Timing of Menarche and the Origins of Conduct Disorder

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Context: Precocious onset of menses (ie, age ≤11 years) has repeatedly been identified as a risk factor for higher rates of delinquency or conduct disorder (CD) in girls. Although this association is often conceptualized as environmentally mediated (via processes such as affiliation of early-menstruating youth with older, more deviant peers), such conclusions are premature as biological and genetic explanations have yet to be fully considered.

Objective: To uncover the origins of the association between CD and timing of menarche.

Design, Setting, and Participants: The sample consisted of a population-based birth cohort of 708 mid-adolescent female twins assessed as part of the ongoing Minnesota Twin Family Study. We conducted 2 sets of analyses: standard bivariate analyses to uncover possible common genes and moderator analyses to evaluate possible moderation of genetic influences on CD by timing of menarche.

Main Outcome Measures: Conduct disorder was assessed via individual semistructured interviews with mothers and adolescents. Menarcheal status and age at menarche were assessed via the Pubertal Development Scale.

Results: The results argued against common genetic influences but did provide evidence of etiological moderation of CD by timing of menarche. The heritability of CD was strongest (67%) in girls with average timing of menarche (ie, age 12-13 years) and substantially weaker (8%) in those with early onset. Those with late initiation of menses (ie, age >13 years) similarly exhibited weaker genetic influences (29%). Shared environmental influences showed the opposite pattern, as they were far stronger for those with precocious and delayed onset vs those with average onset.

Conclusions: Our findings provide indirect support for psychosocial interpretations of the impact of precocious menarche and, to a lesser extent, delayed menarche on CD development. Further, they lend support to the notion that in some cases, genetic influences on psychopathology may be strongest in the “average, expectable” environment.

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signal pleiotropy in which 1 gene has effects on multiple traits, in this case contributing to early pubertal timing and a tendency toward acting-out behaviors. Consistent with this possibility, Comings et al8 reported that the oft-reported link between father abandonment and daughters’ early menarche and behavioral problems5,16 is actually a function of the androgen receptor gene (an X-linked gene passed from fathers to their daughters). A second theory centers on gene-gene interactions in which gene-regulated hormonal influences activate genetic influences on CD (as found for eating pathology [K. L. Klump, PhD, P. Perkins, PhD, S.A.B., M.M., and W.G.I., unpublished data, January 2006]). In both cases, we would expect to observe moderate to strong genetic correlations linking timing of menarche with acting-out behaviors.

Another set of hypotheses falls under the rubric of environmental moderation of the genetic influences on CD (gene-environment interactions).2,7 One possibility is that early menarche exacerbates or potentiates the expression of the genetic influences on CD.5,24 Alternatively, it may be that early menarche acts as an environmental main effect, effectively suppressing genetic influences on CD in early-maturing girls. The latter case would yield largely environmental mediators of CD in early matures and is thus clearly consistent with psychosocial interpretations.7,11-13

The current study sought to evaluate these competing hypotheses in a sample of mid-adolescent female twins. We first made use of a bivariate biometric model to evaluate whether CD and menarchal timing covaried as a result of common genetic influences (as measured via a genetic correlation). We next examined whether and how timing of menarche moderated genetic and environmental contributions to CD. Together, these analyses allowed us to evaluate several possible mechanisms underlying the association between timing of menarche and CD symptoms.

METHODS

PARTICIPANTS

The sample was drawn from participants in the ongoing Minnesota Twin Family Study, a population-based, longitudinal study of same-sex adolescent twins born in the state of Minnesota and their parents. Twin families were ascertained from birth records and located using public databases. More than 90% of twin births between 1971 and 1985 have been located. Families were excluded from the study if either twin had a cognitive or physical handicap that would preclude completing our day-long, in-person assessment or if the family lived more than 1 day’s drive from our Minneapolis, Minn, laboratory. Of eligible families, 83% agreed to participate. Parents in participating families had slightly albeit significantly more years of education than parents in nonparticipating families. In socioeconomic status, 1 symptom. Previous studies22,23 have indicated that each type of symptom endorsement by both mother and child counted as only 1 symptom present in themselves.

MONOZYGOTIC TWIN PAIRS

Of these, 436 were monozygotic (MZ) (identical) twins and 272 were dizygotic (DZ) (fraternal) twins. Participants ranged in age from 13.6 to 16.9 years, averaging 14.8 years, during their first follow-up visit. Monozygotic twins are slightly more common than DZ twins in the population from which our sample was drawn.17 From 1971 to 1984, there were 4,09 MZ twin pairs and 2,60 like-sex DZ twin pairs per 1000 births, for an MZ-DZ ratio of 1.57:1.00. The preponderance of MZ twin pairs reflects this, with an MZ-DZ ratio of 1.60:1.00.

ZYGOSITY DETERMINATION

Zygosity was determined by the agreement of several separate estimates: (1) parents completed a standard zygosity questionnaire; (2) Minnesota Twin Family Study staff evaluated visage, hair color, and face and ear shape for physical similarity; and (3) ponderal and cephalic indices and fingerprint ridge counts were measured. A serological analysis was performed when the 3 estimates did not agree. This method was found to be highly accurate.18,20

CONDUCT DISORDER

A DSM-III-R symptom-count variable was used in the study (DSM-III-R was current at the time of the assessment). This variable corresponds to the number of endorsed criterion A symptoms of CD. During their follow-up visit, all of the participants and their parents were assessed in person by trained bachelor’s- and master’s-level interviewers for DSM-III-R mental disorders. Conduct disorder was assessed using the Diagnostic Interview for Children and Adolescents—Revised.15 Of the 13 possible symptoms, only symptom 9 (“has forced someone into sexual activity with him or her”) was not assessed. Mothers and twins were interviewed by separate interviewers. The reporting period consisted of symptoms present in the last 3 years. Mothers reported on symptom presence in both twins whereas twins reported only on symptom presence in themselves.

Following the interview, a clinical case conference was held in which the evidence for every symptom was discussed by at least 2 advanced clinical psychology doctoral students. Mother and child interviews were not discussed during the same case conference. As necessary, audiotapes from the interview were replayed or the participant was recontacted for clarification. Only the symptoms judged to be clinically significant in both severity and frequency were considered present. As actual diagnoses were not used in the current study, duration rules were excluded. The reliability of the consensus process was good, with a k statistic of 0.79 for diagnoses of CD.

After clinically significant symptoms were assigned, computer algorithms were used to sum the number of assigned symptoms using a combined informant approach. A symptom was considered present if it was endorsed by either the mother or the child. Symptom endorsement by both mother and child counted as only 1 symptom. Previous studies22,23 have indicated that each type of informant contributes a considerable amount of valid information not contributed by other informants, allowing for a more complete assessment of symptoms.

In this way, we created a symptom count corresponding to CD criteria in DSM-III-R. Symptom counts rather than diagnoses were used primarily to increase statistical power, as diagnostic prevalence rates in community-based samples such
14th birthday. As done in prior work, these 44 girls were added to the delayed group, enabling us to maximize the number of participants with timing of menarche data. Our study made use of the final, dichotomously coded variables.

**Table 1. Descriptive Data for Age at Menarche and Conduct Disorder**

<table>
<thead>
<tr>
<th>Age at Menarche</th>
<th>CD Symptoms, Mean (SD), No.</th>
<th>Girls With ≥3 CD Symptoms, %*</th>
<th>Girls With ≥2 CD Symptoms, %*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early (n = 136)†</td>
<td>0.45 (1.01)</td>
<td>5.8</td>
<td>9.5</td>
</tr>
<tr>
<td>Average (n = 427)‡</td>
<td>0.32 (1.07)</td>
<td>4.5</td>
<td>5.7</td>
</tr>
<tr>
<td>Late (n = 125)§</td>
<td>0.23 (0.78)</td>
<td>1.6</td>
<td>4.0</td>
</tr>
<tr>
<td>Full sample (n = 688)</td>
<td>0.32 (1.01)</td>
<td>4.1</td>
<td>5.9</td>
</tr>
</tbody>
</table>

Abbreviation: CD, conduct disorder.

*The rates should be considered upper estimates of the possible disorder prevalences in our sample, as duration requirements were omitted.
†Early age at initiation of menses included girls aged 9 years (n = 2), 10 years (n = 13), and 11 years (n = 121).
‡Average age at initiation of menses included girls aged 12 years (n = 214) and 13 years (n = 213).
§Late age at initiation of menses included girls aged 14 years (n = 70), 15 years (n = 3), and 16 years (n = 8) and girls who had not begun menstruating at the time of this assessment (n = 44).

as the Minnesota Twin Family Study are lower than in clinically referred samples. Also, available data indicate that patterns of genetic and environmental influence are similar for categorical and dimensional models of psychopathology. To better approximate normality, we rank-normalized and Blom-transformed our CD symptom count (the skew following transformation was 2.0).

**TIMING OF MENARCHE**

The Pubertal Development Scale was used to assess pubertal development in the areas of height spurts, body hair growth, skin changes, breast development, and menarche, or initiation of menstruating. Our study made use of the final, dichotomously coded variable, onset of menses. Menarche data were available for 688 of the 708 participants. By convention, girls who had begun menstruating (n = 644) were then split into 3 groups: those with precocious menarche (ie, onset at age ≤11 years; 20% of the sample), those with an average timing of menarche (ie, onset at age 12-13 years; 62% of the sample), and those with delayed onset of menarche (ie, age ≥13 years; 12% of the sample). The number of menstruating girls in each category is presented in Table 1. Furthermore, there were 44 girls (6%) who had yet to begin menstruating. Of these, 28 were aged 14 or 15 years at the time of their assessment whereas the remaining 16 were within 4 months of their 14th birthday. As done in prior work, these 44 girls were added to the delayed group, enabling us to maximize the number of participants with timing of menarche data.

**STATISTICAL ANALYSES**

The structural equation modeling used in our study uses twin methods. Twin studies make use of the difference in the proportion of genes shared between MZ twins, who share 100% of their genetic material, and DZ twins, who share an average of 50% of their segregating genetic material. Monozygotic and DZ twin correlations are compared to estimate the relative contributions of additive genetic effects (a²), shared environmental effects (c²) (ie, factors that make family members similar to each other), and nonshared environmental effects plus measurement error (e²) (ie, factors that make family members different from each other) to the variance within observed behaviors or characteristics (phenotypes). More information on twin studies is provided elsewhere.

We conducted 2 sets of analyses. First, we made use of a standard bivariate biometric model in which the variance within and the covariance between CD and timing of menarche were separated into their genetic and environmental components. We also computed genetic and environmental correlations that specify the proportion of genetic and environmental overlap between CD and timing of menarche. For example, a genetic correlation of 1.0 would indicate that all genetic influences are common to both phenotypes whereas a correlation of 0 would indicate no genetic overlap. Thus, this model enabled us to explicitly estimate the extent to which genetic influences contributed to the covariation between the phenotypes.

A structural equation modeling program, Mx, was used to perform the model-fitting analyses. The Mx program uses maximum-likelihood model-fitting techniques to fit models to covariance matrices. The χ² statistic provides a goodness-of-fit index of the model to observed variance-covariance matrices. Statistically significant χ² values reflect a poor fit. The Akaike Information Criterion (AIC), which measures model fit relative to parsimony, was also used to determine the best-fitting model among a set of fitted models, with the lowest (or most negative) AIC considered best.

Second, we evaluated whether and how timing of menarche moderated genetic and environmental influences on CD. To do so, we fit a series of nested moderator models (of note, twins are not required to be concordant on the value of the moderator). The first model functioned as a baseline main effects model in which only the genetic, shared environmental, and nonshared environmental path estimates or intercepts were computed. In the second and third models, we respectively added linear and then nonlinear genetic, shared environmental, and nonshared environmental moderators to the model. These models could detect whether there were linear or nonlinear shifts in the amount of genetic and environmental variance in CD with timing of menarche.

Because these models effectively involve fitting a separate biometric model for each individual as a function of their menarcheal timing, they require the use of full-information maximum-likelihood raw data techniques. The Mx program was used to fit models to the transformed raw data. The minimized value of minus twice the log likelihood (−2lnL) in the baseline main effects model was then compared with the −2lnL value obtained in the less restrictive linear moderator model to yield a likelihood-ratio χ² test for the significance of the moderator effects. A significant improvement in fit over the baseline model indicated that the genetic and environmental estimates vary with the timing of menarche. Consistent with previous recommendations, the current models were run a minimum of 5 times using multiple start values to ensure that the obtained estimates minimized the −2lnL value.

**RESULTS**

The Pearson correlation between CD and timing of menarche (ie, 0 = late, 1 = average, and 2 = early) suggested a
modest but significant positive association ($r=0.09$, $P=.02$). However, as Pearson correlations are not ideally suited to examine trichotomous data and may be attenuated by significant genetic and environmental moderation,33 a comparison of the mean number of CD symptoms by timing of menarche (1-way analysis of variance, $F_3=3.45$, $P<.05$) more clearly illustrates their association (Table 1). (These analyses were conducted on Blom-transformed data, which are better suited to statistical analysis because they better approximate normality. However, the corresponding raw symptom counts are presented in Table 1 to facilitate ease of presentation.) When comparing girls with 3 or more symptoms of CD (the number required for diagnosis) across timing of menarche status, those with early menarche were 1.29 times as likely to have CD as those with an average time of menarche. Further, when including girls with a probable diagnosis (ie, ≥2 symptoms of CD), those with early menarche were 1.67 times as likely to have probable CD as those with an average time of menarche and 2.38 times as likely as those with late menarche. Such findings collectively indicate that timing of menarche is linked to the number of CD symptoms present in adolescence. Of note, this association is not confounded with age at assessment, as timing of menarche is not associated with age at assessment ($r=0.01$, $P=.76$).

To further determine whether this association is specific to CD symptoms beginning in childhood (ie, child onset) or adolescence (ie, adolescent onset),35 we next examined the association between timing of menarche and childhood-onset CD (as measured by lifetime CD evaluated at the intake assessment at age 11 years). We compared timing of menarche in those participants with (n=117) and without (n=572) childhood-onset CD symptoms using an independent samples t test. The mean age at menarche did not differ (mean ages at menarche, 12.34 and 12.47 years, respectively; $P=.24$), indicating that girls with early-onset CD did not have an earlier age at menarche. We next evaluated whether girls with precocious menarche had more early-onset CD symptoms than those with average or late timing of menarche. The mean number of symptoms again did not vary (mean number of symptoms, 0.25 and 0.23, respectively; $P=.53$). Such findings collectively indicate that early-onset menarche is not associated with higher rates of childhood-onset CD but instead appears to be specific to adolescent-onset CD (ie, those symptoms present between ages 11-14 years, as presented in Table 1). Moreover, these results lend support to the notion that early menarche precedes increases in the rate of CD symptoms.

**BIVARIATE MODEL**

Consistent with prior research,14 we found that although 42% of DZ pairs were discordant for timing of menarche, only 28% of MZ pairs were discordant, findings that offer a preliminary indication of genetic influences on menarcheal timing. We thus tested an ACE bivariate model in which the variance attributable to genetic factors (A), shared environmental factors (C), and unique environmental factors plus measurement error (E) were all estimated. The full model, presented in Figure 1, provided an adequate fit to the data ($\chi^2_1=17.44$, AIC=−4.56). The genetic correlation was near 0 and not significant ($r_{\text{genetic}}=−0.06$), indicating that the genetic contributions to CD do not overlap with those for timing of menarche. In contrast, the shared environmental correlation was estimated at 1.0 and accounted for roughly 95% of the covariance between CD and timing of menarche (that shared environmental influences account for only 2% of the variance in timing of menarche and yet account for such a high proportion of covariance reflects the modest correlation between these 2 phenotypes). Consistent with this, dropping the genetic and nonshared environmental covariance terms significantly improved the fit of the model ($\chi^2_3=18.49$, AIC=−7.51). Additionally dropping the shared environmental covariance term, however, significantly worsened the fit ($\chi^2_4=22.13$, AIC=−5.87, change in $\chi^2=3.65$, $P=.06$). These findings thereby suggest that shared environmental, rather than genetic, factors largely account for the association between CD and timing of menarche.

**MODERATOR MODEL**

Test statistics for a series of nested models are reported in Table 2. Constraining parameter estimates to be constant across timing of menarche resulted in a significant decrement of fit. The optimal fit of the nonlinear model suggests that the magnitude of genetic and environmental forces impacting CD vary both linearly and nonlinearly with timing of menarche. Of note, omitting those girls who had yet to begin menstruating and were younger than 14 years did not alter the findings in any meaningful way. For the best-fitting quadratic model, we then made use of the estimated paths and moderators (Table 3) to cal-
In the main effects model, genetic, shared environmental, and nonshared environmental parameter estimates do not vary by timing of menarche. In the linear model, genetic, shared environmental, and nonshared environmental parameter estimates vary linearly. In the nonlinear model, genetic, shared environmental, and nonshared environmental parameter estimates vary both linearly and quadratically. Each model is compared with the model just preceding it when calculating the change in $\chi^2$ and degrees of freedom. Significant changes in $\chi^2$ indicate that the less restrictive model (ie, that model with more estimated parameters and therefore fewer df) provides a better fit to the data. By this standard, the nonlinear moderation model fits the data best.

### Table 2. Fit Statistics for Nested Models of Genetic, Shared Environmental, and Nonshared Environmental Parameter Estimates in Conduct Disorder*

<table>
<thead>
<tr>
<th>Model</th>
<th>$-2\ln L$</th>
<th>df</th>
<th>Change in $\chi^2$</th>
<th>Change in df</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main effects</td>
<td>1766.12</td>
<td>673</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Linear moderation</td>
<td>1755.02</td>
<td>670</td>
<td>11.10</td>
<td>3</td>
<td>.01</td>
</tr>
<tr>
<td>Nonlinear moderation</td>
<td>1742.47</td>
<td>667</td>
<td>12.55</td>
<td>3</td>
<td>.006</td>
</tr>
</tbody>
</table>

Abbreviations: NA, not applicable; $-2\ln L$, minus twice the log likelihood.

*In the main effects model, genetic, shared environmental, and nonshared environmental parameter estimates do not vary by timing of menarche. In the linear model, genetic, shared environmental, and nonshared environmental parameter estimates vary linearly. In the nonlinear model, genetic, shared environmental, and nonshared environmental parameter estimates vary both linearly and quadratically. Each model is compared with the model just preceding it when calculating the change in $\chi^2$ and degrees of freedom. Significant changes in $\chi^2$ indicate that the less restrictive model (ie, that model with more estimated parameters and therefore fewer df) provides a better fit to the data. By this standard, the nonlinear moderation model fits the data best.

### Table 3. Unstandardized Path and Moderator Estimates in the Best-Fitting Models for Conduct Disorder by Timing of Menarche*

<table>
<thead>
<tr>
<th></th>
<th>$a$</th>
<th>$c$</th>
<th>$e$</th>
<th>$A_1$</th>
<th>$C_1$</th>
<th>$E_1$</th>
<th>$A_2$</th>
<th>$C_2$</th>
<th>$E_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimate (95% CI)</td>
<td>$-0.539^\dagger$ (−0.790 to −0.351)</td>
<td>0.717† (0.489 to 0.928)</td>
<td>0.389† (0.295 to 0.539)</td>
<td>−0.665† (−0.900 to −0.303)</td>
<td>0.078† (−0.043 to 0.204)</td>
<td>0.025</td>
<td>0.393† (0.172 to 0.519)</td>
<td>0.430† (0.208 to 0.544)</td>
<td>0.061† (0.001 to 0.199)</td>
</tr>
</tbody>
</table>

Abbreviations: $a$, genetic path estimate; $A_1$, linear moderator of genetic path estimate; $A_2$, nonlinear moderator of genetic path estimate; $c$, shared environmental path estimate; $C_1$, linear moderator of shared environmental path estimate; $C_2$, nonlinear moderator of shared environmental path estimate; $e$, nonshared environmental path estimate; $E_1$, linear moderator of nonshared environmental path estimate; $E_2$, nonlinear moderator of nonshared environmental path estimate.

*For girls with late-onset menarche (coded as 0), the genetic and environmental variance components can be obtained by squaring the genetic ($a$, shared environmental $(c)$, and nonshared environmental $(e)$ path estimates. For girls with average or early timing of menarche, linear ($i.e., A_1, C_1, E_1$) and nonlinear ($i.e., A_2, C_2, E_2$) moderators were added to these genetic and environmental paths using the following equation: $\text{variance}_{\text{genetic}} = (a + A_1[\text{timing}])^2 + c + (c + C_1[\text{timing}] + C_2[\text{timing}])^2 + (e + E_1[\text{timing}] + E_2[\text{timing}])^2$. Accordingly, for girls with early-onset menarche, the unstandardized genetic variance is $(-0.539 + (-0.665 \times 2) + [0.393 \times 4])^2 = 0.088$. The variance component estimates calculated in this way are standardized and presented in Figure 2.

$^\dagger$The paths or moderators are significant at $P<.05$ as indicated by CIs that do not overlap with 0.

### Figure 2. Standardized genetic ($A$), shared environmental ($C$), and nonshared environmental ($E$) variance contributions to conduct disorder by timing of menarche.

Categorize and plot the standardized genetic and environmental variance components for each group. Because late status was coded as “0,” the path estimates functioned as intercepts. Thus, the genetic and environmental variance components for girls with late onset of menarche were obtained simply by squaring these path estimates. For those with average (ie, “1”) and early (ie, “2”) onset of menarche, linear (ie, $A_1, C_1, E_1$) and nonlinear (ie, $A_2, C_2, E_2$) moderators were added to these genetic and environmental paths using the following equation: $\text{variance}_{\text{genetic}} = (a + A_1[\text{timing}] + A_2[\text{timing}^2])^2$. These estimates were then standardized for each group (Figure 2). Although potentially problematic in moderator models, standardization does ease presentation of results. Moreover, in this case, the shifts in $A$, $C$, and $E$ parameters look essentially identical in the unstandardized figure (not shown) (likely owing to the relatively constant variance in CD across menarcheal groups). Further, although residual skewness in the distribution of the phenotype can induce “a gentle trend for all variance components to be attenuated similarly at low levels of the moderator,”33 this effect was not present.

Genetic influences on CD were strongest (67%) for girls with an average age at menarche and were significantly smaller (as evidenced by the significant linear and nonlinear moderation parameters) for girls with early or late initiation of menses. This effect was particularly pronounced for those with early initiation of menses, as genetic influences on CD are quite modest (8%) for this group. In contrast, environmental influences appeared to be particularly salient for girls with early menarche and far less important for girls with on-time development. Shared environmental influences were weakest for those with an average age at menarche and stronger for those with early or late menarche. Nonshared environmental influences similarly appeared strongest for early-
maturing girls as compared with on-time- or late-maturing girls (these effects were only nonlinearly moderated).

**COMMENT**

The primary aim of our study was to evaluate possible mechanisms underlying the association between the timing of menarche and CD symptoms in girls during mid adolescence. We began by confirming previous findings suggesting that those with precocious timing of menarche have higher rates of adolescent CD symptoms as compared with those with average or late initiation of menses.\(^1,3\) We then conducted 2 sets of structural equation analyses: (1) a bivariate model to determine whether CD and timing of menarche covaried as a function of genetic influences, and (2) biometric moderator analyses to evaluate whether and how timing of menarche impacted the etiology of CD. Our results supported neither genetic overlap nor exacerbation of the genetic influences on CD as a function of early menarche.\(^2,6\) Instead, we found that adolescent CD was largely environmental in origin for those with precocious and, to a lesser extent, delayed timing of menarche. Moreover, we found that although CD was particularly heritable for those with an average age at menarche, it was only minimally heritable for those with an early onset of menses, results that collectively provide support for an environmentally mediated link between adolescent CD and early menarche.

These findings mesh well with existing genetically informative literature. Only 1 other study has, to our knowledge, incorporated information on genetic relatedness into the examination of the link between menarcheal timing and adolescent behavioral outcomes. Dick et al\(^6\) compared rates of substance use in a subsample of 99 extremely discordant DZ twin pairs (ie, age at menarche differed by \(\geq2\) years). Using this within-family design, they found evidence that the well-documented association between early menarche and the rate of substance use exists only in urban, not rural, settings. Similarly, several genetically informative, between-family studies\(^1,3,5\) have robustly supported contextual amplification of menarcheal timing effects via several mechanisms, including neighborhood disadvantage, harsh and inconsistent parental discipline, and a mixed-sex composition of the schools (vs all-girl schools). Such findings are quite consistent with our study’s findings of predominantly environmental mediation of CD in early-maturing girls. In contrast, our findings are not consistent with those of Comings et al,\(^8\) who reported that the androgen receptor gene was responsible for the association of father absence with early menarche and behavioral problems in the daughters. It should be noted, however, that other investigators\(^9\) were also unable to reproduce the original findings.\(^8\)

However, there are limitations to our study. First, as these data were not evaluated longitudinally and as the magnitude of genetic influences on delinquency varies across adolescence,\(^26\) we cannot be sure whether these effects will persist to later ages. Second, as the link between early pubertal timing and increased CD is less certain among boys,\(^3\) only girls were examined in the current study. As puberty in boys and girls involves different social and biological phenomena, it remains unclear whether these findings would generalize to boys. Future research should seek to evaluate the impact of early pubertal timing on CD longitudinally and in boys. Third, as with most behavioral genetic research, the current findings have only limited clinical utility. However, they do tentatively suggest that those with early-onset menarche may be somewhat more amenable to treatment of their adolescent-onset CD symptoms than those with later timing of menarche. Fourth, as with all twin studies, this study relies on the equal environments assumption for interpretation of the results. Evaluating the equal environments assumption was beyond the scope of our study (although it does appear tenable for many mental disorders).\(^37\)

Finally, the 3-year assessment interval for CD symptoms allows for the possibility that symptoms desisted prior to initiation of menses. However, shortening the CD assessment interval to roughly 1 year did not appreciably alter our conclusions. We found that 80% of the symptoms were present within this interval and that their relationship with the timing of menarche remained unchanged. The nonlinear moderator model again fit the data best, with generally similar results (ie, CD was primarily environmental, and particularly shared environmental, in origin in girls with early-onset menses). Such findings further increase confidence in our results.

The findings presented herein have 2 important and interrelated implications. First, our findings of largely environmental mediation of CD for those girls with precocious menarche and, to a lesser extent, delayed menarche offer indirect support for psychosocial interpretations\(^7,11\) of the impact of these pubertal transitions. Thus, rather than resulting from masked genetic commonalities or an exacerbation of the genetic influences on CD, previous findings\(^1,3,5\) of contextual amplification of menarcheal timing effects may represent potent environmentally mediated influences on adolescent girls’ mental health. Future research should seek to clarify which of the aforementioned contextual modulators may operate in this way.

Second, our findings expand the understanding of genetic influences on both CD and psychopathology in general. Although researchers often conceptualize gene-environment interactions such that high-risk environments exacerbate genetic influences on a disorder,\(^17\) our findings highlight another, somewhat older conceptualization of gene-environment interplay, that related to the “average, expectable” environment.\(^38\) In this case, genetic influences are thought to be most strongly expressed under normal to optimal environmental conditions. More extreme or unfavorable conditions may act as “environmental main effects,” such that differences in the trait are a function of differences in environmental circumstances rather than differences in genetic makeup.\(^38\) Findings from a study by Turkheimer et al\(^34\) of the moderation of genetic and environmental influences on IQ by socioeconomic status provide a nice example of this phenomenon. Turkheimer and colleagues found that individual differences in IQ were largely genetic in origin only for those children who grew up in families with a middle to high socioeconomic status. However, for chil-
dren from disadvantaged backgrounds, individual differences in IQ were primarily a function of shared environmental influences. When viewed in conjunction with those of our study, such findings suggest that there may be particular disadvantageous conditions that exert an environmentally mediated effect on psychological or behavioral outcomes, effectively suppressing the normal expression of genetic influences. Future research should seek to clarify the means through which different forms of gene-environment interplay impact the development of mental illness.

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REFERENCES


