

**Familial Liability to Epilepsy and Attention-Deficit/Hyperactivity Disorder:
A Nationwide Cohort Study**

Supplementary Information

Supplementary Table S1. Sensitivity analyses of the within-individual and full-sibling association between epilepsy and ADHD

Supplementary Table S2. Odds ratios (ORs) and 95% confidence interval (CI) from sensitivity analyses stratified by sex

Supplementary Table S3. Genetic and environmental parameter estimates with Bootstrap standard errors and 95% confidence interval

Table S1. Sensitivity analyses of the within-individual and full-sibling association between epilepsy and ADHD

Model	N of individuals	Within-individual OR (95% CI)	N of pairs	Full siblings OR (95% CI)
Crude Estimates	1,899,654	3.53 (3.39-3.68)	1,829,684	1.56 (1.46-1.67)
Model 1	1,899,654	3.68 (3.45-3.89)	1,829,684	1.54 (1.40-1.69)
Model 2	514,345	3.11(2.90-3.34)	223,520	1.72 (1.49-1.99)
Model 3	na	na	1,829,684	1.46 (1.37-1.56)
Model 4	na	na	1,829,684	1.13 (1.06-1.21)

¹ Odd's ratios (OR) represent the risk of ADHD in individuals with a relative with epilepsy, compared to the risk in individuals without a relative with epilepsy. ² Excluding crude estimates, all estimates are adjusted for sex and birth-year of both outcome and exposure person.

Model 1. Stricter definition of exposure and outcome. 2 >= ADHD and epilepsy diagnoses from the National Patient register. Information from the PDR were excluded, as were individuals with only a diagnosis of status epilepticus (ICD codes G41,345Q) and no other epilepsy diagnosis.

Model 2. Restricted birth-cohort born 1994-1999, excluding all individuals with a record of death or migration during follow-up.

Model 3. OR comparing the risk of ADHD in individuals with a relative with epilepsy, to the risk in individuals without a relative with epilepsy, adjusting for epilepsy in the outcome person.

Model 4. OR comparing the risk of ADHD in individuals with a relative with epilepsy, to the risk in individuals without a relative with epilepsy, adjusting for ADHD in the exposure person.

Table S2. Odds ratios (ORs) and 95% confidence interval (CI) from sensitivity analyses stratified by sex

Within Individual			
		OR (95% CI)	N
Male		3.41 (3.24-3.59)	972,428
Female		3.56 (3.32-3.81)	927,226
Full-siblings			
Exposure person	Outcome person	OR (95% CI)	N
Male	Male	1.66 (1.49-1.85)	483,218
Female	Female	1.52 (1.29-1.78)	432,264
Male	Female	1.64 (1.42-1.89)	457,101
Female	Male	1.43 (1.27-1.60)	457,101

¹Odds ratios (ORs) and 95% confidence interval (CI) expressing the association between epilepsy and ADHD, stratified by sex. OR are presented for the within-individual association in the full cohort and for the within-family association in full-siblings. ²N refers to number of individuals for the within individual analysis and number of pairs for the full sibling-analyses. ³All models were adjusted for birth-year of both exposure and outcome person.

Table S3. Genetic and environmental parameter estimates with Bootstrap standard errors and 95% confidence interval

Parameter	Estimate	SE	Lower bound 95% CI	Upper bound 95% CI	p-value
rG	.21	.10	.02	.40	.028
rC	.32	.24	-.16	.79	.191
rE	.36	.07	.23	.49	<.001
% PC due to A	40	16	9	70	.011
% PC due to C	11	7	-3	25	.135
% PC due to E	49	9	32	67	<.001
% ADHD due to A	75	3	70	81	<.001
% ADHD due to C	7	1	5	9	<.001
% ADHD due to E	18	2	15	21	<.001
% Epilepsy due to A	28	8	12	44	.001
% Epilepsy due to C	10	4	2	18	.013
% Epilepsy due to E	62	4	54	71	<.001

¹ Reported parameter estimates were derived based on data from available pairs of full-siblings (914,842), maternal half-siblings (136,962) and paternal half-siblings (134,502) in the full cohort. Reported standard errors (SE), 95% confidence intervals (CI) and p-values were derived using bootstrap resampling (see method section for details). rG, genetic correlation; rC, shared environmental correlation; rE, non-shared environmental correlation. PC, phenotypic correlation; A, additive genetic effects; C, shared environmental effects; E, non-shared environmental effects.