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Association between co-twin sex and eating disorders in opposite sex twin pairs: Evaluations in North American, Norwegian, and Swedish samples

Janet A. Lydecker [a], Emily M. Pisetsky [b], Karen S. Mitchell [a,c,d,e], Laura M. Thornton [f], Kenneth S. Kendler [c,g], Ted Reichborn-Kjennerud [h,i,j], Paul Lichtenstein [k], Cynthia M. Bulik [l], Suzanne E. Mazzeo [a,c,m,*]

[a] Department of Psychology, Virginia Commonwealth University, Richmond, VA, USA
[b] Department of Psychology, University of North Carolina, Chapel Hill, NC, USA
[c] Virginia Institute for Psychiatric & Behavioral Genetics, Virginia Commonwealth University, Richmond, VA, USA
[d] Women's Health Sciences Division, National Center for PTSD, VA Boston Healthcare System, USA
[e] Department of Psychiatry, Boston University, Boston, MA, USA
[f] Department of Psychiatry, University of North Carolina, Chapel Hill, NC, USA
[g] Department of Psychiatry, Virginia Commonwealth University, Richmond, VA, USA
[h] Division of Mental Health, Norwegian Institute of Public Health, Oslo, Norway
[i] Institute of Psychiatry, University of Oslo, Norway
[j] Department of Epidemiology, Columbia University, New York, NY, USA
[k] Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Sweden
[l] Departments of Psychiatry and Nutrition, University of North Carolina, Chapel Hill, NC, USA
[m] Department of Pediatrics, Virginia Commonwealth University, Richmond, VA, USA

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ABSTRACT

Objective: These three studies examined the hypothesis that prenatal exposure to sex hormones influences twins' risk for eating disorders based on co-twin sex, such that individuals with a female co-twin would be more likely than individuals with a male co-twin to meet diagnostic criteria for an eating disorder.
Methods: Male and female twins from the United States (N=2607), Norway (N=2796) and Sweden (N=16,458) with known co-twin sex and zygosity were assessed for eating disorders.
Results: In the U.S. and Swedish samples, sex was significantly associated with eating disorder diagnoses, and although co-twin sex was not associated with eating disorders overall, it was associated with broadly defined bulimia nervosa in the Swedish sample. The effects for bulimia were not sustained when monozygotic twins were excluded, suggesting that the effects of prenatal sex hormones play a minor role in influencing eating disorders. Sex and co-twin sex were not associated with eating disorders in the Norwegian sample.
Conclusion: The prenatal sex hormone hypothesis, which proposes that prenatal hormone exposure is associated with later eating disorder symptomatology, was not supported in these three population-based twin samples.

Introduction

The significant preponderance of anorexia (AN) and bulimia nervosa (BN) in women compared with men suggests that sex is a significant risk factor for these disorders. In the United States, AN affects 0.9% of women and 0.3% of men; BN affects 1.5% of women and 0.5% of men [1]. Both environmental (e.g., thin-ideal internalization) [2] and biological (e.g., estrogen gene activation) [3,4] hypotheses have been proposed to explain this discrepancy. Exposure to sex hormones prenatally, including estrogen, testosterone and progesterone, might play an important role in the development of these conditions [3–9]. These hormones might influence future behavior during prenatal development (i.e., organizational effect) [10], or elicit behaviors at the time of hormone exposure, such as puberty (i.e., activational effect) [11]. Twin studies offer a unique opportunity to investigate organizational effects of prenatal sex hormones on eating behavior by estimating prenatal sex hormone exposure from twin pair sex composition. Specifically, it is hypothesized that individuals with a female co-twin are more vulnerable to eating disorders because of prenatal exposure to additional estrogen, whereas those with a male co-twin have lower risk for these conditions because of prenatal exposure to testosterone [12,13].

In terms of organizational effects, direct research on prenatal levels of sex hormones and their relation to adult behavior presents ethical and practical challenges. Therefore, proxies for measuring prenatal exposure to hormones have been used in human studies. One proxy is the sex composition of a twin pair. Among human twins, females sharing a prenatal environment with male co-twins

* Corresponding author at: 806 W. Franklin Street, PO Box 842018, Richmond, VA 23220.
E-mail address: semazzeo@vcu.edu (S.E. Mazzeo).

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are more similar to males in cerebral lateralization [14], sensation seeking, rule-breaking [15], and social attitudes [15]. These similarities provide evidence of the organizational effects of prenatal hormone exposure. Finger length ratio, also a proxy for prenatal testosterone exposure, is negatively associated with disordered eating [3,9].

Evidence for activational effects of prenatal estrogen is seen in the association between developmental stage and age of eating disorder onset. The peak age of eating disorder onset is typically around puberty [3,12], when estrogen and progesterone levels increase substantially in girls. For example, in female singletons, binge eating is positively related to increased progesterone and decreased estradiol associated with menstrual cycle timing [5,7]. Further, heritability of disordered eating characteristics (e.g., weight preoccupation, body dissatisfaction), which are minimal pre-pubertally, increase to account for approximately 50% of the variance observed post-pubertally [4].

Animal models support both organizational and activational effects of hormones. Studies on multiple births in rats, an animal model for prenatal sex hormone exposure, have found that uterine position influences the masculinization of behavior after birth [16], suggesting that intrauterine environment facilitates organizational effects of hormones. Further, in female rats, perinatal testosterone exposure was positively related to increased caloric intake and higher body mass as adults [17], also suggesting organizational effects of testosterone. Evidence of activational effects comes from findings that adult female rats with higher circulating estrogen levels showed decreased caloric intake and increased exercise compared with female rats with lower estrogen levels [18,19]. Early exposure to androgens makes the brain less responsive to estrogen as it matures [10], indicating that organizational and activational effects are linked.

Several human studies have investigated the association between prenatal sex hormone exposure and disordered eating, with somewhat inconsistent results. Two recent investigations found no effect of co-twin sex on the likelihood that the other twin had an eating disorder [20,21]. Specifically, Raevuori and colleagues [21] found no difference in the prevalence of broadly defined AN or BN between opposite sex (OS) and same sex (SS) female twins in the Finnish Twin Registry. Results remained non-significant after grouping twins by zygosity and twin pair sex composition. Similar results were obtained in a study involving adolescents from the Swedish Twin Study of Child and Adolescent Development [20]. However, three studies [3,9,13] did identify an association between prenatal hormone exposure and disordered eating, using finger length [3,9] and co-twin sex [13] as proxies for prenatal hormone exposure. Of these, Culbert and colleagues [13] controlled for the effects of socialization by comparing disordered eating in OS female twins with female non-twins having at least one male sibling [13]. OS female twins reported less disordered eating than female non-twins, suggesting the difference is not simply related to having a male sibling, but rather to prenatal sex hormone exposure. However, this result did not control for potential confounds such as sibling age, birth order, or the presence of other siblings of either sex, and did not include non-twins with sisters as a comparison group.

Zygosity is a confounding factor in studies using co-twin sex as a variable. Although OS twin pairs are exclusively dizygotic (DZ), SS twin pairs can be either DZ or monozygotic (MZ). The study that found significantly higher disordered eating in SS female twins [13] also investigated whether zygosity was associated with this risk. SS female twins remained at a higher risk for eating disorders, even when MZ twin pairs were excluded. However, more research is needed to establish whether twins with a female co-twin are at a higher risk independent of genetic effects, given that other studies [20,21] have not found a link between co-twin sex and eating disorder symptomatology after excluding MZ twins from their analyses.

Another possible explanation for inconsistencies in earlier research is the use of different measures of disordered eating. The study that found a positive effect of co-twin sex on disordered eating [13] and the study that found a negative association of finger length with disordered eating [3] used the Minnesota Eating Behavior Survey (MEBS). The male study that found a negative association of finger length with disordered eating [9] used a male-specific measure and the Eating Disorder Examination Questionnaire, whereas studies that did not support the prenatal sex hormone hypothesis used eating disorder diagnostic status [21], or the Eating Disorder Inventory (EDI) [20,21]. Compared with other eating disorder measures, the MEBS places greater emphasis on compensatory behaviors and includes these behaviors on a subscale distinct from that measuring binge eating [22]. Notably, continuous measures [3,9,13,20] assessed symptomatology at the time of the study, whereas eating disorder diagnostic status was over the lifetime [21].

Inconsistencies might also be related to sample differences. Studies that found an effect of co-twin sex used samples from the Midwestern region of the United States, whereas those that did not used samples from Sweden [20] and Finland [21]. The current paper includes three additional registries that include eating disorder diagnostic variables from three independent samples of male and female twins—one from the Mid-Atlantic region of the United States (Study 1), one from Norway (Study 2), and one from Sweden (Study 3). Thus, these studies extend previous work examining the prenatal sex hormone exposure hypothesis by including new geographical regions and men.

Method

Study 1: Mid-Atlantic U.S. sample

Participants

This sample comes from a project utilizing the population-based Virginia Twin Registry, now the Mid-Atlantic Twin Registry (MATR), which was approved by Virginia Commonwealth University's Institutional Review Board. A description of the sample and recruitment was published previously [23].

Participants were OS (n=481) and SS (n=1022) female twins (M_{age}=40.44, SD=8.34). Of the SS females, 614 were MZ, and 408 were DZ. OS (n=317) and SS (n=787) male twins were also included (M_{age}=42.33, SD=9.19). Of the SS males, 492 were MZ and 295 were DZ. Participants with more than one co-sibling were excluded because prenatal hormone exposure cannot be reliably estimated in higher-order multiples. Lifetime diagnoses of eating disorders by sex, co-twin sex (i.e., OS or SS) and zygosity, as well as percentages of all participants within that group, are included in Table 1.

Assessment of eating disorder symptomatology

Self-report eating disorder items. Items assessing eating disorder diagnostic criteria were adapted from the Structured Clinical Interview for *DSM-IV* (SCID) [24] to be consistent with the self-report format of the questionnaire, and assessed all criteria from the *Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV)*[25] for AN, BN and binge eating disorder (BED) over the participant's lifetime. Several types of response options were used for the items: the majority were Likert-type, but free write-in (frequency of binges per month and duration of amenorrhea), and yes/no (ever having binged, binge characteristics, and lack of compensatory behaviors for BED) were also used. Because of the relative rarity of threshold ("narrow") eating disorders, we also included individuals meeting subthreshold ("broad") criteria. Diagnostic algorithms, described in detail elsewhere [26], were constructed for narrow and broad versions of each disorder from items associated with each criterion.