ASD and ADHD have a similar burden of rare protein-truncating variants


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Abstract

Autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) are substantially heritable, but individuals with psychiatric diagnoses often do not have blood drawn as part of routine medical procedure, making it difficult to collect large cohorts for genetic study. To overcome this challenge, we drew upon two Danish national resources: the Danish Neonatal Screening Biobank (DNSB) and the Danish national psychiatric registry. We have previously validated the use of archived bloodspots from the DNSB for genotyping and sequencing, and we recently performed common variant analysis on dried bloodspot material in both ASD and ADHD. Here, we present exome sequences from over 13,000 DNSB samples, finding that ASD and ADHD show a strikingly similar burden of rare protein-truncating variants, both significantly higher than controls. Additionally, the distributions of genes hit by these variants are not distinguishable between the two disorders, suggesting that many risk genes may be shared between them. These results motivate a combined analysis across ASD and ADHD, which—in conjunction with incorporation of the gnomAD reference database as additional population controls—leads to the identification of genes conferring general risk for childhood psychiatric disorders, including the novel gene MAP1A.