Sex Differences in the Relationship between Frontal White Matter Microstructure and Impulsivity in Adolescents

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Adolescence is a critical period for brain development, with the largest maturational changes occurring in the frontal cortex (Giedd et al., 1999). During this time, there also is a greater propensity for adolescents to seek out novel stimulation and engage in risk-taking behavior (Trimpop et al., 1999). Further, brain changes during adolescence have been reported to occur in a sex-specific manner (Yurgelun-Todd et al., 2002). As alterations in frontal white matter microstructure have been shown to correlate with measures of impulsivity, the objective of the present study was to examine the relationship between frontal white matter diffusion (fractional anisotropy (FA) and trace) and impulsive behavior (using the Bar-On Emotional Quotient Inventory) in healthy adolescents, as well as sex differences in the diffusion measurements. **Methods:** Twenty well-screened, neurologically and psychiatrically healthy adolescents (aged 12.3 ± 2.9 yrs.; 12 females, 8 males) participated in the present study. Diffusion tensor imaging (DTI) measurements were acquired on a 3.0 Tesla Siemens Trio scanner using a diffusion weighted twice-refocused spin echo EPI sequence and an eight element receive RF coil. Multiple diffusion weighed images were acquired using a single diffusion "b" weighting value of 1000 sec/mm^2. Apparent diffusion coefficient tensor values were calculated using a pixel-wise least squares fit to log images and an approximately calculated "b" weight matrix. FA and trace (diffusivity) of the calculated tensor were determined from axial images using region of interest (ROI) analyses. Voxels (11cm^3) were manually placed on a single slice from an echoplanar image, in the genu and splenium of the corpus callosum and two bilateral white matter (WM) regions within the anterior cingulate cortex (Figure 1, FA map with ROIs indicated in red).

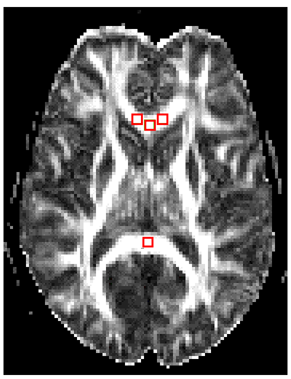

Figure 1.

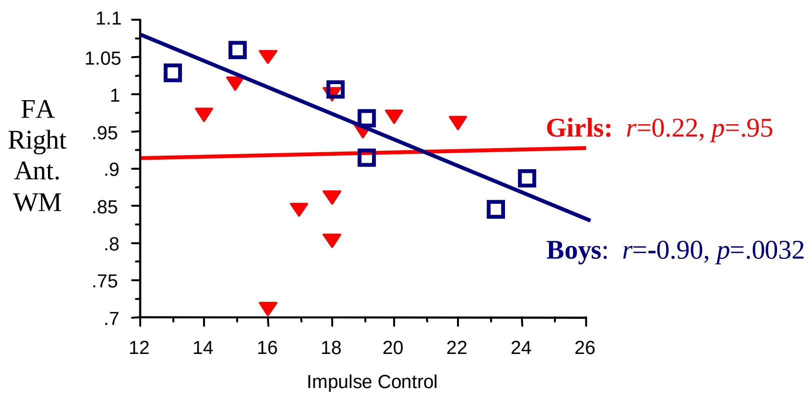

Figure 2.

Results: A significant relationship between FA in the right anterior WM region and impulse control was observed in male adolescents (r=-0.90, p<.001; Figure 2). Associations between FA and impulsivity for the whole group or females did not reach statistical significance (r=-0.30, p=.22 and r=0.22, p=.95, respectively). Overall regional differences were present for FA, with significantly higher FA being observed in the right anterior WM region (p<.0001) relative to the other regions examined. In addition, males displayed significantly higher FA in the left anterior WM region as compared to females (p<.05). Regional differences also were apparent for trace in males and females, with lower trace being observed in the splenium relative to the anterior regions (p<.01). **Conclusion:** Results from the current study demonstrate that in healthy adolescents, sex-specific differences are observed for the relationship between maturation of white matter coherence and impulsive behavior, with this association only present in males. These findings are consistent with previous reports in adult psychiatric and substance abuse populations that have described a significant association between frontal measures of FA and impulsive behavior (Hoptman et al., 2002; Moeller et al., in press). A number of investigations have proposed that a key element of cerebral maturation is the progressive reallocation of cognitive and emotional regulatory systems from lower subcortical regions to higher-order executive control regions of the prefrontal cortex, and others also have explored this hypothesis in recent years (Rubia et al., 2000). The present findings raise questions about the neurobiological basis of some of the emotional and behavioral changes commonly observed during adolescent development and suggest that frontal white matter microstructure may be one mechanism by which these changes occur.