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Pubertal Development Moderates the Importance of Environmental Influences on Depressive Symptoms in Adolescent Girls and Boys

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Abstract

Prevalence differences in depressive symptoms between the sexes typically emerge in adolescence, with symptoms more prevalent among girls. Some evidence suggests that variation in onset and progression of puberty might contribute to these differences. This study used a genetically informative, longitudinal (assessed at ages 12, 14, and 17) sample of Finnish adolescent twins ($N = 1214$, 51.6% female) to test whether etiological influences on depressive symptoms differ as a function of pubertal status. These tests were conducted separately by sex, and explored longitudinal relationships. Results indicated that pubertal development moderates environmental influences on depressive symptoms. These factors are more important on age 14 depressive symptoms among more developed girls relative to their less developed peers, but decrease in influence on age 17 depressive symptoms. The same effects are observed in boys, but are delayed, paralleling the delay in pubertal development in boys compared to girls. Thus, the importance of environmental influences on depressive symptoms during adolescence changes as a function of pubertal development, and the timing of this effect differs across the sexes.

Keywords

Pubertal development; Depressive symptoms; Moderation; Genetics

Introduction

Adolescent depression is a relatively common psychiatric disorder, with a prevalence of approximately 14% in the U.S. (Office of Applied Studies 2005). Adolescent depressive

symptoms can be a predictor of adult depression (Aalto-Setälä et al. 2002), which remains a dominant human health concern. Women suffer from depression at nearly twice the rate of men, and many epidemiological studies have observed that this sex difference becomes evident during adolescence (Cyranowski et al. 2000) and seems to coincide with the onset of puberty (Angold et al. 1998). However, our understanding of the factors contributing to this sex difference in prevalence remains incomplete, as does our knowledge of potential changes in the sources of variance underlying depressive symptoms during this dynamic developmental period.

Researchers have posited various hypotheses regarding the relationship between puberty and depression or depressive symptoms. Some researchers have found that pubertal status, as defined by Tanner Stage, influences female depression (Angold et al. 1998): only after midpuberty (Tanner Stage III or higher) were girls more likely to be depressed than boys. Others have suggested that gonadal hormones that circulate during puberty cause mood disturbances (Born et al. 2002). Interestingly, one research group reported that, while estrogen modestly influenced negative affect among adolescent girls, the additional consideration of negative life events improved the prediction of negative affect (Brooks-Gunn and Warren 1989). Another report indicated that testosterone and estradiol levels, but not luteinizing hormone or follicle stimulating hormone levels, were positively associated with depression in adolescent girls (Angold et al. 1999). In summary, a wealth of evidence supports the presence of a relationship between hormone levels and depression. However, whether this association is causal or correlative remains unclear.

The onset of pubertal development is earlier on average for girls than for boys. Girls begin to exhibit one sign of pubertal development, the growth of pubic hair, 6–12 months earlier than boys (Pinyerd and Zipf 2005), and gonadarche begins around a year earlier in girls (Blakemore et al. 2010). A previous report of pubertal development for the sample used in the current analyses (Dick et al. 2001) was consistent with earlier development in girls: girls reported higher scores on the Pubertal Development Scale than boys at ages 12 and 14. This difference in timing could lead to girls' exposure to novel biological or psychosocial risk factors at earlier ages than boys.

In addition to physiological changes experienced during puberty, adolescents experience a shift in social roles, affiliations, and expectations, with regard to both adults and peers (Angold and Costello 2006; Cyranowski et al. 2000; Nolen-Hoeksema and Girgus 1994). These environmental changes may be experienced as negative and/or stressful, and might thereby contribute to depression risk (Sandberg et al. 2001). These variables could play a role in the observed sex difference in depression prevalence: girls report more negative life events than do boys (Ge et al. 1994). Changing environmental factors, in conjunction with the aforementioned biological influences on depression that become relevant during puberty, create a complex and dynamic model of risk (Cyranowski et al. 2000).

Genetic factors further complicate the biological component of the relationship between pubertal development and depression. Pubertal timing is strongly influenced by genetic factors: heritability estimates have exceeded .90 (Eaves et al. 2004) though others have been more moderate (.49 for age at menarche, Towne et al. 2005). Depressive symptoms are genetically influenced to a lesser degree. Most heritability estimates are modest to moderate, ranging from ~.25 to .56 (Glowinski et al. 2003; Rijdsdijk et al. 2003; Tambs et al. 1997), though others have reported much higher (Kendler et al. 2008) or lower (Silberg et al. 1999) estimates. There is some evidence for sex differences in heritability: one study reported heritability estimates ranging from .25 to .48 for males, and from .45 to .56 for females (Tambs et al. 1997). In addition, the heritability of many psychiatric phenotypes, including depression, begins to increase during adolescence and into adulthood (Bergen et al. 2007),

raising the possibility that factors relevant during this time—such as pubertal development or timing—might be modifying relevant genetic or environmental influences underlying depression.

Despite a longstanding interest in the association of puberty and depression or depressive symptoms, few if any studies have investigated whether the degree of pubertal development moderates etiological factors impacting depressive symptoms. Documenting such moderation would not preclude prior hypotheses (such as effects of gonadal hormones, for example), but the identification of such a relationship could help explain the changes in etiological factors contributing to depression across adolescence. We undertook the current analyses to further explore the relationship between pubertal development and depressive symptoms and examine whether there are differences in the timing or the nature of this relationship across the sexes. As described above, previous findings indicate that there is a robust association between pubertal development (as determined by hormone levels, Tanner Stage, etc.) and depressive symptoms. Therefore, we tested whether this effect is due to moderation of the etiology (i.e., contributions of genetic and/or environmental influences) of depressive symptoms by level of pubertal development, and whether such moderation changes across time.

Hypotheses

At the phenotypic level, we predict that sex differences in depressive symptoms will coincide with pubertal development, with girls endorsing higher levels of depressive symptoms than boys as they mature. Previous studies have not investigated whether pubertal development moderates the etiology of depressive symptoms. However, given past findings regarding changes in heritability across adolescence, we predict that the heritability of depressive symptoms will increase as pubertal development proceeds. We do not have specific hypotheses regarding whether this will be due to an increase in the importance of genetic factors, versus a decrease in the importance of environmental factors, in more developed adolescents. Furthermore, since boys begin puberty later than girls, we hypothesize that moderation effects, if present, will be observed at later ages (though at roughly the same point in pubertal development) than in girls. To summarize, we expect to find that pubertal development moderates the etiology underlying depressive symptoms, and we expect to see this moderation affecting boys at a later age than girls.

Method

Sample

FinnTwin12 is an ongoing longitudinal study with the purpose of investigating genetic and environmental influences on health-related behaviors (Kaprio et al. 2002). From 1994 to 1998, Finnish families with twins born between 1983 and 1987 were identified from Finland's population registry and enrolled in the study. FinnTwin12 consists of two stages: the first used questionnaires to assess all twins and parents at baseline when the twins were age 12 (87% participation rate, $N = 2,724$ families), with a follow-up of all twins at ages 14 and 17. The second stage consisted of intensive assessments of a subsample of this group: 28% of the subsample consisted of twins selected because of parental scores on the Malmö-modified Michigan Alcoholism Screening Test (Seppa et al. 1990) and assumed to be at risk for alcohol problems (Dick et al. 2005; Rose et al. 2004). The current analyses were based on the intensive subsample, in which psychiatric interview data on depressive symptoms were available. A previous study (Rose et al. 2004) indicated that this subsample does not differ from the unselected sample in their use of alcohol in adolescence, suggesting that results from the analyses herein are generalizable to the unselected population.

Only same-sex monozygotic (MZ) and dizygotic (DZ) twins were included in the current analyses. Complete or partial data were available for 167 female MZ twin pairs, 138 female DZ twin pairs, 169 male MZ twin pairs, and 163 male DZ twin pairs. Zygosity was determined using a well-validated questionnaire completed by both co-twins at baseline, as described elsewhere (Kaprio et al. 1995). Confirmation of zygosity came from genetic testing of DNA from twin pairs participating in the ongoing fourth wave of data collection. The ethics committee of the Helsinki and Uusimaa University Hospital District, Finland, and the institutional review board of Indiana University approved data collection.

Measures

Pubertal Development—Pubertal development was assessed at ages 12 and 14 using the Pubertal Development Scale (Petersen et al. 1988), in which items are related to changes in physical development experienced during puberty (hair growth, acne, etc.). An average score was computed across the five items (as in (Dick et al. 2001)). For twin modeling, this was converted into a Z-score, separately by sex, to facilitate use as a moderating variable (see below). Raw scores on the Pubertal Development Scale are abbreviated as “PDS scores”, while transformed scores are abbreviated as “zPDS scores”. We note that the use of a standardized PDS score was used to facilitate interpretation of tests for moderation; however, this also creates a measure that is something of a hybrid between pubertal development and pubertal timing relative to same-sex peers.

Depressive Symptoms—Depressive symptoms at ages 12 and 14 were measured using the Children’s Depression Inventory (CDI) (Kovacs 1991); at age 17, a subscale of the General Behavior Inventory (GBI) (Depue 1987) was used. These scales have been described previously (Edwards et al. 2010). Descriptive statistics for age 12 depressive symptoms are included to test the previous observation that sex differences in depression emerge after age 13 (Angold et al. 1998; Hankin and Abramson 2001), though we note that Tanner Stage (Angold et al. 1998) or hormone levels (Angold et al. 1999) might be more powerful predictors of prevalence difference than age. Twin modeling was conducted on age 12 zPDS scores as a moderator of age 14 depressive symptoms, and age 14 zPDS scores as a moderator of age 17 depressive symptoms.

Stressful Life Events—Post hoc analyses made use of items regarding life events experienced between ages 12 and 14. These included events such as parental divorce, death of a loved one, serious illness, etc. Twins also indicated whether they experienced these changes in a positive or negative way, using a scale of 1–5.

Statistical Analyses

Descriptive statistics were obtained from SAS 9.1.3. Significance values were corrected for sampling as twin pairs using PROC GENMOD where appropriate. Twin modeling was conducted in Mx (Neale et al. 2006) using the raw continuous data option. In twin modeling, liability to measured phenotypes of interest (in this case, standardized scores of pubertal development, and depressive symptom scores) is partitioned into several latent sources of variance: additive genetic factors (A), non-additive genetic factors (D), shared environment (C), and unique environment (E). The A variance component reflects the extent to which genetic factors influence the trait of interest. The correlation between latent genetic influences (A) between the twins varies by zygosity, since MZ twins share all of their genetic variation, and DZ twins share on average half of their genetic variation identical by descent: specifically, the intraclass correlation of the phenotypes should be higher for MZ pairs than for DZ pairs if the phenotype is genetically influenced. The C variance component represents environmental exposures that contribute to twins’ increased phenotypic similarity, and does so to an equal degree for MZ and DZ twins based on the assumption

that both types of twin, when reared together, equivalently share outcome-relevant aspects of their environment. The E variance component represents factors unique to each twin, and reduces twin similarity for a phenotype of interest; in addition, E includes error variance (and thus cannot be excluded from the model).

Variance components are estimated by comparing the intraclass correlation between MZ twins to that of DZ twins (Fig. 1). This correlation is a function of both genetic and shared environmental factors. As indicated above, if the correlation of MZ twins (r_{MZ}) exceeds that of DZ twins (r_{DZ}), genetic factors likely influence the trait at least to some degree. If r_{DZ} is approximately half r_{MZ} , shared environmental factors likely play little role in the variance of the trait; however, if $r_{DZ} > \frac{1}{2} r_{MZ}$, shared environmental factors contribute to the outcome, because we expect DZs to be but half as alike as MZs based on genetic sharing alone. If $r_{DZ} < \frac{1}{2} r_{MZ}$, non-additive genetic effects are likely important. If only twins are included in the model, C and D cannot be estimated simultaneously.

In multivariate models, such as those used in the current analyses, genetic and environmental relationships between phenotypes are estimated by taking into consideration both the within-pair correlation for MZ and DZ twins, as well as the correlations across phenotypes for MZ twins and DZ twins. Multivariate models are powerful methods for deriving these relationships, since more information is available for estimating variance components than in univariate models. Again, if only twins are included in the model, C and D cannot be estimated simultaneously.

In the first step of our modeling, we fit univariate twin models to depressive symptoms at ages 14 and 17, separately. For the current data, twin correlations did not suggest the presence of D effects; therefore, the full model included C but not D. Next, we fit moderation models that allowed for genetic and environmental influences on depressive symptoms to change as a function of zPDS score. Specifically, we investigated whether there was evidence that zPDS moderated the etiology of later depressive symptoms.

Since previous studies have indicated that pubertal development is genetically influenced (Eaves et al. 2004; Mustanski et al. 2004), we fit moderation models that accounted for genetic and environmental sources of variance on zPDS as well as for potential genetic and environmental correlations between pubertal development and depressive symptoms (Fig. 2). We also test for moderation of the genetic and environmental influences on depressive symptoms. The full details of this model can be found in Purcell (Purcell 2002); Fig. 2 presents the genetic portion of the moderation model tested in the current analyses. Briefly, moderation is accounted for in the model by the addition of an estimated coefficient multiplied by the value of the moderator (here, zPDS). This term is added to both the shared genetic/environmental factor loading and to the genetic/environmental factor loading specific to the variable being moderated (here, depressive symptoms). If this term (β^*zPDS) can be set to 0 without a significant deterioration in model fit, we conclude that there is no significant moderation.

In the present analyses, we focus on the moderation component of the model and limit our presentation of results to these moderation effects, because this is our primary question. In order to determine whether the relationship between pubertal development and depressive symptoms changes across time, we examined this relationship across different ages: we assessed moderation by age 12 zPDS on age 14 depressive symptoms, and by age 14 zPDS on age 17 depressive symptoms. In order to facilitate model fitting, these models were not run simultaneously.

Models were estimated using a full information maximum likelihood estimation method. The fit of submodels nested within the full model was assessed as a function of the change

in the value of twice the log likelihood (2LL) of the data, which is distributed as a chi-square statistic with degrees of freedom equal to the difference in the number of parameters estimated between models. A significant $\Delta\chi^2$ indicates a significant deterioration in model fit, which would result in rejection of the nested model. We also used the Akaike Information Criterion (Akaike 1987) (AIC) to select models. A lower AIC value indicates a better balance between the explanatory power of a model and parsimony.

All models were fit separately by sex, as this allowed us to easily explore potential differences between the sexes with regard to timing and sources of variance. Model fitting proceeded by first testing whether the A or C variance components could be removed from the model without a significant deterioration in fit. Once sources of variance were established, we tested whether moderation paths could be dropped from the model, testing the genetic, shared environmental (where applicable), and unique environmental factors in turn. Essentially, this test assesses whether the etiology of depressive symptoms changes as a function of pubertal development.

Results

Descriptive Statistics

Descriptive statistics, and tests of sex differences by phenotype, are provided in Table 1. Boys' and girls' physical pubertal development scores differed significantly at ages 12 and 14, with boys developing later than girls, as is expected. At age 12, there were no sex differences in depressive symptoms. However, at ages 14 and 17, girls' depressive symptom scores were higher than boys'.

Twin Modeling in Girls

Preliminary univariate twin modeling in girls revealed that shared environmental influences could be dropped from the model for depressive symptoms at ages 14 and 17 (Table 2A, B). These findings were incorporated into twin modeling that tested for moderation effects: we limited our model to the variance components on depressive symptoms shown to be significant in the initial univariate models (see Table 3A, B). Since shared environmental influences were not included in the multivariate models for girls, reference to "environmental influences" should be understood to mean "unique environmental influences", encompassed by the E variance component.

We did not detect genetic moderation on depressive symptoms at age 14 or age 17. However, age 12 zPDS moderated environmental influences on age 14 depressive symptoms, and age 14 zPDS moderated environmental influences on age 17 depressive symptoms. Interestingly, the direction of this effect changed over time: environmental influences on age 14 depressive symptoms were more important in more developed age 12 girls than in less developed girls; however, environmental influences on age 17 depressive symptoms were less important in more developed girls than in less developed girls. Figure 3a, b depict changes in the total genetic and environmental variance of age 14 and age 17 depressive symptoms as a function of zPDS.

Twin Modeling in Boys

Preliminary univariate modeling in boys indicated that a CE model fit best for age 14 depressive symptoms, and an AE model fit best for age 17 depressive symptoms (Table 2C, D). Again, these findings were incorporated in models that subsequently investigated moderation effects (Table 3C, D). In contrast to our findings in girls, we did not observe moderation of unique environmental influences on age 14 depressive symptoms by age 12 pubertal development. However, we did observe moderation of unique environmental

influences on age 17 depressive symptoms by age 14 zPDS scores. The effect of this moderation was that unique environmental influences on age 17 depressive symptoms were more influential among more developed boys than among less developed boys. Figure 3c, d depict changes in the total genetic and environmental variance of age 14 and age 17 depressive symptoms as a function of physical pubertal development (as quantified by zPDS scores).

Discussion

Many previous studies have identified a phenotypic association between pubertal development and depressive symptoms (Angold and Costello 2006). Beginning in adolescence and thus coinciding with the onset and continuation of puberty, girls report higher levels of depressive symptoms than do boys (Angold et al. 1998), raising the possibility that there is a direct relationship between pubertal development and depressive symptoms, and this relationship might differ across the sexes. This relationship is likely multifactorial, involving biological, social, and other environmental changes that become relevant during adolescence (Cyranowski et al., 2000). Twin studies have found that the heritability of depression or depressive symptoms changes during this time (Bergen et al. 2007), which leads us to question whether physical pubertal development might be moderating genetic and/or environmental influences on depressive symptoms during this developmentally dynamic period.

Our results confirm that a complex and dynamic relationship exists between physical pubertal development and depressive symptoms. Specifically, pubertal development moderates the influence of environmental factors on depressive symptoms. The direction of these moderation effects changes across time, and begins in girls at an earlier age than in boys, paralleling the earlier onset of puberty in girls relative to boys. Among more physically developed girls, unique environmental influences on depressive symptoms were more important at age 14, and less important at age 17 (relative to less developed girls). Among boys, we did not observe any relationship between age 12 pubertal development and age 14 depressive symptoms. However, age 14 pubertal development positively moderated unique environmental influences on age 17 depressive symptoms such that environmental influences on depressive symptoms were more important among more developed boys—a result that parallels the relationship seen in girls between age 12 zPDS and age 14 depressive symptoms. These results represent an important contribution to our understanding of the phenotypic relationship between physical pubertal development and depressive symptoms, and improve our understanding of the etiology of depressive symptoms during this developmental period.

That physical development moderates environmental, but not genetic, influences on depressive symptoms, is important and would not necessarily be expected given previous findings that the heritability of psychopathologies increases as individuals mature (Bergen et al. 2007). Such findings could potentially result from the examination of standardized variance components without regard for unstandardized measures. Figure 4, which depicts standardized variance components for girls' age 17 depressive symptoms as a function of zPDS, is provided as a contrast to Fig. 3 in order to demonstrate this point. The heritability of depressive symptoms increases in girls from age 14 to age 17 (Fig. 4); however, reference to Fig. 3b reveals that this "increase" in heritability is merely a function of the decreasing influence of environmental factors. Thus, total genetic variance is largely unchanging: heritability only appears dynamic because it is a proportion of the total variance. This fact underscores the need to examine both variance standardized and unstandardized sources of variance when possible.

Thus, though depressive symptoms might be subject to genetic innovation (“new” genetic influences becoming relevant) and genetic attenuation (decreasing influence of genetic factors that were previously relevant) across adolescence as suggested by previous studies, the current results suggest that the influence of environmental factors on adolescents is a critical component of changes in their propensity to experience depressive symptoms. Furthermore, the timing of such changes in sensitivity appears to be attributable in part to pubertal development. Among girls more developed at age 12, environmental factors are more influential; however, those same girls “mature out” of high environmental sensitivity by age 17. Among boys, the relative increase in importance of environmental factors is delayed relative to girls (though normal given the difference in onset of pubertal development). Age 12 pubertal development does not moderate the importance of environmental factors on age 14 depressive symptoms, but we observe in 17-year-old boys the same phenomenon found in 14-year-old girls: more developed boys are more sensitive to environmental influences on depressive symptoms than are less developed boys. In the absence of data beyond age 17, we cannot determine whether the relative importance of environmental factors decreases for these boys later, as it does for girls. We plan to analyze later follow-ups to address this question.

At age 12, the sexes do not differ in their endorsement of depressive symptoms, but by age 14 girls report higher levels of symptoms, a difference that persists to age 17. Again, without later data we cannot know whether boys “catch up” with girls in terms of depressive symptoms, but evidence from other studies would suggest that these sex differences persist throughout adulthood (Lindeman et al. 2000). This persistence could be partially attributable to continued relevance of environmental influences experienced during adolescence; to environmental factors that only become relevant in early adulthood; and/or to later genetic innovation.

So why do we find greater influence of unique environmental effects among more physically developed adolescents? More developed adolescents are more likely to associate with older or more deviant peers, as has been previously reported (Stattin and Magnusson 1990; Westling et al. 2008). It is possible as well that “early bloomers” gain exposure to *new* environmental influences, such as stressful social situations like peer pressure, family discord, or social bullying, that are simply not a part of less developed individuals’ lives. Individuals who develop early are more likely to be exposed to alcohol, tobacco, and drug use (Costello et al. 2007; Dick et al. 2001) and experiment sexually early in life (Phinney et al. 1990). As they mature, adolescents might be treated differently by adults in their lives and be subject to changing expectations (Waylen and Wolke 2004).

Some of these novel environmental considerations might differ across sexes or affect boys and girls differentially. For example, family discord appears to disproportionately affect adolescent girls in a negative way (Zahn-Waxler et al. 2006). Girls might be more susceptible to body image stereotypes (Hankin and Abramson 1999), which could impact self-esteem and contribute to depressive symptoms. Girls also report being more upset by peer sexual harassment than do boys (American Association of University Women 2001). In addition, and particularly relevant to our findings, a recent study (Natsuaki et al. 2009) found that more developed girls were more sensitive to interpersonal stress, which contributed to their higher levels of internalizing problems. Thus, a multitude of environmental factors might impact on adolescents’ risk of depression; some of these might happen to one sex more frequently; and one sex might have a stronger response to these factors. We note further that many of the environmental risk factors we’ve described are less likely to be experienced prior to puberty. Exposure to such novel environmental factors is qualitatively different than a shift in sensitivity to unchanging environmental factors (for

example, neighborhood of residence); unfortunately, we cannot distinguish between these possibilities—which are not mutually exclusive—with the models used in these analyses.

Our results offer a novel contribution to our understanding of how these traits interrelate, as previous research has not addressed the moderation of physical pubertal development on the etiology of depressive symptoms. Unfortunately, it makes it difficult to contextualize our findings. A number of researchers have proposed that biological vulnerabilities, including genetic influences and pubertal timing/development, in combination with stressful life events, lead to sex differences in depression prevalence (Hyde et al. 2008). Our phenotypic data support the existence of sex differences that emerge during adolescence. However, the design of our study does not enable us to directly address causal influences on sex differences in prevalence. Results from twin modeling suggest that the phenomena underlying depressive symptoms—that is, a combination of genetic influences and changing sensitivity to environmental factors—are quite similar in boys and girls. However, there is a striking difference between the sexes that emerges from these analyses: that is, the timing of moderation effects, with effects observed earlier in girls than in boys. The mechanism by which this difference might lead to sex differences in prevalence is not clear and could be multifactorial.

However, given that previous studies have indicated that adolescent girls report more negative life events than do adolescent boys (Ge et al. 1994), and our results indicate that environmental factors are critical components of liability to depression, we might hypothesize that differential experiences of life stress during a critical developmental period contribute to the sex difference in depression prevalence. In light of these findings, we conducted post-hoc tests to determine whether 14-year-old (the only age for which data were available) girls reported more stressful life events than did boys. Girls not only reported significantly ($P = 0.044$) more events than boys, they also reported feeling more stressed by these events ($P < 0.0001$), which is consistent with a previous finding that girls are more sensitive to environmental effects than are boys (Dick et al. 2007). Neither age 12 nor age 14 PDS was correlated with the number of stressful events reported (maximum $r < 0.02$) for either sex, indicating that individuals are not experiencing more stressors because they are more developed. Additional research is needed to determine the extent to which differences in life events influence depressive symptoms in this sample.

These analyses represent basic research on the interrelationships of genetic influences, pubertal development, and depression. Additional studies will be necessary to identify mechanisms underlying these relationships. At this stage, potential clinical implications—such as goals for treatment, intervention, or prevention—of these results can only be speculative. However, based on these findings, parents and clinicians would be prudent to consider the link between pubertal development and depressive symptoms, noting that, as development proceeds, adolescents might be particularly sensitive to environmental influences on depressive symptoms. These results indicate that the relevant risk period is later for boys than for girls, paralleling the timing of boys' development relative to girls'.

These findings should be considered in light of several limitations. First, the sample size available for these analyses is modest, limiting our statistical power. Second, only self-reports of depressive symptoms are used, and there is some evidence that parental reports of depressive symptoms differ from self-reports (Laitinen-Krispijn et al. 1999). Third, our standardization of PDS scores—which was calculated to facilitate with the moderation model—complicates the interpretation of pubertal development: it is possible that individuals with low Z-scores have progressed through pubertal development substantially but are still “behind” their peers: in other words, the Z-score variable could be interpreted as a hybrid of development and timing. In addition, previous studies have implied that the

manner in which pubertal development is operationalized—e.g., age, timing, perceived timing relative to peers, Tanner Stage—can result in different interpretations of the relationship between pubertal development and depression (Conley and Rudolph 2009). However, there is no obvious reason that our results would change substantively had a non-transformed variable been used. Acknowledging these limitations in the context of our study's strengths, including a representative sample and longitudinal assessments, we conclude that the influence of environmental factors on adolescent depressive symptoms differs as a function of physical pubertal development.

Our phenotypic results replicate the phenomenon of sex differences in depression prevalence, though we included subclinical measures of depression and thus might not be directly comparable to previous studies. Twin modeling indicated that pubertal development influences the etiology of depressive symptoms similarly across the sexes; specifically, development moderates environmental influences on depressive symptoms, but does not moderate genetic influences on these symptoms. Importantly, these effects occur later in boys than in girls. In summary, these analyses underscore a complicated relationship between pubertal development and depressive symptoms, and indicate that the influence of environmental factors on liability to depressive symptoms changes as a function of development.

References

- Aalto-Setälä T, Marttunen M, Tuulio-Henriksson A, Poikolainen K, Lonnqvist J. Depressive symptoms in adolescence as predictors of early adulthood depressive disorders and maladjustment. *American Journal of Psychiatry*. 2002; 159:1235–1237. [PubMed: 12091207]
- Akaike H. Factor analysis and AIC. *Psychometrika*. 1987; 52:317–332.
- Lipson, J., editor. American Association of University Women. *Hostile hallways: Bullying, teasing, and sexual harassment in school*. Washington, DC: 2001.
- Angold A, Costello EJ. Puberty and depression. *Child and Adolescent Psychiatric Clinics of North America*. 2006; 15:919–937. ix. [PubMed: 16952768]
- Angold A, Costello EJ, Erkanli A, Worthman CM. Pubertal changes in hormone levels and depression in girls. *Psychological Medicine*. 1999; 29:1043–1053. [PubMed: 10576297]
- Angold A, Costello EJ, Worthman CM. Puberty and depression: The roles of age, pubertal status and pubertal timing. *Psychological Medicine*. 1998; 28:51–61. [PubMed: 9483683]
- Bergen SE, Gardner CO, Kendler KS. Age-related changes in heritability of behavioral phenotypes over adolescence and young adulthood: A meta-analysis. *Twin Research and Human Genetics*. 2007; 10:423–433. [PubMed: 17564500]
- Blakemore SJ, Burnett S, Dahl RE. The role of puberty in the developing adolescent brain. *Human Brain Mapping*. 2010; 31:926–933. [PubMed: 20496383]
- Born L, Shea A, Steiner M. The roots of depression in adolescent girls: Is menarche the key? *Current Psychiatry Reports*. 2002; 4:449–460. [PubMed: 12441025]
- Brooks-Gunn J, Warren MP. Biological and social contributions to negative affect in young adolescent girls. *Child Development*. 1989; 60:40–55. [PubMed: 2702873]
- Conley CS, Rudolph KD. The emerging sex difference in adolescent depression: Interacting contributions of puberty and peer stress. *Development and Psychopathology*. 2009; 21:593–620. [PubMed: 19338700]
- Costello EJ, Sung M, Worthman C, Angold A. Pubertal maturation and the development of alcohol use and abuse. *Drug and Alcohol Dependence*. 2007; 88(Suppl 1):S50–59. [PubMed: 17275214]
- Cyranowski JM, Frank E, Young E, Shear MK. Adolescent onset of the gender difference in lifetime rates of major depression: A theoretical model. *Archives of General Psychiatry*. 2000; 57:21–27. [PubMed: 10632229]
- Depue, R. *General behavior inventory*. Ithaca, NY: Department of Psychology, Cornell University; 1987.

- Dick DM, Pagan JL, Holliday C, Viken R, Pulkkinen L, Kaprio J, et al. Gender differences in friends' influences on adolescent drinking: A genetic epidemiological study. *Alcoholism, Clinical and Experimental Research*. 2007; 31:2012–2019.
- Dick DM, Rose RD, Pulkkinen L, Kaprio J. Measuring puberty and understanding its impact: A longitudinal study of adolescent twins. *Journal of Youth and Adolescence*. 2001; 30:385–399.
- Dick DM, Viken RJ, Kaprio J, Pulkkinen L, Rose RJ. Understanding the covariation among childhood externalizing symptoms: Genetic and environmental influences on conduct disorder, attention deficit hyperactivity disorder, and oppositional defiant disorder symptoms. *Journal of Abnormal Child Psychology*. 2005; 33:219–229. [PubMed: 15839499]
- Eaves L, Silberg J, Foley D, Bulik C, Maes H, Erkanli A, et al. Genetic and environmental influences on the relative timing of pubertal change. *Twin Research*. 2004; 7:471–481. [PubMed: 15527663]
- Edwards AC, Sihvola E, Korhonen T, Pulkkinen L, Moilanen I, Kaprio J, et al. Depressive symptoms and alcohol use are genetically and environmentally correlated across adolescence. *Behavior Genetics*. 2010; 1007/s10519-010-9400-y
- Ge X, Lorenz FO, Conger RD, Elder GH, Simons RL. Trajectories of stressful life events and depressive symptoms during adolescence. *Developmental Psychology*. 1994; 30:467–483.
- Glowinski AL, Madden PA, Bucholz KK, Lynskey MT, Heath AC. Genetic epidemiology of self-reported lifetime DSM-IV major depressive disorder in a population-based twin sample of female adolescents. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. 2003; 44:988–996.
- Hankin BL, Abramson LY. Development of gender differences in depression: Description and possible explanations. *Annals of Medicine*. 1999; 31:372–379. [PubMed: 10680851]
- Hankin BL, Abramson LY. Development of gender differences in depression: An elaborated cognitive vulnerability-transactional stress theory. *Psychological Bulletin*. 2001; 127:773–796. [PubMed: 11726071]
- Hyde JS, Mezulis AH, Abramson LY. The ABCs of depression: Integrating affective, biological, and cognitive models to explain the emergence of the gender difference in depression. *Psychological Review*. 2008; 115:291–313. [PubMed: 18426291]
- Kaprio J, Pulkkinen L, Rose RJ. Genetic and environmental factors in health-related behaviors: Studies on Finnish twins and twin families. *Twin Research*. 2002; 5:366–371. [PubMed: 12537860]
- Kaprio J, Rimpela A, Winter T, Viken RJ, Rimpela M, Rose RJ. Common genetic influences on BMI and age at menarche. *Human Biology*. 1995; 67:739–753. [PubMed: 8543288]
- Kendler KS, Gardner CO, Lichtenstein P. A developmental twin study of symptoms of anxiety and depression: Evidence for genetic innovation and attenuation. *Psychological Medicine*. 2008; 38:1567–1575. [PubMed: 18578897]
- Kovacs, M. The child's depression inventory (CDI). North Tonawanda, NY: Multi Health Systems; 1991.
- Laitinen-Krispijn S, van der Ende J, Verhulst FC. The role of pubertal progress in the development of depression in early adolescence. *Journal of Affective Disorders*. 1999; 54:211–215. [PubMed: 10403167]
- Lindeman S, Hamalainen J, Isometsa E, Kaprio J, Poikolainen K, Heikkinen M, et al. The 12-month prevalence and risk factors for major depressive episode in Finland: Representative sample of 5993 adults. *Acta Psychiatrica Scandinavica*. 2000; 102:178–184. [PubMed: 11008852]
- Mustanski BS, Viken RJ, Kaprio J, Pulkkinen L, Rose RJ. Genetic and environmental influences on pubertal development: Longitudinal data from Finnish twins at ages 11 and 14. *Developmental Psychology*. 2004; 40:1188–1198. [PubMed: 15535766]
- Natsuaki MN, Klimes-Dougan B, Ge X, Shirtcliff EA, Hastings PD, Zahn-Waxler C. Early pubertal maturation and internalizing problems in adolescence: Sex differences in the role of cortisol reactivity to interpersonal stress. *Journal of Clinical Child and Adolescent Psychology*. 2009; 38:513–524. [PubMed: 20183638]
- Neale, MC.; Boker, SM.; Xie, G.; Maes, HH. Mx: Statistical modeling. 7. Richmond, VA: Dept. of Psychiatry, Virginia Commonwealth University; 2006.
- Nolen-Hoeksema S, Girgus JS. The emergence of gender differences in depression during adolescence. *Psychological Bulletin*. 1994; 115:424–443. [PubMed: 8016286]

- Office of Applied Studies. Results from the 2004 national survey on drug use and health: National findings. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2005.
- Petersen AC, Crockett L, Richards M, Boxer A. A self-report measure of pubertal status: Reliability, validity, and initial norms. *Journal of Youth and Adolescence*. 1988; 17:117–133.
- Phinney VG, Jensen LC, Olsen JA, Cundick B. The relationship between early development and psychosexual behaviors in adolescent females. *Adolescence*. 1990; 25:321–332. [PubMed: 2375259]
- Pinyerd B, Zipf WB. Puberty-timing is everything! *Journal of Pediatric Nursing*. 2005; 20:75–82. [PubMed: 15815567]
- Purcell S. Variance components models for gene-environment interaction in twin analysis. *Twin Research*. 2002; 5:554–571. [PubMed: 12573187]
- Rijsdijk FV, Snieder H, Ormel J, Sham P, Goldberg DP, Spector TD. Genetic and environmental influences on psychological distress in the population: General health questionnaire analyses in UK twins. *Psychological Medicine*. 2003; 33:793–801. [PubMed: 12877394]
- Rose RJ, Dick DM, Viken RJ, Pulkkinen L, Kaprio J. Genetic and environmental effects on conduct disorder and alcohol dependence symptoms and their covariation at age 14. *Alcoholism, Clinical and Experimental Research*. 2004; 28:1541–1548.
- Sandberg S, Rutter M, Pickles A, McGuinness D, Angold A. Do high-threat life events really provoke the onset of psychiatric disorder in children? *Journal of Child Psychology and Psychiatry and Allied Disciplines*. 2001; 42:523–532.
- Seppa K, Sillanaukee P, Koivula T. The efficiency of a questionnaire in detecting heavy drinkers. *British Journal of Addiction*. 1990; 85:1639–1645. [PubMed: 2289065]
- Silberg J, Pickles A, Rutter M, Hewitt J, Simonoff E, Maes H, et al. The influence of genetic factors and life stress on depression among adolescent girls. *Archives of General Psychiatry*. 1999; 56:225–232. [PubMed: 10078499]
- Stattin, H.; Magnusson, D. Pubertal maturation in female development. Hillsdale, NJ: Lawrence Erlbaum Associates; 1990.
- Tambs K, Harris JR, Magnus P. Genetic and environmental contributions to the correlation between alcohol consumption and symptoms of anxiety and depression. Results from a bivariate analysis of Norwegian twin data. *Behavior Genetics*. 1997; 27:241–250. [PubMed: 9210795]
- Towne B, Czerwinski SA, Demerath EW, Blangero J, Roche AF, Siervogel RM. Heritability of age at menarche in girls from the Fels longitudinal study. *American Journal of Physical Anthropology*. 2005; 128:210–219. [PubMed: 15779076]
- Waylen A, Wolke D. Sex ‘n’ drugs ‘n’ rock ‘n’ roll: The meaning and social consequences of pubertal timing. *European Journal of Endocrinology/European Federation of Endocrine Societies*. 2004; 151(Suppl 3):U151–159. [PubMed: 15554900]
- Westling E, Andrews JA, Hampson SE, Peterson M. Pubertal timing and substance use: The effects of gender, parental monitoring and deviant peers. *Journal of Adolescent Health*. 2008; 42:555–563. [PubMed: 18486864]
- Zahn-Waxler, C.; Crick, NR.; Shirtcliff, EA.; Woods, KE. The origins and development of psychopathology in females and males. In: Cicchetti, D.; Cohen, DJ., editors. *Developmental psychopathology*. 2. Vol. 1. Hoboken, NJ: Wiley; 2006. p. 76-138.

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Fig. 1. Standard full twin model. Latent genetic (A), shared environmental (C), and unique environmental (E) factors influence variance of the observed variable zPDS. *Twin 1* and *Twin 2* are phenotypically correlated due to genetic and shared environmental correlations. The genetic correlation between MZ twins is 1; the genetic correlation between DZ twins is .5. The shared environmental correlation for both MZ and DZ twins is 1

Fig. 2.

Current full model allowing for correlation between traits and moderation by zPDS. Observed variables and latent genetic variables for Twin 1 are depicted: an identical structure exists for latent shared environmental and unique environmental variables; the same structure exists for Twin 2. Genetic correlation between traits, within individual, is represented by path labeled a_C (where “c” stands for “common”); moderation of this genetic correlation by zPDS is represented by the $\beta_C zPDS$ term. Genetic influences specific to depressive symptoms (DS) are represented by the path labeled a_{DS} ; moderation of this path by zPDS is represented by the $\beta_{DS} zPDS$ term

Fig. 3. Changes in total genetic and unique environmental variance as a function of zPDS score. Extreme zPDS scores (−2 to +2) are used for illustrative purposes. Results are presented for **a** girls' age 14 depressive symptoms; **b** girls' age 17 depressive symptoms; **c** boys' age 14 depressive symptoms; and **d** boys' age 17 depressive symptoms. In the legend, "A" represents latent additive genetic factors, "C" represents shared environmental factors (*panel c* only), and "E" represents unique environmental latent factors. In *panel a*, note that environmental variance of age 14 depressive symptoms is increased in more developed girls (i.e., those with a high PDS Z-score); in contrast, environmental variance in age 17 depressive symptoms is decreased in more developed girls (*panel b*). A similar trend is observed among boys, but it occurs later

Fig. 4. Standardized variance components underlying girls' age 17 depressive symptoms, as a function of pubertal development. Extreme zPDS scores (-2 to +2) are used for illustrative purposes. Among girls who are more developed at age 14, the heritability of age 17 depressive symptoms is higher. However, as demonstrated in Fig. 3b, this "increase" in heritability does not correspond to an increase in genetic variance, but rather to a decrease in total environmental

Table 1
Descriptive statistics for pubertal development scores (prior to transformation) and depressive symptom scores

Phenotype	Range		Mean ($\pm$ SE)		Sex differences in mean b^* , p
	Boys	Girls	Boys	Girls	
Age 12 PDS	1.0–2.4	1.0–3.2	1.32 (.01)	1.68 (.02)	–.36, < .0001
Age 14 PDS	1.0–3.6	1.4–3.8	2.02 (.02)	2.84 (.02)	–.82, < .0001
Age 12 CDI	27–59	27–66	35.1 (.21)	35.2 (.25)	–.07, .86
Age 14 CDI	27–54	27–56	32.8 (.27)	33.8 (.28)	–.95, .04
Age 17 GBI	9 ^{**} –37	10–40	13.6 (.20)	16.3 (.27)	–2.6, < .0001

* Boys' score is the reference

** Due to missing data

Table 2

Univariate model fitting for depressive symptoms

Model #	Model description	Comparison	Δdf	$\Delta\chi^2$	$\chi^2 P$ -value	ΔAIC
<i>A. Girls, age 14 depressive symptoms</i>						
1	Full	n/a	342	(2094.79)	n/a	1,410.79
2	AE model	2 vs. 1	1	0.95	0.33	-1.05
3	CE model	3 vs. 1	1	3.24	0.07	1.24
<i>B. Girls, age 17 depressive symptoms</i>						
1	Full	n/a	436	(2762.67)	n/a	1,890.67
2	AE model	2 vs. 1	1	0.26	0.61	-1.74
3	CE model	3 vs. 1	1	2.27	0.13	0.27
<i>C. Boys, age 14 depressive symptoms</i>						
1	Full	n/a	315	(1892.67)	n/a	1,262.67
2	AE model	2 vs. 1	1	6.95	< .01	4.95
3	CE model	3 vs. 1	1	0.00	1.00	-2.00
<i>D. Boys, age 17 depressive symptoms</i>						
1	Full	n/a	410	(2342.20)	n/a	1,522.20
2	AE model	2 vs. 1	1	0.00	1.00	-2.00
3	CE model	3 vs. 1	1	3.66	0.06	1.66

Models in bold text were incorporated into subsequent moderation models (Table 3)

Table 3

Models testing moderation effects

Model #	Model description	Comparison	Δdf	$\Delta\chi^2$	$\chi^2 p$ -value	ΔAIC
<i>A. Girls, age 12 zPDS moderating age 14 depressive symptoms</i>						
1	Full	n/a	(834)	(3,219.78)	n/a	(1551.78)
2	Drop moderation of genetic influences	2 vs. 1	2^a	1.26	0.53	-2.74
3	Drop moderation of unique environmental influences	3 vs. 2	2	5.94	0.05	1.94
<i>B. Girls, age 14 zPDS moderating age 17 depressive symptoms</i>						
1	Full	n/a	(881)	(3,755.88)	n/a	(1,993.88)
2	Drop moderation of genetic influences	2 vs. 1	2	2.25	0.33	-1.75
3	Drop moderation of unique environmental influences	3 vs. 2	2	4.619	0.10	0.62
<i>C. Boys, age 12 zPDS moderating age 14 depressive symptoms</i>						
1	Full	n/a	(667)	(2,576.58)	n/a	(1,242.58)
2	Drop moderation of shared environmental path	2 vs. 1	1 ^b	0.53	0.26	-1.47
3	Drop moderation of unique environmental influences	3 vs. 2	2	1.34	0.51	-2.66
<i>D. Boys, age 14 zPDS moderating age 17 depressive symptoms</i>						
1	Full	n/a	(850)	(3,352.65)	n/a	(1,652.65)
2	Drop moderation of genetic paths	2 vs. 1	2	0.87	0.65	-3.13
3	Drop moderation of unique environmental paths	3 vs. 2	2	28.19	< .001	24.19

The full model was based on results from univariate model testing (Table 2). Models in bold were adopted as the final model for that analysis; estimates from those models are described in the text

^aThis test has 2 degrees of freedom because there are two genetic moderation parameters; one that is a component of the genetic path shared between zPDS and depressive symptoms, and one that is a component of the genetic path specific to depressive symptoms. See Purcell (2002) for details

^bThis test has one degree of freedom because the full model does not include a "C" path that is shared by zPDS and depressive symptoms