DIFFUSION CHANGES IN FRONTAL WHITE MATTER IN PRENATALLY COCAINE EXPOSED CHILDREN

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Introduction

Cocaine easily crosses the fetal blood-brain barrier and accumulates in the CNS (1, 2). Various mechanisms such as hypoxia or disruption of the monoaminergic system as potential causes of brain injury in children prenatally cocaine exposed, PCE, have been therefore suggested. Hypoxia places the hippocampus and frontal white matter, FWM, at risk, and may also affect development. The neurotransmitters of the monoaminergic system greatly influence the developmental trajectory of their targets. These possible mechanisms of injury may alter tissue microstructure. Therefore, the purpose of our study was to examine the brains of the cocaine exposed children versus their control group for microstructural abnormalities that may relate to emerging developmental issues. DTI was employed for its ability to detect such changes.

Subject Population and Methods

A prospective longitudinal study was designed to evaluate the neurodevelopmental outcome of children whose mothers used (mostly crack) cocaine during pregnancy compared to matched controls. Subjects were matched on: high vs. low perinatal risk; level of Socioeconomic Status (SES); first vs. subsequent births; African-American vs. other reported race. This group of 11-12 year old children consists of 28 exposed subjects and 25 non-exposed subjects. During MR scanning and data processing, researchers were blinded to the drug exposure status of each child.

The MRI datasets were collected on a Siemens 3T Allegra equipped with gradients capable of 40mT/m, interfaced to a Syngo console. The MRI scanning protocol consisted of a high resolution 3D gradient echo scan for volumetric analysis and a 6 direction DTI acquisition. For the DTI sequence, a spin-echo diffusion weighted EPI pulse sequence was utilized with b values = 0, 250, and 1000 s/mm², FOV = (210 mm)², matrix = 128², slice thickness = 3.5 mm, TR = 4200 ms, TE = 90 ms, and NEX = 4 yielding an acquisition time of 4 min. In house developed software was used for the tensor processing. FA and <D> maps were used for analysis. FWM structures studied included right and left callosal fibers, right and left projection fibers. A semi-automated region shrink segmentation technique was implemented relying on intensity thresholding where ROIs were segmented off the FA images. The mean and standard deviations of FA and <D> were tabulated. Two tailed student t tests, α ≤ 0.05, were conducted probing for differences between the cocaine exposed and control group for each structure. Linear relationships between two variables were assessed using the Pearson correlation coefficient, α ≤ 0.05.

Results & Discussion

An increase of <D> in 2 of 4 FWM areas in the PCE population was noticed, right projection fibers and left callosal fibers. The PCE population showed a trend of decreased FA in these same areas, but no significance. Interestingly, significant negative correlations of <D> and one significant positive correlation of FA with brain volume were noticed in the unexposed population. Controversially, no significant correlations were found in either FA or <D> with brain volume in the PCE population. Adult cocaine exposure has been reported to cause damage to the FWM(3). Our results are concordant with the published results as we found significant increase in FWM <D> and trend of FA reduction. Possible microstructural changes from PCE include alterations to cytoskeletal structure, axonal thickness, myelin thickness, and neuronal density. Changes in these areas may explain an increase in <D> or a decrease in FA and may also lead to degradation in brain function and development. Therefore, our data suggest a link between PCE and microstructural alteration in FWM in children, potentially causing a developmental disruption at the microstructural level.

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