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ScienceDirect
Comprehensive Psychiatry 50 (2009) 20–25
Comprehensive PSYCHIATRY
www.elsevier.com/locate/comppsych

Prospective associations of early-onset Axis I disorders with developing eating disorders

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Abstract

Objective: The purpose of this study is to analyze the developmental relationships of adolescent-onset Axis I mental disorders and eating disorders (EDs).
Method: One thousand three hundred eighteen adolescent twins born from 1983 to 1987 completed a professionally administered semistructured psychiatric interview at the age of 14 years and a questionnaire follow-up at the age of 17.5 years.
Results: Eating disorders at the age of 17.5 years were significantly predicted by major depressive disorder (odds ratio, 5.9; 95% confidence interval, 2.6-15.3) and generalized anxiety disorder (GAD) (odds ratio, 4.7; 95% confidence interval, 1.8-15.6) at the age of 14 years, when baseline EDs were excluded. Early-onset major depressive disorder in combination with GAD increased the likelihood of developing EDs compared with either mood or anxiety disorders alone. Similar risks and trends were evident in within-family analyses of twin pairs discordant for baseline predictors and ED outcome.
Conclusions: Depressive disorder and GAD that manifest at that age of 14 years predict future EDs. Analysis of discordant twins suggested that early-onset depressive disorder and GAD prospectively relate to EDs in adolescence, even after familial factors are taken into account.

1. Introduction

The developmental relationships of juvenile eating disorders (EDs) and other mental disorders are poorly understood. To date, only few studies have examined the longitudinal relationships of EDs and other psychopathology in adolescence. In general, these studies are suggestive of the existence of longitudinal relationships between depression, attention-deficit/hyperactivity disorder (ADHD), substance use, and EDs, but the sequence in the development of these disorders remains unknown because of inconclusive and mixed results. In some studies, EDs have preceded other forms of psychopathology [1,2], whereas in others, EDs have followed the same disorders [3-6].

Once comorbidity is established, several etiologic mechanisms are possible; one disorder may affect the expression of another, a third mediating factor may exist, or comorbidity may be caused by a common underlying factor, such as common genes. Studying twins discordant for a particular disorder offers an elegant way to control familial background [7,8]. In fact, if the within-twin-pair analyses replicate the association found among twins as individuals, it rules out the confounding effects associated with shared family background, that is, family structure or family history of disorder. The importance of these tests is highlighted because most of the prospective associations in clinical patients and population rests in individuals.

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doi:10.1016/j.comppsych.2008.05.004

Thus, using a large prospective adolescent sample, we addressed the predictive value of Axis I disorders for the development of EDs. To control for familial factors, we studied the associations among twins discordant for predictive baseline disorders and later EDs.

2. Methods

2.1. FinnTwin12 study design

FinnTwin12 is an ongoing longitudinal twin study launched in 1994 to investigate developmental genetic epidemiology of health-related behaviors [9]. From 1994 to 1998, all Finnish families with twins born in 1983 to 1987 were identified from Finland's Population Register Centre and included in the Finnish Twin Cohort [10]. The FinnTwin12 study has a 2-stage sampling design. The first-stage study included questionnaire assessments of all twins and parents at baseline, starting with the initial family questionnaire (87% participation rate, 2724 families) conducted during autumn of the year in which each twin cohort reached 11 years old, with follow-up of all twins at the age of 14 and 17 1/2 years. Nested in this epidemiologic, population representative study was an intensive assessment of a subsample of 1035 families, comprising about 40% of all twins, most (72%, 748 families) selected at random. A modest part of the subsample (28%, 287 families) was enriched with twins assumed to be at elevated familial risk for alcoholism, based on one or both parents' elevated scores on the 11-item lifetime version of the Malmö-modified Michigan Alcoholism Screening Test [11]. Details about the subsample have been described earlier [9]. However, we have performed a series of model-fitting analyses to diverse phenotypes to test for potential bias introduced by the sample enrichment, and we find no evidence that model-fitting results were systematically affected [12].

In this subsample, both twins and parents were interviewed using the adolescent version of Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA) [13], a highly reliable instrument providing lifetime diagnoses for alcohol dependence, major depressive disorder (MDD), anxiety disorders, conduct disorder (CD), oppositional defiant disorder (ODD), ADHD, and EDs. Assessments of nonresponders at each stage revealed no evidence of selection for family type, parental age, area of residence, zygosity, sex of the twin, or other systematic bias. All the interviewers had previous interview experience and were professionals, Masters of Psychology and Healthcare or registered nurses trained at Indiana University's Institute of Psychiatry Research, Indianapolis, IN, using standard COGA-interview training procedures (The Collaborative Study on the Genetics of Alcoholism) [14]. The interviews were highly age standardized; the mean age at interviews was 14.19 years, with 75% of interviews completed between 14 years and 14.3 months of age, and all interviews were completed before the age of 15 years. The final sample consisted of 1852 interviewed boys (n = 945, 51%) and girls (n = 907, 49%). The participation rate was 90%.

Later, during 2000 to 2005, at the average age of 17 1/2 years, the participants from all 5 birth cohorts were approached again. All twins received a follow-up questionnaire including ED assessments. A total of 1545 interviewed adolescents (83% participation rate) born 1983 to 1987 replied at the age of 17 years (mean age, 17.6 years; 754 females, 49%, and 791 males, 51%). The complete ED status data at follow-up was available for 1318 adolescents (671 females, 49%, 641 males, 51%). Nonrespondents did not significantly differ from respondents in baseline disorder status, sex, or age. Zygosity of twins was determined from well-validated questionnaire method supplemented by information from parents, photographs, and genotyping [15,16]. Data collection was approved by the ethics committee of Helsinki University, Finland, and the institutional review board of Indiana University.

2.2. Baseline assessments

The Finnish translation of the adolescent SSAGA (C-SSAGA-A) collected full information on MDD generalized anxiety disorder (GAD), ADHD, ODD, and CD, as well as alcohol abuse and dependence diagnoses. All disorders were assessed according to *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (*DSM-IV*) criteria [17] without considering impairment.

Eating disorders were analyzed in the same interview using both full *DSM-IV* criteria and broader ad hoc definition (meeting at least 2/4 of current diagnostic criteria).

2.3. Eating disorders at follow-up

At follow-up, the adolescents were asked: Do you have or do you think that you have ever had an ED? Six alternatives were given: (1) yes, anorexia nervosa, (2) yes, bulimia nervosa, (3) yes, both anorexia and bulimia nervosa, (4) yes, another type of an ED, (5) I have not had an ED, and 6) I do not know. The reliability of questionnaire assessments have been studied by authors in Finnish population previously, and despite their simplicity, they showed satisfactory and more specific and sensitive detection of lifetime EDs compared with the longer and more elaborate EDI subscales [18].

2.4. Statistical analysis

Logistic regression analyses were conducted to test the predictive value of Axis I disorders for the development of EDs. Conditional logistic regression were performed among twins discordant for significant predictors at baseline and also discordant for ED outcome.

First, a univariate logistic regression model to study the association with ED and another Axis I disorder was examined. Second, other Axis I mental disorders were added to the model. Finally, to investigate whether Axis I