N-acetylaspartate within frontal and parietal white matter differentially predicts intellectual functioning in normal brain

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Background

Previous research has found relatively low correlations between the quantity of brain tissue and intelligence quotient (IQ) in normal cohorts, with the "quality" of neuronal circuitry, dendritic arbor, synaptic number, and metabolic efficiency hypothesized to account for the remaining variance in IQ (Andreasen et. al., 1996). N-acetylaspartate (NAA), a metabolic marker of neuronal density and/or viability, has since been correlated with broad measures of cognition in brain regions including the cerebellum (Rae et. al., 1998), frontal white matter (Valenzuela et. al., 2000), and parietal white matter (Jung et. al., 1999a/b) in cohorts of normal subjects. Here we sought to determine 1) the regional distribution of brain metabolites in multiple brain regions in normal human subjects, and 2) the concurrent regional influence of these metabolites on a broad measure of brain function as measured by IQ.

Methods

Sample: Twenty neurologically healthy controls (17 male, 3 female) were recruited from the local college population: Mean age = 24.8 (+/-5.4); education = 14.3 (+/-1.4); Full Scale IQ = 113.2 (+/-7.7). All subjects were administered the 2-subtest version of the Wechsler Abbreviated Scale of Intelligence, a reliable (r_{xx} = .96) and valid (r_{12} = .87 with WAIS-III) measure of intelligence (WASI Manual, 1999), and scanned on a separate occasion. MR Imaging/Spectroscopy: All MR acquisitions were carried out on a 1.5 Tesla GE clinical MR scanner using a birdcage quadrature head coil. A PRESS pulse sequence (TE = 40 ms, TR = 2000 ms, 128 averages), including water suppression, was prescribed within four brain regions (Figure 1) based on prior morphometric (i.e., caudate nucleus, cerebellum) and/or spectroscopic studies (frontal white matter, parietal white matter, cerebellum) of brain-IQ correlations. All voxels were 12.6 cm^3 except the caudate nucleus voxel (6 cm^3). Metabolic values for choline (Cho), creatine (Cre) and NAA were determined using Magnetic Resonance User Interface (MRUI) and were corrected for percent tissue within each voxel. Statistics: Paired t-tests with Bonferroni correction for multiple comparisons (.05/18) were used to determine regional differences of metabolic values across voxels. Stepwise linear regression was used to relate all metabolic measures to general intellectual functioning.

Results

Levels of choline, creatine, and NAA across the four voxels of interest are presented in Figure 2. Paired-Sample t-tests yielded significant NAA differences between parietal and frontal white matter (t = 4.4, p <.001). Cre was significantly lower in frontal and parietal regions compared to the caudate and cerebellum (all p < .001). Regression Analysis yielded two predictors for Full Scale IQ (parietal NAA t = 4.6, p < .001; frontal NAA t = -3.2, p = .006). Note that parietal NAA was directly, and frontal NAA was inversely related to intelligence scores and that the variance of IQ scores accounted for by the NAA regression equation was substantial (r^2 = .68). An index of the regression equation for NAA prediction of Full Scale IQ [96.83 + (8.75 x parietal NAA) – (7.72 x frontal NAA) is presented in Figure 3.

Figure 1

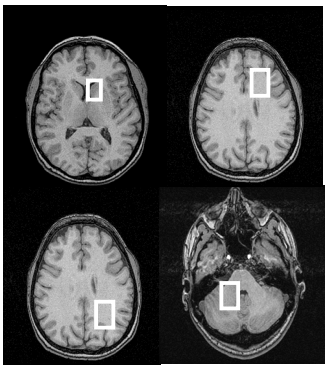


Figure 2

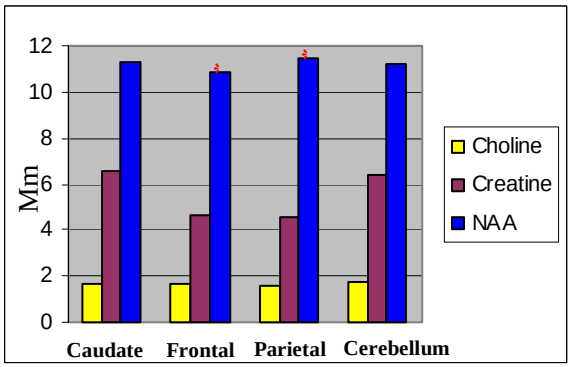
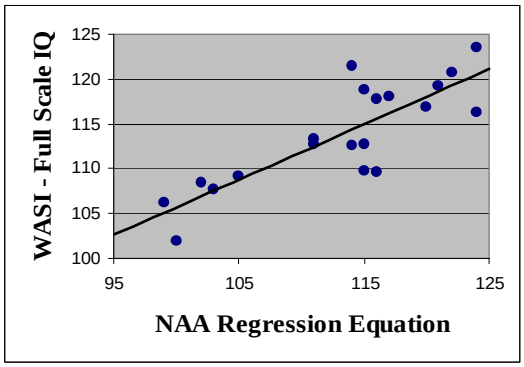


Figure 3



Discussion

While previous clinical research of damaged brain tissue consistently supports levels of NAA associated with neuronal viability and function (Barker, 2002), our findings suggest that, in normal appearing brain tissue, regionally optimal NAA levels may underlie individual differences in higher cognitive functioning. Specifically, a gradient of higher parietal and lower frontal NAA was found to be associated with increasing levels of general intellectual ability. Future research utilizing spectroscopic imaging will be essential to determine more completely the regional variations of NAA and concurrent associations with cognition in larger, more heterogeneous subject pools including both normal and clinical samples.

References

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