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Heritability and genome-wide SNP linkage analysis of temperament in bipolar disorder.

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Abstract

BACKGROUND: The many attempts to identify genes for bipolar disorder (BD) have met with limited success, which has generally been attributed to genetic heterogeneity and small gene effects. However, it is also possible that the categorical phenotypes used in genetic studies of BD are not the most informative or biologically relevant. We have explored aspects of temperament as quantitative phenotypes for BD through the use of the Temperament Evaluation of Memphis, Pisa, Paris, and San Diego Auto-questionnaire (TEMPS-A), which is designed to assess lifelong, milder aspects of bipolar symptomatology and defines five temperaments: hyperthymic, dysthymic, cyclothymic, irritable, and anxious.

METHODS: We compared temperament scores between diagnostic groups and assessed heritability in a sample of 101 families collected for genetic studies of BD. A genome-wide SNP linkage study was then performed in the subset of 51 families for which genetic data was available.

RESULTS: Significant group differences were observed between BD subjects, their first-degree relatives, and independent controls, and all five temperaments were found to be significantly heritable, with heritabilities ranging from 21% for the hyperthymic to 52% for the irritable temperaments. Suggestive evidence for linkage was observed for the hyperthymic (chromosomes 1q44, 2p16, 6q16, and 14q23), dysthymic (chromosomes 3p21 and 13q34), and irritable (chromosome 6q24) temperaments.

LIMITATIONS: The relatively small size of our linkage sample likely limited our ability to reach genome-wide significance in this study.

CONCLUSIONS: While not genome-wide significant, these results suggest that aspects of temperament may prove useful in the identification of genes underlying BD susceptibility.

KEYWORDS: Bipolar disorder; Genetic linkage; Heritability; TEMPS-A; Temperament

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