Replicated association of Synaptotagmin (SYT1) with ADHD and its broader influence in externalising behaviours.


Abstract

Attention-Deficit/Hyperactivity Disorder (ADHD) is a common psychiatric disorder, affecting both children and adults. The Soluble N-ethylmaleimide sensitive factor Attachment Receptors (SNARE) complex has been implicated in ADHD pathophysiology since it is a key component of neurotransmitter release events and neurodevelopment processes, and SNPs in this complex have been associated with ADHD. Here we aim to analyse the effects of SNARE complex variants on ADHD susceptibility and its clinical heterogeneity in affected adults. We tested the association between ADHD and polymorphisms on the SNARE genes STX1A (rs2228607), SYT1 (rs1880867 and rs2251214), VAMP2 (26bp Ins/Del) and SNAP25 (rs6108461 and rs8636) on a sample comprised of 548 adults with ADHD and 644 non-affected controls. Regarding clinical heterogeneity, we further investigated the effects of associated SNPs on age at onset of impairment due to ADHD and on relevant externalising behaviours (i.e. school suspensions/expulsions and problems with law/authority) and comorbidities (i.e. Substance Use Disorder, Oppositional Defiant Disorder, Conduct Disorder and Antisocial Personality Disorder). We replicated a previously reported association between SYT1-rs2251214 and ADHD in adulthood. This SNP was also associated with age at onset of impairment due to ADHD symptoms and with a range of externalising phenotypes. These findings involving SYT1 suggest that variation in neurotransmitter exocytosis mechanisms may represent an underlying genetic factor shared by a spectrum of externalising behaviours and disorders, including - but not restricted to - ADHD.