The aging brain and changes in GABA concentrations

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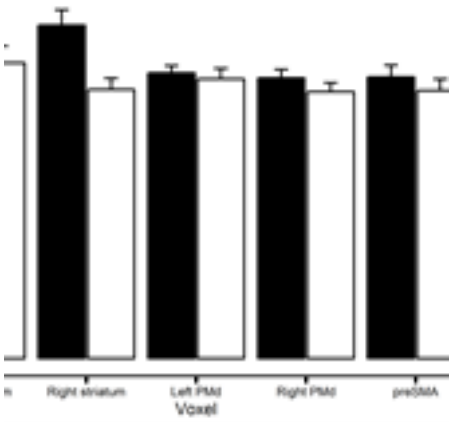
Introduction Gamma-aminobutyric acid (GABA) is the main inhibitory neurotransmitter in the human brain. Previous literature revealed a decline in GABA concentration in frontal and parietal regions as a result of age (Gao et al., 2013; Porges et al., 2017). Nevertheless, it is not clear whether this age-related decline in GABA concentration is specific to these regions or a widespread effect. Therefore, we aimed to investigate age-related changes in GABA concentrations within several cortical and subcortical regions. Since regional GABA concentration has been found to be correlated with various behavioral measures (Puts & Edden, 2012; Stagg, 2014), insight into the effect of healthy aging on brain chemistry may increase our understanding of the underlying neural mechanisms that contribute to cognitive and motor deficits in older adults. Methods A total of 30 healthy right-handed young (14 men, mean age = 23.2) and 29 healthy right-handed older adults (13 men, mean age = 67.5) participated in this study. GABA+ concentrations were acquired in nine different voxels using the MEGA-PRESS spectral editing method on a Philips 3T Achieva Magnetic Resonance scanner (Philips Healthcare, The Netherlands) with a 32 channel receiver head coil. The following acquisition parameters were used: 14 ms editing pulses at 7.5 ppm (edit-OFF) and 1.9 ppm (edit-ON), TE = 68 ms, TR = 2 s, 320 averages, 2 kHz spectral width, MOIST water suppression. Voxels of interest were bilateral primary motor cortex (3x3x3cm^3), bilateral dorsal premotor cortex (4x2.5x2.5cm^3), bilateral striatum (3x3x3cm^3), presupplementary motor area (3x3x3cm^3), right inferior frontal cortex (4x2.5x2.5cm^3) and occipital cortex (3x3x3cm^3). Additionally, a T1 scan was acquired in order to calculate the cerebrospinal fluid (CSF) fraction of each voxel. The obtained MRS spectra were analyzed using the Gannet software toolkit (Edden, Puts, Harris, Barker, & Evans, 2013) and GABA+ concentrations were calculated relative to water. Differences in GABA+ concentrations between young and older adults were tested with a mixed model with age group and voxel as fixed factor, participant as random factor and CSF as covariate (JMP Pro 12). Significant interaction effects were further investigated using unpaired student's t-tests with Bonferroni correction. Results Older adults had

lower GABA+ concentrations in all voxels in comparison with young adults (Figure 1). Statistical analysis however indicated that there was no effect of age on GABA+ concentrations ($F_{1,106.4} = 0.317$, $p = .574$), but there was an interaction between age and voxel ($F_{8, 404.8} = 2.009$, $p = .0442$). Between-group post hoc analysis showed lower GABA+ concentrations within right striatum in older adults compared to young adults ($t = -2.86$, $p = .0045$). GABA+ concentrations did not significantly differ between young and older adults in all other voxels (all $p \geq .1604$). Conclusions In the present study, we found a decline in GABA+ concentrations with age, however, this decline was only present within right striatum. Within bilateral primary motor cortex, bilateral dorsal premotor cortex, left striatum, presupplementary motor area, right inferior frontal cortex and occipital cortex, the decline in GABA+ concentrations was not significant. This suggests that biochemical changes as a result of healthy aging are not uniform across the human brain. However, it is possible that the regional concentration of macromolecules (i.e. part of the edited GABA+ signal) changes as a function of age, thereby masking the decline in GABA concentrations.

Figure 1



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