LONGITUDINAL GENETIC STABILITY OF THE CBCL JUVENILE BIPOLAR PHENOTYPE

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Introduction

Many prior investigations of children with Juvenile Bipolar Disorder (JBD) yield a profile on the Child Behavior Checklist (CBCL) that includes elevation about a T-score of 70 on the Attention Problems (AP), Aggressive Behavior (AGG), and Anxious/Depressed (A-D) subscales of CBCL. This profile has been shown to be separable from other common child psychiatric disorders. The genetic and environmental contributions to its stability from ages 7 to 12 is currently unknown and available studies have reported conflicting outcomes for subjects who are diagnosed as having JBD as a child. This study uses the CBCL-JBD as a quantitative phenotype of JBD based on parental ratings of the behavior of their children.

We have shown previously that this profile shows evidence of heritability of this phenotype using cross-sectional analyses of Dutch twin data (Hudziak et al., in press). The phenotype has been shown to be separable and distinct, shares less than 50% overlap with ADHD, is different from children who have inattention, aggression, or anxious/depressed syndromes only.

Objective

To assess the developmental stability and change of the CBCL-JBD across ages 7, 10, and 12 years in a large population-based twin sample and to estimate the genetic architecture of the CBCL-JBD phenotype across childhood.

Methods

The CBCL-JBD (Achenbach, 1991) was used to measure eight behavioral and emotional syndromes. Three syndrome scores known to distinguish between problems with attention only and Bipolar-ADHD were selected - Attention Problems (AP), Aggressive Behavior (AGG), and Anxious/Depressed (A-D).

Data Analyses

Means, variances, and twin correlations were calculated using the statistical software program Mx. Differences in mean scores were tested by likelihood-ratio χ² tests. Differences in variances were tested by χ² tests on variances (using a χ² test that has been shown to be adequate for dichotomous variables and to provide approximate normal distribution before analysis). Transformed scores were used in the correlation and structural equation modeling. Mx model fitting was performed on transformed data with Mx. The basic model was a Cholesky decomposition of longitudinal data. The basic model is below:

• The significance of the A and C factors or sibling interaction was tested by dropping these variance components, using the χ² difference test. We also computed likelihood-based 95% confidence intervals.

Results

The summary of twin correlations at each age end of the cross-twin-crossex-age correlations is shown below. The twin correlations within age show that at each age, the DZ correlations appear smaller than half the MZ correlations. This suggests that genes and shared family environment both explain familial resemblance in CBCL-JBD. The cross-sex correlations at ages 7 and 10 years and the other twin correlations constrained to be equal for first-born with second-born and second-born with first-born twins. As can be seen, the past behavior of the co-twin is more predictive for the current behavior of this or her twin in MZ pairs, than it is in DZ pairs. Based on this pattern of cross-sex-cross-age correlations for MZ and DZ pairs, it may be expected that longitudinal stability in bipolar disorder is explained by genetic factors and by the shared environment.

References


Discussion

• The CBCL-JBD measure is stable across ages and we have quantified the genetic and environmental contributions to its stability from ages 7 to 12.

• The influence of additive genetic effects on variation in JBD was found to be relatively high at each age, increasing from 63% at age 7 to 75% at age 12 years.

• The effects of the shared environment tend to decrease. At age 7, 20% of the variation in CBCL-JBD is explained by the influence of the common family environment and this percentage decreases to 5% at age 12 years.

• The small remaining part of the variance at each age was explained by unique, or individual-specific environmental influences.

• Similar genes may underlie the disorder in boys and girls.

• About 80% of the stability on JBD in childhood is due to additive genetic effects, and about 10% of stability is explained by shared environmental effects.

Limitations

1. Data on maternal report may not generalize to other informants. Our group is currently collecting data on other informants by father and teacher report in order to test for these factors.

2. We did not directly interview the parents or children in this study and therefore cannot present data on the number of children who would meet criteria for DSM IV Bipolar Affective Disorder.

3. Data in this report are limited to children up to the age of 12. Because the expression of Bipolar Affective Disorder is often in adolescence or early adulthood, these data and the estimates of heritability resulting would apply best to childhood bipolar disorder.

Conclusions

• Roughly 80% of the stability in childhood CBCL-JBD is due to additive genetic effects.

• The estimates for males and females are quite similar.


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