Quantitative Magnetic Resonance Imaging (MRI) and Proton Magnetic Resonance Spectroscopic Imaging (MRSI) of Dorsolateral Prefrontal Cortex in Children with Fetal Alcohol Syndrome.

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Introduction

Biological measures of CNS dysfunction after prenatal alcohol are needed for differential diagnoses of Fetal Alcohol Syndrome (FAS) from other developmental psychopathologies (e.g., ADHD) and among the various fetal alcohol effects (e.g.,FAS from Alcohol-Related Neurodevelopmental Disorder [ARNDs]). Basic/animal research demonstrates specific CNS neuroanatomical changes and neurochemistry in humans by measuring brain volumes and CNS levels of certain neurochemicals, esp. the neuron-specific N-acetyl-aspartate (NAA). We have previously reported significant decreases in the ratio of NAA/Cr, a putative index of “neuronal brain viability”, in the right cerebellum and the left and right anterior cingulate cortex (Cortese et al., ISMRM 2000) of children exposed prenatally to alcohol. The present study sought to quantify the absolute value of [NAA] and volume of the dorsolateral prefrontal cortex in children diagnosed with FAS.

Methods

Subjects

Children with FAS were recruited from an ongoing prospective study of the effects of prenatal alcohol exposure (Jacobson, et al, 1994) and through FAS parent groups. We assessed cerebral anatomy and chemistry via MRI and MRSI in children with confirmed diagnoses of FAS (n=5; 7 to 10 yrs; 1 boy/4 girls), and in controls (n=5; 9 to 12 yrs; 1 boy/4 girls).

MR Acquisition

MRI and 1H MRSI were performed using a 1.5-T General Electric Signa scanner (Horizon hardware, 5.7 software). MR images were acquired using a multi-slice spin-echo sequence (TR=2300ms, TE=280ms) in four 15-mm thick oblique slices with a 2.5-mm interslice gap. A 32 X 32 circular phase encoding scheme and field of view of 24 X 24 yielded a nominal voxel size of 0.8ml. T1 weighted images (TR=400ms, TE=20ms) were obtained from identical slices as the MRSI studies. Using a 3 dimensional “spoiled” gradient echo sequence (SPGR), 124 contiguous slices (1.5-mm thick) of anatomical data were acquired in the coronal plane (TE=5ms, TR=25ms, acquisition matrix 256x256, field of view = 24cm, flip angle = 10).

Analysis

VOI spectra were analyzed using a semi-automated non-linear least squares fitting procedure, and provided numerical results for Cho, Cr, and NAA peak areas (IMAX/CXS, Dr. Peter Barker). Absolute levels of metabolites were calculated using a phantom replacement method designed by Soher et al. (1996). The NIH IMAGE software (version 1.16) was used to compute all neuroanatomical volumetric measurements. Gray matter volumes are reported bilaterally for the dorsolateral prefrontal cortex. Statistical comparisons between the groups were made using unpaired t-tests with the Bonferroni correction.

Results

Gray matter volumes in both left and right dorsolateral prefrontal neocortex were significantly decreased in the FAS subjects compared to controls (p's<0.02; Figure 1).

Discussion

With the small number of subjects in this analysis, there was a significant correlation between the size of the dorsolateral prefrontal cortex and [NAA] levels on both sides (r=0.443; control: r=-0.289). The results of the present study demonstrate significant decreases in the size and neuronal functioning (i.e., reduced [NAA]) of the dorsolateral prefrontal cortex in FAS. These results are also consistent with prior research by others (e.g., Mattson, et al., 1999) demonstrating executive dysfunction in children with FAS, for example, problems with working memory, attentional shifting and planning. Such executive functions are known to be disrupted by damage to the dorsolateral prefrontal neocortex. This study implies that MRI and MRSI assessments can be sensitive to the structural and functional consequences, respectively, of prenatal exposure to alcohol in the dorsolateral prefrontal cortex, and may validate the behavioral measures as indices of specific neuronal dysfunction.

References


