Genetic and Environmental Contributions to ADHD Using the Conners' Rating Scales-Revised

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Objective

To test the genetic architecture of ADHD by using the Conner's Rating Scale Revised (CRS) - ADHD Index (ADHD-I).

Questions

1. What percentage of children, by gender, meet CRS criteria for clinical deviance on the ADHD-I?
2. Are rates of ADHD-I more or less common in our general community twin sample compared to DSM rates of ADHD?
3. What are the estimates of the genetic and environmental contributions to ADHD-I and are there gender differences?

Sample

Mother reports on 1,472 (1596) 7-year-old twin pairs from the Netherlands Twin Registry.

Twin Type	N
Monozygotic Males (MZm)	236
Dizygotic Males (DZm)	240
Monozygotic Females (MZf)	264
Dizygotic Females (DZf)	224
Dizygotic Opposite Sex (DOS)	508
Unknown zygosity	124
Total zygosity known	1472
Total	1596

Measures

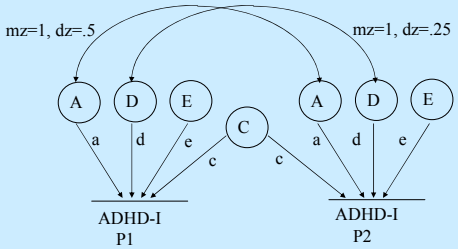
- The Conners' Parent Rating Scale–Revised: Short Form (Conners, Sitarenios, Parker, & Epstein, 1998).
- Consists of 27 items rated on a 4-point Likert scale for symptom severity.
- The ADHD index was developed specifically to discriminate children with ADHD from matched controls using t-tests followed by discriminant analysis to identify the 12 items which most discriminated.
- The ADHD index displayed a kappa of .904. Internal consistency coefficients for all four scales are above .81 for males and females. Test-retest reliability coefficients for scales were between .62 and .85 over a period of 6 to 8 weeks.

Data Analysis

Means, variances, and twin correlations were calculated using the statistical software program Mx and are presented below. Differences in mean scores were tested by likelihood-ratio χ^2-tests. Because the ADHD-I scale from the Conners-Revised Form was not normally distributed, the data were square-root transformed to approximate normal distribution.

All model fitting was performed on transformed data with MX. The basic model was an ACE or ADE model with and without sex and interaction effects. The possible presence of an interaction component was tested by equating the variances between MZ and DZ twins. The basic model is shown below.

The significance of the A, D, and C factors or sibling interaction was tested by dropping these variance components, using the χ^2- difference test. We also computed likelihood-based 95% confidence intervals.



Results

Percentage of Twins Clinically Deviant

	Male	Female
T Score > 65	6.8 %	8.1 %
T Score > 70	3.4 %	5.1 %

Mean square root transformed ADHD-I scores and standard deviations by Sex and Zygosity

Twin Type	Mean ADHD-I Score (SD)
Monozygotic Males	2.60 (1.33)
Dizygotic Males	2.63 (1.36)
Monozygotic Females	2.09 (1.32)
Dizygotic Females	2.16 (1.36)
Dizygotic Opposite Sex, eldest male	2.41 (1.38)
Dizygotic Opposite Sex, eldest female	2.32 (1.42)
All males	2.62 (1.37)
All females	2.12 (1.34)

Twin-Twin Correlations

Twin Type	Correlation
Monozygotic Males	.794
Dizygotic Males	.289
Monozygotic Females	.768
Dizygotic Females	.287
DOS – male eldest	.253
DOS – female eldest	.265

Model Fitting Results

	-2 log likelihood	Number of estimated parameters	Compared to model	Δ df	Δ chi²	p
1. Fully saturated	9409.520	30	-	-	-	-
2. Equal variances MZ/DZ	9412.306	26	1	4	2.785	.594
3. ADE, with sex differences	9414.886	18	1	12	5.366	.945
4. ACE, with sex differences	9428.179	18	1	12	18.659	.097
5. AE	9434.226	16	3	2	19.340	.000
6. ADE, equal ADE boys and girls	**9415.860**	**15**	**3**	**3**	**.975**	**.807**

Model Estimates

Source of Variance	Standardized Estimate	CI (low-high)
A	.2882	.051 - .515
D	.4992	.269 - .740
E	.2126	.186 - .244

Summary of Model Fitting

The difference in χ^2 indicates the goodness-of-fit of the model, compared to a saturated model. First, variance differences between MZ and DZ twins were tested. The fit of a model that constrained the variances to be equal was compared to the fit of a fully saturated model in which all variances and covariances were freely estimated. The variances were not significantly different, as a result an interaction component was not included.

Second, an ADE model was fit to the data. This model provided a very good fit to the data (χ^2 (12)=5.366, p=.945). Dominance contributed significantly to the variance of ADHD scores (χ^2 (2)=19.340, p=.000). The factor loadings of A, D and E were not significantly different between boys and girls (χ^2 (3)=.975, p=.807).

The ADE model without sex differences was the best fitting model. The additive genetic factor explained 29% of the variance, the dominant genetic factor 50% and the unique environmental factor 21%. The confidence intervals are provided above.

Discussion

The Conners-Revised ADHD-I combines the strengths of both DSM and CBCL taxonomic approaches in the study of ADHD. Here we report on heritability estimates for DSM ADHD more in line with those reported for AP and AGG of the CBCL (70%) than with studies which use DSM-IV categorical, yes/no data, which report heritability estimates in the 90-95% range.

In addition, these data, which allow for gender sensitive analyses (comparing data on females to females, males to male), fosters the perception that the DSM-IV ADHD items identify too few females as suffering from ADHD.

Finally, our model fitting identifies the contribution of genetic dominance. This model, which identifies genetic dominance as the primary influence on ADHD, has not been reported previously for ADHD. Our group has found evidence of genetic dominance on AP from the CBCL, but not in all age groups and not by all informants. In the ADE model we identify modest additive genetic influences (29%), moderate dominant genetic influences (50%), and modest unique environmental contributions (21%). If such models are replicated, evidence of genetic dominance argues for a different approach to identifying heritable phenotypes of the genetic study of ADHD. The issue of the ADE model versus models reported by others such as the AEi model can only be solved as we increase the sample sizes, types of samples (such as adopted sib designs, unrelated designs, and multi-informant designs).

Limitations

1. Like other factor analytically derived approaches the ADHD-I, does not retain all 18 items of the DSM-IV, thus use of the ADHD-I is not a direct test of DSM-IV ADHD. The ADHD-I is closer in content to DSM than other measures of ADHD.
2. Data on maternal report may not generalize to children of older ages or to other informants. Our group is currently collecting data on older twins by father and teacher report in order to test for these factors.
3. We did not directly interview the parents or children in this study and therefore cannot present data on the number of children who exceeded ADHD-I cut-off's who also met DSM-IV diagnostic criteria for ADHD. In order to test for these data, our group is currently interviewing a subset of this sample in order to determine those relations.

Conclusions

Use of the Conners' Parent Report Scale-Revised ADHD-I to estimate genetic and environmental contributions to ADHD combines the strengths of categorical and quantitative taxonomic approaches in the study of ADHD.

Our data are consistent with prior reports that ADHD is predominantly influenced by genetic factors that are both dominant and additive.