Methylation of the dopamine transporter gene in blood is associated with striatal dopamine transporter availability in ADHD: a preliminary study


Abstract

Dopamine transporters (DAT) are implicated in the pathogenesis and treatment of attention deficit hyperactivity disorder (ADHD) and are upregulated by chronic treatment with methylphenidate, commonly prescribed for ADHD. Methylation of the DAT1 gene in brain and blood has been associated with DAT expression in rodents’ brains. Here we tested the association between methylation of the DAT1 promoter derived from blood and DAT availability in the striatum of unmedicated ADHD adult participants and in that of healthy age-matched controls (HC) using Positron Emission Tomography (PET) and [11 C]cocaine. Results showed no between-group differences in DAT1 promoter methylation or striatal DAT availability. However, the degree of methylation in the promoter region of DAT1 correlated negatively with DAT availability in caudate in ADHD participants only. DAT availability in VS correlated with inattention scores in ADHD participants. We verified in a post-mortem cohort with ADHD diagnosis and without, that DAT1 promoter methylation in peripheral blood correlated positively with DAT1 promoter methylation extracted from substantia nigra (SN) in both groups. In the cohort without ADHD diagnosis, DAT1 gene expression in SN further correlated positively with DAT protein expression in caudate; however, the sample size of the cohort with ADHD was insufficient to investigate DAT1 and DAT expression levels. Overall, these findings suggest that peripheral DAT1 promoter methylation may be predictive of striatal DAT availability in adults with ADHD. Due to the small sample size, more work is needed to validate whether DAT1 methylation in blood predicts DAT1 methylation in SN in ADHD and controls.