Supplementary Online Content


eMaterial.

eFigure 1. Risks for TS/CTD Among First-, Second-, and Third-Degree Relatives of TS/CTD Probands in the Swedish National Patient Register (1969-2009) Compared With Matched Population Controls, Excluding Probands and Relatives With Intellectual Disability or Pervasive Developmental Disorders.

eFigure 2. Time Living Together in the Same Household Through Childhood and Adolescence for Different Types of Siblings in Sweden

This supplementary material has been provided by the authors to give readers additional information about their work.
Sensitivity analyses

We found a relatively high prevalence of comorbid Mental Retardation (MR) and Pervasive Developmental Disorders (PDD) in our cohort of patients with chronic tic disorders. While these neurodevelopmental disorders are not exclusion criteria for TS/CTD, we decided to run sensitivity analyses, excluding all probands and relatives with either comorbid MR or PDD in order to appreciate their potential impact on our estimates of familial risk. The pattern of results showed slightly (non-significantly) smaller risks for first-degree relatives (OR= 16.93 (12.00-23.90), second-degree relatives (OR = 2.25 (1.18-4.29) and third-degree relatives (OR = 1.97 (1.07-3.64) (eFigure 1). We therefore conclude that our estimates are largely independent of these comorbidities.

Further testing of the assumption of negligible shared environmental effects

Our model-fitting analyses are based on the assumption that full siblings and maternal half siblings are very similar with regard to shared environmental exposures, which is supported by data from Statistics Sweden indicating that that the majority (91%) of children continue to live with their mothers after a divorce. We also assumed that paternal half-siblings do not share any of the common environment. However, are these assumptions correct?

Work by our research group (PL, HL) using the tax records has confirmed that the vast majority of maternal half-siblings continue to live in the same building as their mothers throughout childhood and adolescence. As can be seen in eFigure 2 outlining the respective distributions of time registered as living in the same building, full and maternal half-siblings by and large grew up in the same household, supporting our assumption that they shared all of the common environment. The distribution based on paternal half-siblings, on the other hand, was largely bimodal, indicating that about half lived in different buildings, but that the other half were registered as living in the same building throughout childhood and adolescence. To the extent that the shared environment is assumed to reflect time spent in the same household, this violates our assumption that paternal half-siblings do not share any of the common environment. Therefore, we decided not to base our heritability estimates on the comparison of maternal and paternal half-siblings. In addition, there were too few affected paternal half-sibling pairs for this analysis. Additional model fitting work done by our group has demonstrated that even if this annual housing information is parameterized in several ways, the shared environment still did not have a meaningful influence on the heritability estimates of various mental disorders.
Using the same shared housing logic, we can reasonably assume that cousins share very little environment. From our cousin data, we can approximately estimate the heritability of TS/CTD from the tetrachoric correlations to be 0.88 (0.11x8=0.88), which is similar to the heritability estimates based on the full vs maternal half-siblings.

We therefore conclude that, while shared environmental effects cannot be fully ruled out, our data suggests that these are minimal or, at least, clearly less important than genetic effects.
**eFigure 1.** Risks for TS/CTD Among First-, Second-, and Third-Degree Relatives of TS/CTD Probands in the Swedish National Patient Register (1969-2009) Compared With Matched Population Controls, Excluding Probands and Relatives With Intellectual Disability or Pervasive Developmental Disorders.

Legend: First-degree relatives included full siblings, parents, and children. Second-degree relatives included maternal and paternal half siblings, grandparents and grandchildren, uncles/aunts, and nephews/nieces. Third-degree relatives consisted of first cousins.
eFigure 2. Time Living Together in the Same Household Through Childhood and Adolescence for Different Types of Siblings in Sweden