White matter alterations related to attention-deficit hyperactivity disorder and COMT val(158)met polymorphism: children with valine homozygote attention-deficit hyperactivity disorder have altered white matter connectivity in the right cingulum (cingulate gyrus).


Abstract

INTRODUCTION: In this article, the COMT gene val(158)met polymorphism and attention-deficit hyperactivity disorder (ADHD)-related differences in diffusion-tensor-imaging-measured white matter (WM) structure in children with ADHD and controls were investigated.

PATIENTS AND METHODS: A total of 71 children diagnosed with ADHD and 24 controls aged 8-15 years were recruited. Using diffusion tensor imaging, COMT polymorphism and ADHD-related WM alterations were investigated, and any interaction effect between the COMT polymorphism and ADHD was also examined. The effects of age, sex, and estimated total IQ were controlled by multivariate analysis of covariance (MANCOVA).

RESULTS: First, an interaction between the COMT val(158)met polymorphism and ADHD in the right (R) cingulum (cingulate gyrus) (CGC) was found. According to this, valine (val) homozygote ADHD-diagnosed children had significantly lower fractional anisotropy (FA) and higher radial diffusivity (RD) in the R-CGC than ADHD-diagnosed methionine (met) carriers, and val homozygote controls had higher FA and lower RD in the R-CGC than val homozygote ADHD patients. Second, met carriers had higher FA and axial diffusivity in the left (L)-uncinate fasciculus and lower RD in the L-posterior corona radiata and L-posterior thalamic radiation (include optic radiation) than the val homozygotes, independent of ADHD diagnosis. Third, children with ADHD had lower FA in the L-CGC and R-retrolenticular part of the internal capsule than the controls, independent of the COMT polymorphism.

CONCLUSION: Significant differences reported here may be evidence that the COMT gene val(158)met polymorphism variants, as well as ADHD, could affect brain development. ADHD and the COMT polymorphism might be interactively affecting WM development in the R-CGC to alter the WM connectivity in children with val homozygote ADHD.