The serotonin transporter gene polymorphism 5-HTTLPR moderates the effects of stress on attention-deficit/hyperactivity disorder.


Introduction
The role of the serotonin transporter gene polymorphism 5-HTTLPR in attention-deficit/hyperactivity disorder (ADHD) is unclear. Heterogeneity of findings may be explained by gene–environment interactions (GxE), as it has been suggested that S-allele carriers are more reactive to psychosocial stress than L-allele homozygotes. This study aimed to investigate whether 5-HTTLPR genotype moderates the effects of stress on ADHD in a multisite prospective ADHD cohort study.

Methods
5-HTTLPR genotype, as well as the number of stressful life events in the past 5 years and ongoing long-term difficulties, was determined in 671 adolescents and young adults with ADHD, their siblings, and healthy controls (57.4% male, average age 17.3 years). Linear mixed models, accounting for family relatedness, were applied to investigate the effects of genotype, experienced stress, and their interaction on ADHD severity at time point T2, while controlling for ADHD severity at T1 (mean follow-up time 5.9 years) and for comorbid internalizing problems at T2.

Results
The interaction between genotype and stress significantly predicted ADHD severity at T2 (p = .006), which was driven by the effect on hyperactivity–impulsivity (p = .004). Probing of the interaction effect made clear that S-allele carriers had a significantly more positive correlation between stress and ADHD severity than L-allele homozygotes.

Conclusion
The results show that the interaction between 5-HTTLPR and stress is a mechanism involved particularly in the hyperactivity/impulsivity dimension of ADHD, and that this is independent of comorbid internalizing problems. Further research into the neurobiological mechanisms underlying this interaction effect is warranted.