Familial liability to Epilepsy and ADHD: A Nationwide Cohort Study

Isabell Brikell, Laura Ghirardi, Brian M. D’Onofrio, David W. Dunn, Catarina Almqvist, Søren Dalsgaard, Ralf Kuja-Halkola, Henrik Larsson

Biological Psychiatry, 2017
DOI: https://doi.org/10.1016/j.biopsych.2017.08.006.

Abstract

Background
Epilepsy and ADHD are strongly associated, however, the underlying factors contributing to their co-occurrence remain unclear. A shared genetic liability has been proposed as one possible mechanism. Our goal was therefore to investigate the familial co-aggregation of epilepsy and ADHD, and to estimate the contribution of genetic and environmental risk factors to their co-occurrence.

Methods
We identified 1 899 654 individuals born 1987-2006 via national Swedish registers and linked each individual to their biological relatives. We used logistic regression to estimate the association between epilepsy and ADHD, within-individual and across relatives. Quantitative genetic modelling was used to decompose the cross-disorder covariance into genetic and environmental factors.

Results
Individuals with epilepsy had a statistically significant increased risk of ADHD (OR=3·47, 95%CI=3·33-3·62). This risk increase extended to children whose mothers had epilepsy (OR=1·85, 95%CI=1·75-1·96), children whose fathers had epilepsy (OR=1·64, 95%CI=1·54-1·74), full-siblings (OR=1·56, 95%CI=1·46-1·67), maternal half-siblings (OR=1·28, 95%CI=1·14-1·43), paternal half-siblings (OR=1·10, 95%CI=0·96-1·25), and cousins (OR=1·15, 95%CI=1·10-1·20). The genetic correlation was 0·21 (95%CI=0·02-0·40) and explained 40% the phenotypic correlation between epilepsy and ADHD, with remaining variance largely explained by non-shared environmental factors (49%, rE 0·36, 95%CI=0·23-0·49). The contribution of shared environmental factors to the cross-disorder overlap was not statically significant (11%, rC 0·32, 95%CI=0·16-0·79).

Conclusions
This study demonstrates a strong and etiologically complex association between epilepsy and ADHD, with shared familial factors and risk factors unique the individual contributing to co-occurrence between the disorders. Our findings suggest that epilepsy may share less genetic risk with ADHD, as compared to other neurodevelopmental disorders.