School Achievement and Risk of Eating Disorders in a Swedish National Cohort

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Objective: High achievement in school has been associated with increased risk of eating disorders, including anorexia nervosa (AN) and bulimia nervosa (BN), but causality of these relationships is unclear. We sought to examine the association between school achievement and AN or BN in a national cohort and to determine the possible contribution of familial confounding using a co-relative design.

Method: This national cohort study involved 1,800,643 persons born in Sweden during 1972 to 1990 who were still living in Sweden at age 16 years and were followed up for AN and BN identified from inpatient and outpatient diagnoses through 2012. We used Cox regression to examine the association between school achievement and subsequent risk of AN or BN, and stratified Cox models to examine the gradient in this association across different strata of co-relative pairs (first cousins, half siblings, full siblings).

Results: School achievement was positively associated with risk of AN among females and males (hazard ratio [HR] per additional 1 standard deviation, females: HR = 1.29; 95% CI = 1.25–1.33; males: HR = 1.29; 95% CI = 1.10–1.52), and risk of BN among females but not males (females: HR = 1.16; 95% CI = 1.11–1.20; males: HR = 1.05; 95% CI = 0.84–1.31). In co-relative analyses, as the degree of shared genetic and environmental factors increased (e.g., from first-cousin to full-sibling pairs), the association between school achievement and AN or BN substantially decreased.

Conclusion: In this large national cohort study, high achievement in school was associated with increased risk of AN and BN, but this appeared to be explained by unmeasured familial (genetic and environmental) factors.

Key words: achievement, anorexia nervosa, bulimia nervosa, eating disorders, schools

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Eating disorders are an important cause of morbidity and mortality in adolescents and young adults, especially among women.[1-3] The lifetime prevalence of anorexia nervosa (AN) and bulimia nervosa (BN) in women has been reported to be up to 4% and 3%, respectively.[4-6] Both AN and BN have a high risk of premature mortality even when specialized treatment is available.[7,8] Young adults with AN or BN are reported to have more than a 6-fold and nearly 3-fold all-cause mortality, respectively, relative to healthy controls.[7]

Eating disorders are reported to be more common among individuals with high intelligence,[9] perfectionism,[10] high grades in school,[11] or higher achievement in school than would be predicted by intelligence.[12] However, causality of associations between school achievement and eating disorders is unclear. Previous studies have examined factors commonly associated with school achievement, such as parental education or socioeconomic status (SES), with conflicting results. Some[11,13-16] but not all[17-19] have reported associations between high parental education or SES and increased risk of eating disorders. A recent Swedish cohort study of 250,000 youth reported that high parental education was associated with eating disorders among females but not males.[13] However, a Korean study reported that the association between SES and risk of eating disorders among girls was U-shaped, with increased risk among those with either lowest or highest SES.[20]

Confounding by familial factors potentially may explain the association between school achievement and eating disorders. To our knowledge, no studies have used family-based designs to examine the potential contribution of unmeasured familial factors. We conducted a national cohort study in Sweden to do the following: examine the association between school achievement and subsequent risk of AN or BN in a national cohort of 1.8 million native-born Swedes; and use a co-relative design to examine the gradient in this association across different strata of co-relative pairs (e.g., first cousins, half siblings, full siblings) to determine whether observed associations, if any, are explained by unmeasured shared familial (genetic or environmental) factors.

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METHOD

Study Population and Data Sources

We identified 1,861,934 persons who were born in Sweden from 1972 to 1990 and were still living in Sweden at age 16 years. Of this total, 1,800,643 (96.7%) were registered in the National School Register and were included in this study. This study was approved by the Regional Ethical Review Board of Lund University in Sweden.

We linked data from multiple Swedish national registries using an anonymous version of the unique individual 10-digit personal ID number assigned at birth or immigration to all Swedish residents. Our database was created from the following sources: the Multi-Generation Register, providing information on family relationships; Swedish Hospital Discharge Register, containing all discharge diagnoses for Swedish inhabitants during 1964 to 2012; Swedish Outpatient Registry, containing all outpatient diagnoses nationwide during 2001 to 2012; Population and Housing Census, providing information on educational status for the biological parents in every fifth year between 1960 and 1985; and the National School Register, containing the school grade score (similar to a grade point average) for all students at the end of grade 9 (usually age 16 years) during 1988 to 2012.

Exposure and Outcome Ascertainment

The school grade score was recorded on a scale from 1 (lowest) to 5 (overall mean was 3.2) during 1988 to 1997, and on a scale from 10 (lowest) to 320 (overall mean was 207) from 1998 onward. For each year and by gender, we standardized the grade score into a *z* score with mean 0 and SD 1. This standardized variable, which we refer to as school achievement (SA), was our exposure of interest.

The study outcomes were AN and BN, which were identified using *International Classification of Diseases (ICD)* codes in the Swedish Hospital Discharge and Outpatient Registries, and were examined separately. AN was identified by *ICD-9* code 307B and *ICD-10* codes F50.0-F50.1 (*DSM-IV/V* code 307.1), and BN by *ICD-9* code 307F and *ICD-10* codes F50.2-F50.3 (*DSM-IV/V* code 307.51).

Education level among biological parents was examined as a potential confounder and was measured as the mean of the highest education level achieved by both parents. It was categorized into 5 groups (<9, 9, 10 to 11, 12, and >12 years) and modeled as an ordinal variable. Individuals with missing data for 1 parent were assigned the education level of the other parent, and those with missing data for both parents (n = 13,929) were assigned the lowest education level (or, alternatively, exclusion of these individuals in a secondary analysis did not affect the results).

Statistical Analyses

Because our aim was to assess causality, we sought to ensure that our exposure of interest (SA) preceded our study outcomes (AN and BN). Therefore, in our main analyses, we removed prevalent (pre-existing) cases of AN or BN by excluding diagnoses that were made before registration of SA. This resulted in exclusion of 1,249 of 6,122 (20.4%) AN cases and 793 of 4,054 (19.6%) BN cases among females, and 110 of 311 (35.4%) AN cases and 577 of 648 (89.0%) BN cases among males. We also performed secondary analyses in which all prevalent cases were included.

We used Cox proportional hazards regression to compute hazard ratios (HRs) and 95% CIs for the association between SA and risk of AN or BN. Robust standard errors were used to adjust the 95% CIs for correlation within families. The Cox model time scale was follow-up time from SA registration until the first diagnosis of AN or BN, emigration, death, or the end of follow-up (December 31, 2012), whichever occurred first. In all models, we investigated the proportional hazards assumption by including an interaction term between SA and the natural logarithm of time.

In a second analysis, we compared results from the entire population with those from a co-relative design. Using the Swedish Multi-Generation Register, we identified all first-cousin, half-sibling, and full-sibling pairs. We performed stratified Cox regression analyses for all first-cousin, half-sibling, and full-sibling pairs that did not have the same SA score, and extrapolated analyses for monozygotic (MZ) twins, with a separate stratum for each relative pair. The co-relative design allows a comparison of rates of AN or BN in relatives with different levels of SA. The stratified Cox models compute HRs that are adjusted for the familial cluster, and therefore account for shared genetic and environmental factors. MZ twins, full siblings, half siblings, and first cousins share, respectively, 100%, 50%, 25%, and 12.5% of their genes identical by descent. We constructed a final model that includes all 4 types of relative relationships, in which the HR for each relative type is dependent on the degree of genetic resemblance. The logarithm of the HRs was assumed to be a linear function of the proportion of genes shared and the outcome of interest. This model can yield a more robust estimate of the association between SA and eating disorders among MZ twins, for whom data are sparse (e.g., the number of discordant pairs for AN and BN was 0 and 1, respectively, among MZ twin males, and 22 and 14, respectively, among MZ twin females). All statistical analyses were performed using SAS 9.3.

RESULTS

In this cohort of 1,800,643 native-born Swedes, subsequent diagnosis of AN or BN was much more common among females (0.56% and 0.37%, respectively) than males (0.02% and 0.01%, respectively) (Table 1). Incidence rates (per 10,000 person-years) for AN were 3.93 in females and 0.15 in males, and for BN were 2.59 in females and 0.05 in males. The mean age at diagnosis was 20.7 years for AN and

TABLE 1 Descriptive Statistics for Population Born in Sweden From 1972 to 1990 and Registered for School Achievement

	Females (n = 878,365)		Males (n = 922,278)	
	AN	BN	AN	BN
Cumulative prevalence[a], %	0.56	0.37	0.02	0.01
Person-years	12,375,125	12,600,612	13,362,872	13,360,740
Incidence rate[b]	3.93	2.59	0.15	0.05
Mean age at diagnosis (SD)	20.8 (4.6)	23.6 (4.8)	20.6 (4.2)	23.4 (5.4)
Mean school achievement (SD)[c]	0.26 (1.0)	0.16 (1.0)	0.26 (1.0)	0.07 (0.9)

Note: AN = anorexia nervosa, BN = bulimia nervosa.

[a]*Number of cases divided by number of individuals included in the study.*

[b]*Cases per 10,000 person-years.*

[c]*Grade score standardized by year and gender into z score with population mean 0 and SD 1.*