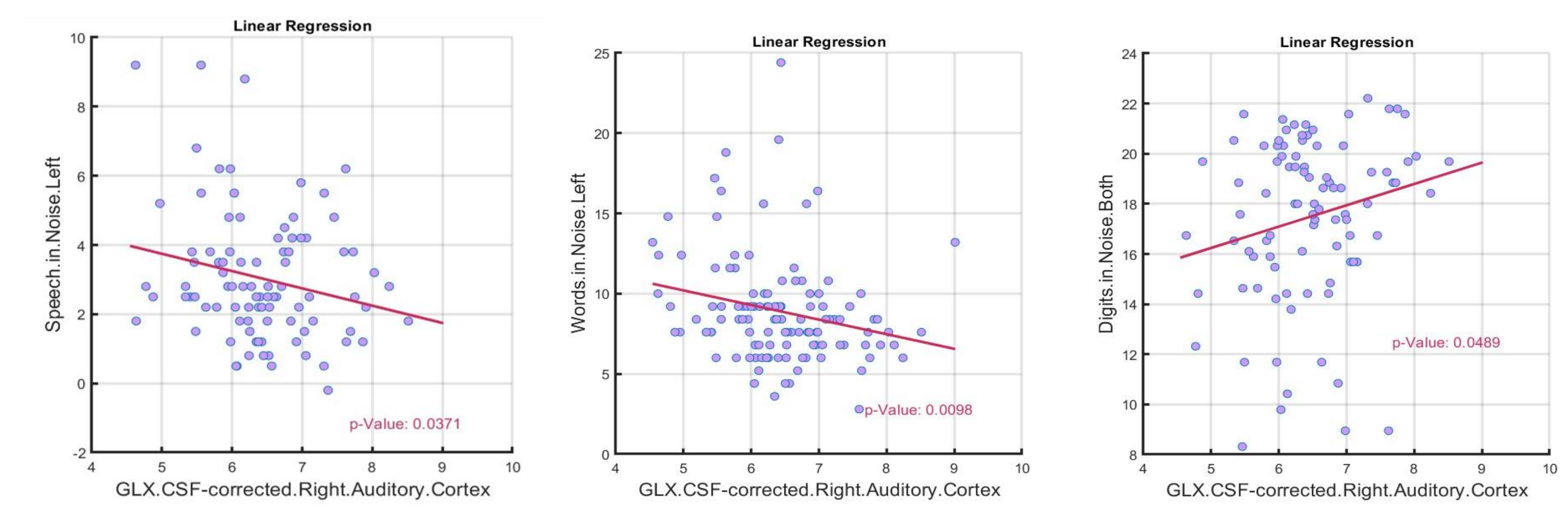
2. Results of GABA Levels in Right Auditory Cortex



3. Results of Glx Level in Right Auditory Cortex

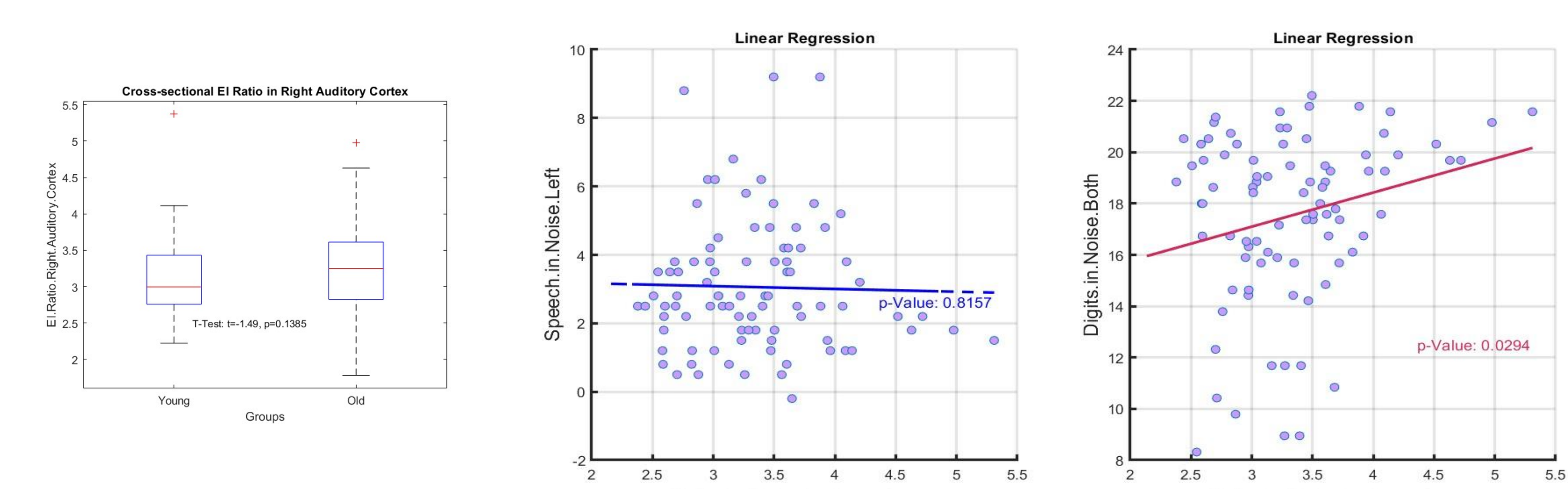


4. Glx Level in Right Auditory Cortex and Three Auditory Performance



Model		Estimated Coefficient	SE	T value	P value
1 AudioSINLeft ~ GLX	Intercept	6.245	1.530	4.083	< 0.001
	GLX Level	-0.500	0.236	-2.116	0.037 *
2 WINLeft ~ GLX	Intercept	14.751	2.242	6.581	< 0.001
	GLX Level	-0.910	0.347	-2.624	0.010 *
3 DINBoth ~ GLX	Intercept	11.987	2.771	4.326	< 0.001
	GLX Level	0.850	0.426	1.997	0.049 *

5. Results of EI Ratio in Right Auditory Cortex



6. T-test Results on Cross-sectional Analysis on GABA, Glx, and EI ratio

Dependent Variable (right auditory cortex)		Descriptive Scores: Mean	Lower	Upper	StdErr	T-Test Results: Mean Diff	Lower	Upper	t	df	p-value
GABA	Young	2.143	2.092	2.193	0.025	-0.135	0.050	0.220	3.135	175.000	0.002*
	Old	2.007	1.957	2.058	0.026						
Glx	Young	6.685	6.464	6.907	0.111	-0.280	0.012	0.548	2.060	178.000	0.041*
	Old	6.405	6.264	6.546	0.071						
EI Ratio	Young	3.123	2.990	3.256	0.067	0.132	-0.307	0.043	-1.488	170.000	0.139
	Old	3.255	3.159	3.350	0.048						

Discussion

- Age is a significant predictor in all the three auditory in noise performance.
- GABA+ (uncorrected and CSF-corrected) in right auditory cortex is a significant predictor of the speech-in-noise performance in left ear in older adults.
- Glx level (uncorrected and CSF-corrected) in right auditory cortex is a significant predictor for all three auditory in noise performance (Speech-in-Noise in the left ear, Words-in-Noise in the left ear, and Digits-in-Noise in both ears) in old adults.
- EI ratio in right auditory cortex is a significant predictor in Digits-in-Noise in both ears in old adults.
- Cross-sectional comparison showed that older adults have lower GABA+ and Glx level compared to the younger cohort.
- EI ratio has no significant differences between young and old groups.
- The results indicate that the age-related change of the concentration of GABA+, and Glx in right auditory cortex may help us understand the age-related hearing loss in the old adults.

Limitations and Future Directions:

- One of the limitation in quantification Glx level is that there is no tissue correction method yet to account for the ratio of Glx expected in gray to white matter. Thus we only corrected for CSF.
- A longitudinal analysis on Glx level may provide more evidence in the trajectory of Glx change in old adults.

References

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