Age related morphometric and metabolic changes in pediatric brains

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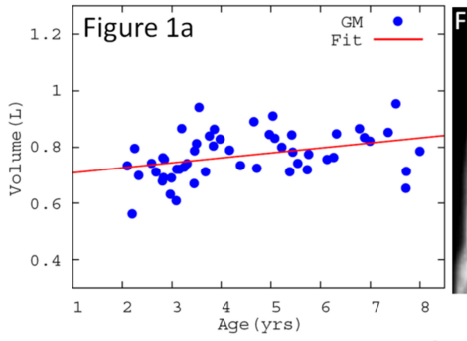
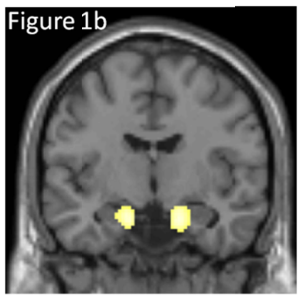
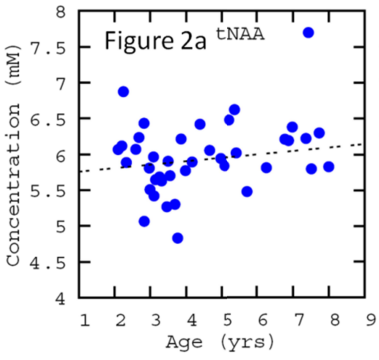
Introduction There is little information about brain growth and metabolic changes in children less than 8 years of age. This gap in knowledge limits interpretation of studies conducted in this young age group because age-related morphometric changes are essential to consider when interpreting neuroanatomical data. Here we employed computerized whole brain analysis to analyze age related morphometric changes, in addition to characterizing metabolic status using proton magnetic resonance spectroscopy (^{1}HMRS) in children 2-7 years of age.

Method A total of 52 children (age 4.5±1.7; 31Male/21Female) anesthetized with sevoflurane or propofol underwent MRI imaging for clinical evaluation. Common clinical diagnoses included seizures, headache, and developmental delay. Exclusion criteria were acute brain trauma, stroke or hemorrhage or processes increasing intracranial pressure. Scanning was performed on a 3.0T Philips whole body scanner, and high resolution T1W and single voxel ^{1}HMRS were performed in each session. T1W TFE sequence was acquired sagittally at voxel dimensions of 0.94mm×0.94mm×1.00mm. For regional morphometric changes, voxel-wise morphometric (VBM) analysis was implemented on the high resolution T1W scans using SPM8 [1,2] with default parameters and 10mm FWHM Gaussian smoothing followed by voxel-wise statistical correlation with age. PRESS ^{1}HMRS sequence was performed in parietal lobe, temporal lobe, insula, or occipital lobe with following parameters TR/TE/2000ms/32ms, receiver bandwidth=1200/2000Hz, number of points=1024/2048, and average =256. Metabolites (tNAA, tCh, tCr, tGlx, mI) concentrations were quantified by using LC model using water concentration as an internal reference. Partial volume effect in water concentration was also considered in the concentration calculation. [3]

Result Global and local morphometric analyses: Total grey (GM), white (WM), and intracranial volumes (TIV) yielded significant correlations with age in the expected positive directions (GM r=0.34 WM r=0.56 TIV r=0.28 P<0.05). Figure 1a shows individual GM volumes for all 52 subjects. Local morphometric analysis using VBM (P<0.05 FWE corrected k>100) indicated that volumes of amygdala, hippocampus, and cerebellum positively correlated with age as shown in Figure 1b. No cluster survived in the direction of negative correlation with age. ^{1}HMRS: Quality of each spectrum was first checked for poor SNR and aberrant baseline, and 13 such spectra were excluded leaving a total of 39 spectra for the analysis. Pearson's correlation coefficients between the metabolites concentrations (tNAA, tCho, tCr, Glx, and mI) against age did not reach the significance for any of the metabolites.







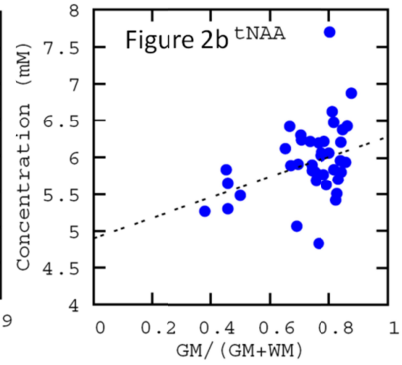


Figure 2a is a plot of tNAA as a function of age. However, partial tissue volume fractions (GM/GM+WM) and metabolites concentrations were significantly (P<0.05) correlated: mI (r=0.42), tNAA (r=0.38 Figure 2b), and tCr (r=0.36).

Discussion We performed MRI and ^{1}HMRS on a 3T MRI to elucidate morphometric and metabolic changes among children younger than 8 years of age. Global tissue volume analysis has shown a monotonically increasing trend as a function of age , and our VBM analysis revealed that the structures belonging to the limbic system (amygdala, hippocampus) and motor control (cerebellum) are prominent areas of structural growth during this period, consistent with other studies in adolescent subjects.[4] In contrast, metabolite concentrations appear to be relatively stable during brain maturation within the age range, although some of the metabolite concentrations are significantly correlated with partial volumes which has also been shown in adult populations.[5]

References 1. Ashburner et al. Neuroimage (2000) 2. Ashburner et al. Neuroimage (2005) 3. Gasparovic et al. MRM (2009) 4. Wilke et al. Exp Brain Res (2007) 5. Posse et al. MRM (2007)