Genetic Structure of Reciprocal Social Behavior

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Objective: The study examined the genetic structure of deficits in reciprocal social behavior in an epidemiologic sample of male twins.

Method: Parents of 232 pairs of 7–15-year-old male twins completed the Social Reciprocity Scale to provide data on their children's reciprocal social behavior. Scale scores were analyzed by using structural equation modeling.

Results: Intraclass (twin-twin) correlations for scores on the Social Reciprocity Scale were 0.73 for monozygotic twins (N=98 pairs) and 0.37 for dizygotic twins (N=134 pairs). The best fitting model of causal influences on reciprocal social behavior incorporated additive genetic influences and unique environmental influences.

Conclusions: For school-age boys in the general population, reciprocal social behavior is highly heritable, with a genetic structure similar to that reported for autism in clinical samples. Continuous measures of reciprocal social behavior may be useful for characterizing the broader autism phenotype and may enhance the statistical power of genetic studies of autism.

TABLE 1. Results of Structural Equation Modeling of Genetic and Environmental Influences on Deficits in Reciprocal Social Behavior in an Epidemiologic Sample of Male Twins (N=232 Pairs)

<table>
<thead>
<tr>
<th>Modela</th>
<th>Maximum Likelihood Analysisb</th>
<th>Akaike’s Information Criterionc</th>
<th>Root Mean Squared Error Approximationd</th>
<th>Parameter Estimates for Components of Best Fitting Models</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\chi^2$ df p</td>
<td></td>
<td></td>
<td>$a^2$ 90% CI $c^2$ 90% CI $e^2$ 90% CI</td>
</tr>
<tr>
<td>ACE</td>
<td>3.5 3 0.31</td>
<td>-2.49 0.04</td>
<td></td>
<td>0.76 0.69–0.80 0.0 0.24 0.19 to 0.29</td>
</tr>
<tr>
<td>AE</td>
<td>3.5 4 0.48</td>
<td>-4.49 0.02</td>
<td></td>
<td>0.76 0.72–0.80 0.0 0.24 0.19 to 0.29</td>
</tr>
<tr>
<td>CE</td>
<td>31.4 4 0.00</td>
<td>23.37 0.24</td>
<td></td>
<td>0.76 0.72–0.80 0.0 0.24 0.19 to 0.29</td>
</tr>
<tr>
<td>E</td>
<td>97.2 5 0.00</td>
<td>87.20 0.39</td>
<td></td>
<td>0.76 0.72–0.80 0.0 0.24 0.19 to 0.29</td>
</tr>
</tbody>
</table>

a Models incorporate effects of additive genetic influences (A), common or shared environmental influences (C), and unique or nonshared environmental influences (E).

b Models with a nonsignificant $\chi^2$ value ($p>0.05$) are judged to have a good fit to the observed data.

c Defined as $-2\chi^2$ minus 2df (two times the number of degrees of freedom). Values $>0.0$ reflect a poor fit of the model to the observed data (5).

d Values <0.05 indicate a very good fit of the model to the observed data (5).

e df=N of observed statistics minus N of free parameters (A, C, and/or E) in the model. N of observed statistics=6.

Results

Deficits in reciprocal social behavior were normally distributed in this epidemiologic sample of twins. For monozygotic twins (N=98 pairs; mean Social Reciprocity Scale score=34.0 [SD=20.3]), the intraclass (twin-twin) correlation was 0.73, twin A variance was 437.2, twin B variance was 388.8, and the covariance was 301.4. For dizygotic twins (N=134 pairs; mean Social Reciprocity Scale mean score=40.4 [SD=23.1]), the intraclass (twin-twin) correlation was 0.37, twin A variance was 515.2, twin B variance was 550.3, and covariance was 195.5.

The results of structural equation modeling applied to these data are shown in Table 1. The best fitting model was the AE model, which incorporated additive genetic influences and unique environment influences. Goodness-of-fit indices for more complex models that incorporated age, dominant genetic effects, rater contrast, and/or rater bias were, without exception, poorer than those derived for the AE model.

Discussion

These findings indicate that for boys in the general population, deficits in reciprocal social behavior are highly heritable. The magnitude of additive genetic influences on reciprocal social behavior in this epidemiologic twin sample was very similar to what has been observed for autism itself in previous behavioral genetic studies (1). The estimation of a relatively small influence of the unique environment parameter (which incorporates measurement error) offers further support for the validity of the Social Reciprocity Scale. Future research on the genetic structure of reciprocal social behavior is warranted; such research should include female subjects, larger samples, and multiple informants. Further research is also needed to examine the relationship between deficits in reciprocal social behavior as measured by the Social Reciprocity Scale and autistic-spectrum deficits ascertained by using conventional autism rating scales.

Since deficits in reciprocal social behavior are the sine qua non of autistic spectrum disorders, and since genetic influences have been implicated in what has been referred to as the “broader autism phenotype,” studies of the causes of autism (particularly genetic linkage studies) may be greatly facilitated by measuring reciprocal social behavior as a continuous variable in families representing the entire range of deficits in the general population. The Social Reciprocity Scale may feasibly be used in large-scale genetic-epidemiologic studies and as a clinical measure of symptoms across the autistic spectrum.

References

3. Piven J, Palmer P, Jacobi D, Childress D, Arndt S: Broader autism phenotype: evidence from a family history study of mul-
Support for Allelic Association of a Polymorphic Site in the Promoter Region of the Serotonin Transporter Gene With Risk for Alcohol Dependence

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Objective: An association between the 5-HTTLPR short variant polymorphism in the promoter region of the serotonin transporter gene and risk for alcohol dependence has been reported from case-control studies that are, however, prone to chance findings related to artifacts of population structure. The authors sought additional evidence for this association from a family-based study.

Method: Ninety-two alcohol-dependent probands and their parents were tested for nonrandom transmission of alleles from heterozygous parents to affected probands.

Results: Preferential transmission of the short allele was found (65 of 102 transmissions from heterozygous parents).

Conclusions: The results suggest allelic association between a variant in the promoter region of the serotonin transporter gene and the risk for alcohol dependence. However, it remains to be seen whether the functional properties of this variant are directly responsible for the increased risk to alcohol dependence.

Studies in rodents and humans have pointed to a relationship between low levels of brain serotonin turnover and high levels of alcohol intake that may play a crucial role in the initiation and maintenance of alcoholism. Decreased availability of the serotonin transporter to radioligands has been found in brain imaging studies of probands with alcohol dependence (1) and in postmortem studies of human brains after alcohol exposure (2). Thus, a polymorphism in the promoter region of the serotonin transporter gene (3) can be considered a good candidate for conferring genetic susceptibility to alcohol dependence. It has been shown that the two common variants of this polymorphic site differ in the effect they have on the transcriptional activity of the gene in vitro (3), although it is unclear which of several activators or silencers of transcription (4) is to be held accountable. Such functional polymorphisms are particularly valuable in tests for association with complex traits such as alcohol dependence. The traditional approach is to compare allele frequencies between afflicted individuals and unrelated matched healthy comparison subjects. In studies using this design, a higher frequency of the short allele has been found in probands with alcohol dependence (5). Other studies have demonstrated an association between the short allele and increased neuroticism (3), a personality trait that in turn figures as a risk factor for alcoholism (6). Since case-control studies are prone to false-positive results caused by population structure (7), we used a family-based study design to investigate the association between risk for alcohol dependence and the 5-HTTLPR polymorphism in the promoter region of the serotonin transporter gene.

Method

Ninety-two inpatients (mean age=35.3 years, SD=6.3, 82.6% of whom were male) from the alcohol detoxification programs of two psychiatric university hospitals in Germany and Hungary and their parents donated blood samples and were interviewed with the Semi-Structured Assessment for the Genetics of Alcoholism (8) after receiving a complete description of the aims and the procedures of the study and after having given written informed consent. Inpatient probands fulfilled DSM-IV criteria for alcohol dependence at a mean age of 26.6 years (SD=7.1). Antisocial personality traits were present in 10 probands (10.9%) and a history of multiple-incidence autism families. Am J Psychiatry 1997; 154: 185–190
