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Early Pubertal Maturation and Internalizing Problems in Adolescence: Sex Differences in the Role of Cortisol Reactivity to Interpersonal Stress

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Abstract

An accumulating body of literature has shown a link between early pubertal maturation and internalizing problems, particularly among girls. Our knowledge is, however, limited with regard to what accounts for this association. Based on a hypothesis that early maturing girls have heightened stress sensitivity that increases the risk of internalizing problems, the present investigation examined the roles of pubertal timing and salivary cortisol reactivity to interpersonal stressors in adolescents' internalizing problems. Results from 110 boys and 106 girls (ages 11–16) indicated that early maturing adolescents had increased internalizing symptoms. Early maturing girls' higher levels of internalizing problems were at least partially attributed to their heightened sensitivity to interpersonal stress. Finally, girls' cortisol reactivity to interpersonal challenge was more strongly associated with internalizing problems than boys' reactivity.

Although biological transformation from child-like physique to a matured body at puberty is a normative process (Simmons, Burgeson, Carltonford, & Blyth, 1987), there are significant interindividual variations in the timing at which a teenager experiences this transition. Such

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individual differences in pubertal timing appear to be implicated in the development of internalizing problems during adolescence, a time when their significant rise is typically observed (Ge, Lorenz, Conger, Elder, & Simons, 1994; Ge, Natsuaki, & Conger, 2006; Hankin et al., 1998; Wichstrom, 1999). A rapidly accumulating body of literature has documented that early pubertal maturation constitutes a significant risk factor for a variety of girls' internalizing problems including depression, anxiety, psychological distress, and low self-esteem (e.g., Alsaker, 1992; Ge, Conger, & Elder, 1996, 2001a; Graber, Lewinsohn, Seeley, & Brooks-Gunn, 1997; Kaltiala-Heino, Kosunen, & Rimpela, 2003; Siegel, Yancey, Aneshensel, & Schuler, 1999; Stattin & Magnusson, 1990; Wichstrom, 2000). However, the mechanisms underlying the association between early pubertal timing and adolescent girls' internalizing problems remain poorly understood.

One plausible hypothesis is that early maturing adolescent girls exhibit higher levels of internalizing problems because they are vulnerable to stressors in their environment. The corollary of this proposition is that early maturing individuals may be more vulnerable to stressors because of the mismatch of external challenges and resources to cope with them. They may be confronted with social expectations and norms elicited by their precocious physical maturity at a time when their cognitive and socioemotional skills and resources are still immature with resources to deal with these challenges because of their immature cognitive and socioemotional skills (Caspi, Lynam, Moffitt, & Silva, 1993; Ge et al., 1996). Hence, when confronted with difficulties and challenges, early maturing girls show heightened reactions to stressors, increasing their negative affect following experiencing stressors (Mendle, Turkheimer, & Emery, 2007). This view is consistent with the stress-diathesis model and the concept of biological sensitivity to context (Boyce & Ellis, 2005). Early maturing girls' heightened sensitivity to environmental threat could be a liability to their adjustment, particularly when the environment consists of adversity. Given that the transition to adolescence is associated with a substantial increase in the number of stressors experienced (Ge et al., 1994), the examination of this hypothesis appears crucial.

In this study, we focused on adolescents' reactivity to interpersonal stressors. Theories of sex differences in internalizing problems have proposed that adolescent girls often have a strong interpersonal orientation that may serve as a liability to their emotional well-being (Cyranowski, Frank, Young, & Shear, 2000; Rose & Rudolph, 2006; Rudolph, 2002; Zahn-Waxler, Shirtcliff, & Marceau, 2008). The premium girls place on affection, closeness, loyalty, social validation, and acceptance in relationships could result in their intensified interpersonal sensitivity, which could tax girls' emotional adjustment when they encounter stressors of an interpersonal nature (Rudolph, 2002). Because girls are more likely than boys to view interpersonal relationships as core to self-definition and identity, conflict and stress within relationships would be more likely to threaten emotional well-being in girls in a salient way (Rudolph, 2002).

It is plausible that early physical maturation could make girls particularly sensitive to stressors of interpersonal nature. Overtly motivated by the desire to socially "fit in," early maturing girls—whose precocious physical appearance already deviates from normatively developing peers—may perceive interpersonal challenges as highly stressful. Indeed, several psychosocial studies have documented a significant statistical interaction between environmental threat and early pubertal maturation, showing that that early maturing girls are sensitive to interpersonal stressors. For instance, Ge et al. (1996) reported that compared to their peers, early maturing girls reacted more strongly to deviant peer pressure and father's hostility with psychological distress. Others have also noted early maturing girls' heightened vulnerability to peer difficulties (Conley & Rudolph, in press) and challenges arising from romantic relationships (Natsuaki, Biehl, & Ge, 2009).

A significant statistical interaction between early pubertal maturation and interpersonal stressors provides suggestive evidence for early maturing girls' heightened sensitivity to interpersonal stressors. However, various alternative interpretations are also viable because the underlying mechanisms that drive such interaction remain unclear. For instance, a Pubertal Timing $\times$ Interpersonal Stress interaction can be interpreted as evidence that biological changes at puberty exerts negative effect only when coupled with additional stressors. This interpretation does not require any assumption of stress sensitivity; instead, it posits that although early timing of maturation alone may not be enough stress to tip the scales toward internalizing psychopathology, the presence of multiple risks may lead to emotional problems. To directly test whether early maturing girls' elevated internalizing symptoms are related to their heightened stress sensitivity, it is important to move beyond the search for an Early Maturation $\times$ Interpersonal Stressor interaction. A potentially fruitful avenue is to directly assess stress sensitivity by looking at individual variation in biological reactivity associated with experience of stress.

Cortisol reactivity represents one of the key biological indicators of stress reactivity. Cortisol is a steroid hormone released by the hypothalamic-pituitary-adrenal (HPA) axis. Activation of this system occurs when neurons in the paraventricular nucleus of the hypothalamus secrete corticotropin-releasing hormone (CRH), which stimulates the release of adrenocorticotropin hormone (ACTH), resulting in the synthesis and release of cortisol. Once released, cortisol also acts on the central nervous system, where it inhibits the release of CRH and ACTH through negative feedback (for details, see Gunnar & Quevedo, 2007). Disruption of this HPA axis cascade has been implicated in the development of symptoms of depression and anxiety (e.g., Gold & Chrousos, 2002; Sapolsky, 2000). Among adolescents with internalizing problems, elevations in basal cortisol and heightened response to interpersonal stressors have been noted (for a review, see Adam, Klimes-Dougan, & Gunnar, 2007).

Furthermore, cortisol secretion is closely intertwined with age, puberty, and sex, which together seem to contribute to adolescent girls' vulnerability to external stressors (Walker, Sabuwalla, & Huot, 2004; Young & Altemus, 2004). For example, basal cortisol levels increase gradually during pubertal transition (Schreiber et al., 2006; Walker et al., 2004). Although the impact of sex hormones on the HPA axis at the onset of puberty is still poorly understood (Rubinow & Schmidt, 1999), sex and stress hormones are thought to be strongly interconnected. At a biological level, sex steroid-related events, such as the timing of puberty, are related to activation of the HPA axis because the hypothalamic-pituitary-gonadal (HPG) and HPA axes interact bidirectionally across every level of the axes, from the brain to the periphery (Viau, 2002). Indeed, the reciprocal connections between sex and stress steroids are so extensive that some steroids operate as end-products of both the HPA and HPG axes, and most sex steroids are stress responsive (e.g., Shirtcliff, Zahn-Waxler, Klimes-Dougan, & Slaterry, 2007). For example, steroids of adrenal origin stimulate growth of several pubertal processes, such as pubic hair, body odor, and acne. Frequently, it is these changes in the maturation of stress steroids that constitute the first sign of puberty (Shirtcliff, Dahl, & Pollak, 2009). Several researchers have also shown that the dramatic alterations in sex steroids seen with the onset of puberty play a potential modulatory role on the HPA axis, possibly contributing to vulnerability for depression in adolescent girls (e.g., Stroud, Papandonatos, Williamson, & Dahl, 2004; Young & Altemus, 2004). Supporting evidence from animal studies has also shown that high doses of estrogen amplify the stress response, which may in turn increase susceptibility to stress-related disorders (Shansky et al., 2004).

Given that sex steroids and puberty are associated with the HPA functioning, an important subject of scientific investigation is to understand sex difference in the levels of cortisol reactivity and how sex moderates the link between cortisol reactivity and internalizing

problems. Because females are more likely than males to develop depression and anxiety-related disorders and symptoms starting around the time of pubertal transition (Ge et al., 1994; Hankin et al., 1998; Kessler, McGonagle, Swartz, Blazer, & Nelson, 1993), it has been speculated that this sex difference in internalizing problems is associated with sex differences in stress reactivity. No clear pattern of sex differences in cortisol reactivity has been established, however; some studies have documented boys producing more elevated levels of cortisol than girls after a standardized psychosocial stress challenge task (Kirschbaum, Wust, & Hellhammer, 1992; Seeman, Singer, Wilkinson, & McEwen, 2001; Uhart, Chong, Oswald, Lin, & Wand, 2006). Although some studies have suggested heightened stress responses in female individuals in the context of tasks of a more interpersonal nature (Stroud, Salovey, & Epel, 2002), others have failed to observe sex differences (e.g., Dorn et al., 1996; Kelly, Tyrka, Anderson, Price, & Carpenter, 2008). Furthermore, it is possible that the relationship between cortisol and psychological indices may be sex specific (Kirschbaum, Klauer, Filipp, & Hellhammer, 1995; Kivlighan, Granger, & Booth, 2005; McCormick, Lewis, Somely, & Kahan, 2007). Even in the absence of sex differences in the level of cortisol reactivity, female participants have been found to report more negative affect after the socially challenging task than male participants (Kelly et al., 2008). Sex differences in cortisol reactivity and the moderating role of sex in the link between cortisol reactivity and internalizing symptoms merit further examination.

This study set out to address the following gaps in the literature regarding pubertal timing, cortisol reactivity, and internalizing symptoms. First, no study that we are aware of has directly tested the joint effects of cortisol reactivity and early pubertal timing in predicting internalizing symptoms. A piece of suggestive evidence comes from a study of a sample of elementary school children (ages 6–9) showing that children with precocious puberty (i.e., premature adrenarche measured by Tanner ratings) had higher levels of basal cortisol and exhibited elevated internalizing symptoms and disorders (Dorn, Hitt, & Rotenstein, 1999). However, existing knowledge remains fragmented because cortisol reactivity and pubertal timing have not been examined together in their relation to adolescent internalizing problems. Second, cortisol reactivity (i.e., changes in cortisol levels in reaction to environmental stressors) has been rarely evaluated. Unlike levels of basal cortisol, cortisol reactivity represents biological stress responses involving transactions between biology and environment. Such a variable provides an opportunity to delve into the underpinnings of the Pubertal Timing $\times$ Interpersonal Stress interaction observed in psychosocial literature. Finally, the examination of pubertal timing, cortisol reactivity, and the moderating role of sex has been largely overlooked in the literature.

THE PRESENT STUDY

The overarching aim of the present study was to examine the role of pubertal timing and stress sensitivity in adolescents' internalizing problems, with special attention to sex differences in their effects. Focusing on biological aspects of stress sensitivity, we examined whether cortisol reactivity to interpersonal stress explained the link between pubertal timing and internalizing problems. Two major hypotheses about girls motivated the present investigation: We predicted (a) that early maturing girls would show higher internalizing problems than their peers, and (b) that the relationship between early maturation and girls' internalizing problems would be mediated by stress sensitivity indexed by cortisol reactivity to interpersonal stress. If these two hypotheses were supported, it would suggest that early maturing girls' elevated levels of internalizing problems are, at least in part, accounted for by their heightened sensitivity to interpersonal stress. Because there is not comparable evidence for boys (Huddleston & Ge, 2003), we did not expect similar links with cortisol reactivity, pubertal timing, and internalizing problems. We tested whether the pubertal timing-internalizing problems and cortisol reactivity-internalizing problems associations

would be more pronounced among girls than boys. This approach is consistent with recent theorizing and findings from a body of literature, indicating gender differences in risk factors and etiological predictors of internalizing problems (see review by Zahn-Waxler et al., 2008).

Several covariates were considered when testing these substantive hypotheses. First, body mass index (BMI) was included because it is documented that BMI is highly correlated with body image, which mediates the relationship between pubertal timing and internalizing problems for girls (Ge, Elder, Regnerus, & Cox, 2001). We also examined children's medication use because salivary biomarkers are sensitive to medications (Hibel, Granger, Cicchetti, & Rogosch, 2007). In addition, we identified adolescents' externalizing problems as a possible covariate because internalizing and externalizing problems often co-occur (Angold, Costello, & Erkanli, 1999).

METHOD

Participants

The present study is based on the data collected from 216 adolescents (110 boys, 106 girls) and their mothers who participated in the Adolescent Emotion Study (AES). The AES is an investigation conducted at the National Institute of Mental Health to examine the role of emotion in the development of psychopathology in adolescence (Klimes-Dougan, Hastings, Granger, Usher, & Zahn-Waxler, 2001; Zahn-Waxler et al., 2001). The AES was approved by the Human Subjects Institutional Review Board at the National Institutes of Mental Health. Families were recruited from the greater Washington, DC, metropolitan area. The average age of the adolescents was 13.30 years ($SD = 1.57$) at the time of recruitment. Families were mainly from middle and upper-middle socioeconomic status. For annual household income, 5.6% of the families had less than \$20,000, 11.2% had between \$20,000 and \$40,000, 18.6% had between \$40,000 and \$60,000, 18.1% had between \$60,000 and \$80,000, 16.3% had between \$80,000 and \$100,000, and 30.2% had more than \$100,000. Most of the mothers (65.7%) and fathers (78.6%) had completed college or graduate degrees. The ethnic composition of the adolescent sample was 70.4% Caucasian, 16.2% African American, 1.9% Hispanic, 2.8% Asian American, and 8.8% mixed race or other. The majority of the adolescents (76.4%) lived in two-parent (biological, adopted, or step-parents) families.

Adolescents and their parents were recruited through announcements (e.g., newspapers, flyers). Eligibility for participation was based on the child's age (between the ages of 11 and 16 years at the time of the initial visit) and competency to complete procedures (e.g., free from debilitating language, cognitive, physical, or psychotic impairment). Because the overarching goal of the AES was to investigate adolescent psychopathology, the recruitment strategy was designed to cover a wide range of emotional and behavioral problems. At the initial telephone interview, abbreviated versions of the Child Behavior Checklist (Achenbach, 1991b) and the Youth Self-Report (Achenbach, 1991c) were administered to the mother and the child for the screening purpose. Approximately equal numbers of early (11–13-year-olds) and midadolescent (14–16-year-olds) boys and girls with low to clinical levels of internalizing and externalizing problems were included in the study. It should be noted that this sampling strategy over-sampled adolescents with elevated problems and masked possible gender differences in incidence of psychopathology. For more information regarding the recruitment method, see Klimes-Dougan et al. (2001).

Measures

Internalizing problems—Adolescents' internalizing problems were assessed by the symptom counts for generalized anxiety disorder (GAD) and major depressive disorder (MDD) on the Diagnostic Schedule for Children, Version IV (Schaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000). Adolescents and their mothers reported whether the participating adolescents experienced the listed problems in the past 12 months. Self- and mother-report of symptom counts in two modules (GAD and MDD) were moderately, yet significantly, correlated ($r_s = .11-.57$). Such modest cross-informant coefficients have been observed in previous studies for internalizing symptoms (Achenbach, 2006; Achenbach, McConaughy, & Howell, 1987). Modest convergence (as indicated by low bivariate correlations among the same construct across informants) is in fact advantageous because orthogonality between informants could potentially facilitate validity of the measure by which one informant's data could address some of the deficiencies in the other informant's data (Kraemer et al., 2003). We thus used a composite of mother- and child-reports of internalizing symptoms. Our rationale for combining anxiety and depression was motivated by the fact that comorbidity between anxiety and depression is much more common than "pure" disorder (Angold et al., 1999), and these two types of psychopathology are often indistinguishable particularly during adolescence (Compas, Ey, & Grant, 1993). Factor analytic work has supported a rationale for combining anxiety and depression into one scale (Achenbach, 1991a). Based on the aforementioned reasons, the four indices of internalizing problems (i.e., mother- and self-report of GAD and MDD) were summed to create a composite score of adolescents' internalizing problems. The Cronbach's alpha of this aggregated measure was .65.

Pubertal timing—Self-rated pubertal maturation was assessed using Tanner criterion of breast and pubic hair stage for girls and genital and pubic hair stage for boys (Marshall & Tanner, 1970; Morris & Udry, 1980). Previous studies have shown moderate agreement (average $k = .50$ across 11 studies) with high correlations (above .7) between self- and physician-ratings of Tanner stage, suggesting that self-reported Tanner stage is a viable alternative to physician examination (Shirtcliff et al., 2009). Breast development and growth of pubic hair were portrayed in pictures, from which girls selected the images that represented their current physical development most closely. Boys indicated their status of physical maturation by selecting the drawings that best described their pubic hair and genital development at that time. Each picture represented one of the five Tanner stages, ranging from Stage 1 (i.e., puberty has not begun) to 5 (i.e., pubertal development has completed). Because girls' pubic hair and breast development were highly correlated ($r = .76$) as were boys' pubic hair and genital development ($r = .82$), we aggregated the scores of two items for each sex to construct adolescents' pubertal status score.

It is important to distinguish pubertal status and timing. Pubertal status refers to an individual's degree of physical maturation, and it is highly confounded with age. Pubertal timing, which is the focus of this study, is a relative concept that connotes social implication; it indicates whether an individual's physical maturation occurs earlier than, at the same time as, or later than that of his or her same-age, same-sex peers. Hence, pubertal timing by definition is derived from a measurement of status and the comparison of that level of development to the level that is normative for the individual's age and sex (Graber, Petersen, & Brooks-Gunn, 1996). Using a procedure that has been used in previous research (Ge, Brody, Conger, Simons, & Murry, 2002; Ge, Conger, & Elder, 2001b), we standardized pubertal status scores within each age and sex to create a pubertal timing variable. This procedure is particularly important for this study because activity in the HPA axis, reflected in salivary cortisol secretions, is confounded with age during adolescence (Walker et al., 2004). Higher scores are indicative of early pubertal timing.

Salivary cortisol reactivity—Salivary cortisol samples were collected during an experimental paradigm and at home for the baseline sample. Adolescents participated in the Social Performance Paradigm (SPP; for more details refer to Klimes-Dougan et al., 2001), an experimental task that is conceptually similar to the widely used Trier Social Stress Test (Kirschbaum, Pirke, & Hellhammer, 1993). In this interpersonally challenging task, the adolescent was first asked to carry on a conversation with an unfamiliar female confederate who feigned being shy and uncommunicative. The adolescent was then asked to prepare and give a 3-min speech in the presence of a two-person audience (one male, one female). Public speaking tasks and the presence of evaluative audience are known to elicit self-report negative affect (Hastings, Zahn-Waxler, & Usher, 2007) and responses in cortisol (Dickerson & Kemeny, 2004). Prior analysis based on the AES also showed that SPP generated significant increases in salivary cortisol levels (Klimes-Dougan et al., 2001). The SPP took place in the late morning ($M = 11:16$ a.m., $SD = 27$ min).

In the SPP task, salivary samples were collected prior to (pretask), 20 min (posttask I), and 40 min (posttask II) after the completion of this experimental task. In this study, we exclusively focused on changes in cortisol levels from pretask to posttask I because the main aim of this study was to examine cortisol reactivity to a socially challenging stress.¹ There was a modest but significant increase in the levels of cortisol from pre- to posttask I (pretask, $M = .18$ $\mu\text{L/dL}$, $SD = .11$; posttask I, $M = .19$ $\mu\text{L/dL}$, $SD = .10$), $t(216) = -1.98$, $p < .05$. The small increases in cortisol between pre- and posttask I might be interpreted as masking a more substantial HPA activation because generally cortisol production follows a steep decline during the morning hours. The bivariate correlation between pre- and posttask I cortisol levels was .46. To capture how cortisol levels changed before and after performing the SPP, we calculated residualized slope of changes in cortisol levels between pre- and posttask I. Residualized scores are an index of cortisol reactivity, representing how much steeper or flatter an individual's slope (i.e., changes in cortisol levels between pre- and posttask) is compared to the average slope. The reliability and utility of residualized scores to underscore biological reactivity has been reported (Llabre, Spitzer, Saab, Ironson, & Schneiderman, 1991). To control for possible elevations that might occur at pretask associated with setting characteristics (e.g., lab visit), a midday baseline sample was collected at home on a different day (usually the weekend prior to the lab visit) at a time that corresponded with the SPP pretask sample ($M = 11:45$ a.m., $SD = 46$ min).

Procedures for salivary collection, storage, and analyses are as follows. Participants were instructed not to eat, drink, or smoke cigarettes 30 min prior to saliva collection. Participants first rinsed their mouth with water, and then chewed Trident sugarless original flavor gum for 60 sec to stimulate saliva flow. Participants then expectorated approximately 5 ml of saliva into a test tube. Samples were stored in a freezer at -25°C . Samples were sent by overnight delivery on dry ice to Pennsylvania State University Behavioral Endocrinology Laboratory where they were stored frozen at -86°C until assayed for cortisol. Each 5 ml sample was thawed and then centrifuged at 3,000 rpm for 15 min. The clear top-phase of the sample was pipetted into appropriate test wells. Samples were assayed for cortisol using a high-sensitivity enzymeimmunoassay kit (Salimetrics, State College, PA). The test used 50 μL of saliva, which had a lower limit of sensitivity of .007 $\mu\text{L/dL}$ (ranged up to 1.2 $\mu\text{L/dL}$), and average intra- and interassay coefficients of variation 4.1% and 8.9%, respectively. All samples were tested in duplicates, and duplicate tests values that varied by more than 5% were retested. The average of the duplicate tests was used in the analyses.

¹We also analyzed recovery in levels of cortisol from posttask I to II because some studies suggest that the dysregulation of the HPA axis can be studied by how individual's levels of cortisol recover to baseline after acute stress (Miller et al., 2007). However, results indicated no significant association between internalizing symptoms and the downward slope between posttask I and II. Thus, this report focuses on immediate reaction of salivary cortisol to stress, rather than recovery from stress.

BMI—Because it is documented that BMI is highly correlated with body image, pubertal timing, and internalizing problems for girls (Ge et al., 2001), we included BMI as a covariate in our model. We calculated BMI based on weight and height measured by research staff when adolescents came to the laboratory.

Medication use—It is important for researchers to monitor children's medication use in studies of the endocrine correlates because salivary biomarkers are sensitive to medications (Hibel et al., 2007). At the time of testing, mothers reported all the medications prescribed and taken by children. Based on a published medication coding system (Schreiber et al., 2006), we categorized the types of medications into seven codes (pain relief and antacids; antibiotics and nonsteroidal cold, allergy, and asthma medications; oral steroids; nonoral steroids; psychotropic medications; hormones; and others). We first explored the effects of specific medications on the study variables. The preliminary analyses indicated that adolescents who were taking psychotropic medications had higher externalizing problems than those who were not ($F = 16.24, p < .01$). In addition, older adolescents were more likely to be on oral contraceptives ($F = 8.33, p < .01$). However, relatively few individuals were taking medications within each category (ranging 0–25), and only 59 children who were taking at least one medication were identified. Therefore, we created a global measure of whether children were on any medication by collapsing seven types of medication. If a child was taking any medication, he or she was coded as 1 and otherwise a code of 0 was assigned.

Externalizing problems—Because internalizing and externalizing problems often coexist (Angold et al., 1999), we included adolescents' externalizing problems as a covariate in the analyses. Mother's rating on the Child Behavior Checklist (Achenbach, 1991b) broadband scale of externalizing problems was used in this study. Validity and reliability of the Child Behavior Checklist has been documented extensively with Cronbach's alpha reported at .93 (Achenbach, 1991b).

Demographic variables—We included annual household income, the child's sex, and age in the models.

RESULTS

Descriptive Analyses

Table 1 provides the means and standard deviations of the study variables in the preliminary analyses. The raw means of pubertal status indicated that, on average, participants were in the middle of pubertal transition. Girls' breast development and pubic hair growth, on average, were between Tanner Stages 3 and 4, although a large variation was observed. A closer examination of the distribution indicated that for breast development, 8.5% of girls were at Stage 1, 5.7% at Stage 2, 24.5% at Stage 3, 41.5% at Stage 4, and 19.8% at Stage 5. As for growth of pubic hair, 3.8% of girls were at Stage 1, 5.7% at Stage 2, 14.2% at Stage 3, 33.0% at Stage 4, and 43.4% at Stage 5. Similarly, the means of boys' genital growth and pubic hair were between Stages 3 and 4 with a standard deviation of one stage. The distribution of boys' genital development indicated that 2.7% were at Stage 1, 10.9% at Stage 2, 26.4% at Stage 3, 46.4% at Stage 4, and 13.6% at Stage 5. As for boys' growth of pubic hair, 2.8% were at Stage 1, 12.8% at Stage 2, 22.0% at Stage 3, 47.7% at Stage 4, and 14.7% at Stage 5. Preliminary analysis indicated that there was no significant sex difference in internalizing problems, cortisol levels in pre- or posttask, or BMI. However, boys ($M = 11.54, SD = 9.90$) had higher levels of externalizing problems than girls ($M = 8.70, SD = 7.29$), $F = 5.66, p < .05$. Girls ($M = .22 \mu\text{l/dl}, SD = .17$) had higher baseline levels of cortisol at midday than boys ($M = .17 \mu\text{l/dl}, SD = .10$), $F = 6.84, p < .01$.

Table 2 presents the bivariate correlations among the study variables. As expected, early pubertal timing was positively associated with internalizing problems ($r = .19, p < .01$). When boys and girls were separately analyzed, the correlation between pubertal timing and internalizing problems was stronger for girls ($r = .25, p < .01$) than for boys ($r = .12, ns$). Cortisol reactivity was positively associated with pubertal timing ($r = .17, p < .01$). This finding indicated that early maturing youths tended to have heightened cortisol reactivity to the laboratory-induced interpersonal stressor. Cortisol reactivity was not significantly associated with internalizing problems in the full sample. However, when girls and boys were analyzed separately, cortisol reactivity was significantly associated with internalizing problems for girls ($r = .20, p < .05$), but not for boys ($r = -.04, ns$). This pattern of results suggested that child's sex was a likely candidate of a moderator in the association between internalizing problems and cortisol reactivity.

As for the covariates, externalizing problems were positively associated with internalizing problems ($r = .33, p < .01$). Adolescents with higher BMI showed higher levels of internalizing problems ($r = .17, p < .01$). Adolescents who were taking at least one medication had higher levels of internalizing problems than their peers who were not ($r = .19, p < .01$). These coefficients suggest that it is important to include externalizing problems, BMI, and medication use as covariates in the subsequent analyses.

Primary Analysis

We used hierarchical multiple regression analysis to test (a) whether pubertal timing was associated with internalizing problems and (b) whether cortisol reactivity accounted partially for the link between pubertal timing and internalizing problems. Because our hypotheses pertained mainly to girls and not to boys, we examined sex differences in pubertal timing and cortisol reactivity by incorporating two interaction terms (i.e., Pubertal Timing $\times$ Sex; Cortisol Reactivity $\times$ Sex). Because of possible moderation by sex in the link between cortisol reactivity and internalizing problems in explaining pubertal timing effects, we performed a series of multiple regression analyses that are sensitive to a moderated mediation model (Muller, Judd, & Yzerbyt, 2005). Moderated mediation occurs when mediation is only significant for a particular subgroup of population, not others (Edwards & Lambert, 2007; MacKinnon, Fairchild, & Fritz, 2007; Muller et al., 2005). This framework is particularly suited for the present study because we expected cortisol reactivity to mediate effects of pubertal timing on internalizing problems for girls, but not for boys. In the analyses reported here, we controlled for potential confounding variables, including medication use, BMI, externalizing problems, midday baseline cortisol levels, and relevant demographic variables (i.e., annual household income, age, and sex of the child). All the predictors were centered at their own mean. Age was centered at 11 years of age. Sex and medication use were dummy coded (girls = 0, boys = 1; no medication = 0, any medication = 1) to facilitate the interpretation of the intercepts. The reference group was set to low-income families whose annual household income was less than \$20,000. Table 3 presents the results from a series of hierarchical multiple regression analyses. The parameter estimates reported in Table 3 are unstandardized coefficients, which indicate increase or decrease in counts of internalizing symptoms with a unit increase of the independent variable.

In the first step of testing our hypotheses, we examined whether pubertal timing predicted adolescents' internalizing problems (Model 1, Table 3). After accounting for the covariates (i.e., medication use, externalizing problems, BMI, household income, and age), sex emerged as a significant predictor, with girls exhibiting more internalizing problems than boys ($b = -3.61, p < .01$). More important, pubertal timing was also a significant predictor of adolescents' internalizing problems ($b = 2.07, p < .05$). This finding suggested early physical maturation operates as a potential risk factor for internalizing problems. The

interaction term between pubertal timing and sex did not reach statistical significance ($b = -1.49$, *ns*).

Model 2 added cortisol reactivity and its interaction with sex to Model 1. In addition to other control variables, midday baseline cortisol levels were also entered into the equation as a covariate. As hypothesized, the inclusion of cortisol stress reactivity resulted in a substantial drop in the size of the coefficient estimate of pubertal timing (b from 2.07 to .69), leaving it statistically nonsignificant in Model 2. Examination of the main effect of cortisol reactivity ($b = 29.41$, $p < .01$) and its interaction with sex ($b = -35.54$, $p < .01$) indicated that girls' cortisol reactivity was significantly associated with internalizing problems and the effect of cortisol reactivity on internalizing problems was significantly stronger for girls than boys. As a follow-up of this interaction, we performed regression analyses separately by sex. The results of post hoc analyses revealed that cortisol reactivity was a significant predictor of internalizing problems for girls ($b = 25.42$, $p < .05$), but not for boys ($b = -5.24$, *ns*). R^2 increased from .22 in Model 1 to .27 in Model 2.

DISCUSSION

Although a robust link has been established between pubertal timing and increased internalizing symptoms among girls, mechanisms that potentially explain this link remain largely unknown. The present investigation was motivated to answer a question looming in the field of pubertal timing research: Are early maturing girls more depressed and anxious than their peers because they are more susceptible to the adverse effects of interpersonal stressors? Using cortisol reactivity to interpersonal challenges as a biological index of stress sensitivity, we tested the hypothesis that early maturing girls' heightened reaction to stress accounts for their higher risk for internalizing problems. This study has several important findings. First, early pubertal timing was significantly linked to adolescents' internalizing problems. Further test of statistical interaction between pubertal timing and gender did not reach statistical significance level, suggesting that the effect of pubertal timing on boys was not significantly different from that on girls. This finding is consistent with past research that has documented a risk for internalizing problems in both early maturing girls (e.g., Ge et al., 1996; 2001a; Graber et al., 1997; Stattin & Magnusson, 1990; Stice, Presnell, & Bearman, 2001; Wichstrom, 2000) and early maturing boys (Ge et al., 2001b; Nadeem & Graham, 2005). Second, our results indicated that at least for girls, early maturers' sensitivity to stressors partially explained their experience of elevated symptoms of depression and anxiety. The findings reported here complement previous psychosocial research that has been conducted with alternative methodologies (e.g., Conley & Rudolph, in press; Ge et al., 1996; Natsuaki et al., 2009). The consistency with existing research enhances our confidence that heightened vulnerability to interpersonal stressors is significantly implicated in the elevated internalizing problems for early maturing girls. To our knowledge, the present study is among the first wave of empirical attempts that assesses biological underpinnings of stress reactivity in an effort to explore mechanisms through which early maturation may exert adverse impact on girls' emotional well-being. Because this area of investigation is still at nascence, further validation is undoubtedly needed.

The finding that girls' heightened stress reactivity appears to explain the association between early maturation and symptoms of depression and anxiety warrants significant attention. Adolescence is a time when stressful life events generally increase, particularly for girls (Ge et al., 1994; Hankin, Mermelstein, & Roesch, 2007). To add to the general increase in stressors in their lives, early maturing girls tend to exacerbate the situation by selecting themselves into stress-inducing environments. For example, they are more inclined to affiliate with older and deviant peers (Magnusson, Stattin, & Allen, 1985; Stattin & Magnusson, 1990). Parents' awkward reaction to their daughter's early sexual maturation

may further add to the developing adolescent's stress load (Brooks-Gunn, Newman, Holderness, & Warren, 1994; Paikoff & Brooks-Gunn, 1991). Thus, girls with heightened interpersonal stress sensitivity, when faced with a greater number of stressors in their lives, are at significant risk for developing internalizing problems.

Our results are also theoretically consistent with the notion that adolescents, particularly girls, are biologically vulnerable to external stressors during pubertal transition (Walker et al., 2004). There is some evidence to suggest that higher levels of circulating sex steroids at the onset of puberty alter adolescent girls' HPA axis, which may contribute to their increased risk for depression (Young & Altemus, 2004). However, more detailed work is needed to scrutinize what makes *early maturation* a liability for girls' interpersonal stress sensitivity and internalizing problems. Clinical studies of children with premature adrenarche have documented that precocious children have higher levels of cortisol (Cizza et al., 2001; Dorn et al., 1999). Our findings in a sample of adolescents with less extreme pubertal timing reveal a similar pattern in cortisol reactivity. Still, it remains unclear how early onset of puberty and over-reactivity in the HPA axis are associated. It is possible that stress exposure in childhood organizes both stress and sex steroid-related processes (Boyce & Ellis, 2005; Ellis, 2004). Future studies are encouraged to tap into biological as well as psychosocial mechanisms linking pubertal timing and stress sensitivity.

The findings also have an important implication for our understanding of sex differences in the link between biological stress reaction and internalizing psychopathology. The results reported here suggest that reactivity to interpersonal stressors for adolescent girls and boys may function quite differently. In this study, although no significant sex difference in the levels of cortisol reactivity was found, the effect of cortisol reactivity on internalizing problems was moderated by sex. That is, heightened cortisol reaction to the interpersonal stressor was associated with symptoms of depression and anxiety for girls, but not for boys. This pattern of findings suggests that boys and girls may experience similar physiological reactions to interpersonal stressors, but such physiological reactions may possibly manifest themselves differently at symptom levels. Girls' preponderance to internalizing psychopathology is often attributed to girls' heightened vulnerability to interpersonal stressors (for a review, see Zahn-Waxler et al., 2008). Expanding this theme, our findings provide a glimpse of a more complex picture: Boys and girls may differ in how biological stress reactions to interpersonal challenges are associated with symptoms. This view is, in fact, consonant with accumulating evidence showing that girls react more strongly with depressive and anxiety symptoms than boys when encountering the same amount of interpersonal stressors (Hankin et al., 2007; Rudolph & Hammen, 1999). Future research needs to investigate the gender specificity of symptom manifestation in diverse stressful contexts. Perhaps responses to interpersonal stressors and associated cortisol reactions in boys and girls may have different implications for different domains of adjustment outcomes.

The results of this study must be interpreted in the context of its methodological limitations. First, this study reports cross-sectional associations. Whether the adverse effect of early maturation persists over time, and if so, whether it would be mediated by cortisol reactivity, remain unanswered questions that are of high priority to address. Evidence for long-term effects of early maturation has been mixed, with some studies showing persistent effects (e.g., Graber, Seeley, Brooks-Gunn, & Lewinsohn, 2004) whereas others did not find such effects (Angold & Costello, 2006). In addition, longitudinal investigations will likely provide a clearer developmental picture of the complex intersections among cortisol reactivity, pubertal timing, and internalizing problems. Second, the interpretation of the results needs to be framed within the sample, the measurement constraints, and the time of assessment. Although the sample size and variation in pubertal status allowed for an

investigation of pubertal timing, future efforts would benefit from capturing a wider range of pubertal transition. In addition, the measure of pubertal timing was constructed based on a snapshot of individuals' physical maturation at the time of assessment. Given that there are variations in tempo individuals complete pubertal transition (Eichorn, 1975), individuals may get different pubertal timing scores depending on the time of assessment (Graber et al., 1996). Third, this study solely focused on stressors of interpersonal nature. Future efforts should be attuned to the differential impact of distinctive types of stressors. Fourth, as with any experimental studies, it is important to consider potential threats to the external validity of the SPP paradigm. Although the SPP was designed to mimic interpersonal stressors and, indeed, elicited cortisol reactions, a question remains as to whether these experimentally evoked reactions in salivary cortisol represent adolescents' biological responses to everyday life stressors. As Miller, Chen, and Zhou's (2007) recent review indicates, different types of stressors may elicit different patterns of HPA axis activity. Fifth, the magnitude of the coefficients were small. It should be emphasized, however, that because of complexity in human behaviors and emotions, effect sizes are necessarily small in outcomes with multiple determinants (Ahadi & Diener, 1989). Finally, because our sample was predominantly middle- and upper-class Caucasian families, generalizability of the findings to other populations may be limited.

Implications for Research, Policy, and Practice

The aforementioned limitations notwithstanding, this study demonstrated that stress reactivity could be one of the potential mechanisms to understand why early maturing girls may become more depressed and anxious than their peers. Interventions aimed at reducing interpersonal stress exposure and/or enhancing resilience and coping skills to combat interpersonal stress may prove effective in preventing early maturing girls' emotional problems. Our findings also highlight the importance of considering the multifaceted nature of development: Adolescents experience not only transformation in secondary sex characteristics and an increase in social stressors but also changes in physiology such as alteration of the HPA axis. The study also serves to increase our understanding of the mechanisms whereby pubertal transitions affect adolescents' emotions and draws attention to their complexity, as such physiological changes impact adjustment differentially in boys and girls. Future research on pubertal transition needs to account for this complexity in development and potential sex differences in the mechanisms for adolescent internalizing problems.

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TABLE 1**Means and Standard Deviations of the Study Variables**

	M	SD
Internalizing Problems	17.01	9.43
Pubertal Status		
Girls: Breast	3.58	1.13
Girls: Pubic Hair	4.07	1.07
Boys: Genital Growth	3.57	0.95
Boys: Pubic Hair	3.58	0.98
Pubertal Timing	0.00	1.00
Midday Baseline Cortisol Levels	0.20	0.14
Cortisol in SPP		
Pretest	0.18	0.11
Posttest	0.19	0.10
Residualized Cortisol Reactivity	<.01	0.09
Age	13.30	1.56
Externalizing Problems	10.15	8.82
BMI	21.32	4.07

Note. Pubertal timing was constructed by standaradizing pubertal status scores within same-sex and same-age peers, SPP = Social Performance Paradigm; BMI = body mass index.

TABLE 2
Bivariate Correlations Between Internalizing Problems, Pubertal Timing, Cortisol Reactivity, and Control Variables

	1	2	3	4	5	6	7	8	9
1 Internalizing Problems	—								
2 Pubertal Timing	.19**	—							
3 Cortisol Reactivity	.06	.17**	—						
4 Midday Baseline Cortisol Levels	.02	.13+	.07	—					
5 Age	.05	.01	.26**	.12+	—				
6 Externalizing Problems	.33**	.05	-.01	-.05	.02	—			
7 Body Mass Index	.17**	.21**	-.03	.07	.21**	-.01	—		
8 Household Income	-.05	-.09	-.07	-.08	.02	-.18**	-.02	—	
9 Medication Use ^a	.19**	.02	.08	0.3	-.01	.07	.05	.06	—
10 Sex ^b	-.10	-.01	.08	-.19**	-.01	.16*	-.11	-.05	-.01

^a0 = no medication used, 1 = at least one medication (e.g., pain relief, antacids, antibiotics, oral steroids, nonoral steroids, psychotropics, hormones, and others) used.

^b0 = girls, 1 = boys.

*
 $p < .05$.

**
 $p < .05$.

+
 $p < .10$.

TABLE 3

Predicting Internalizing Problems as a Function of Pubertal Timing and Cortisol Reactivity

	Model 1		Model 2	
	b	SE	b	SE
Intercept	20.03**	2.05	20.30**	4.08
Medication Use ^a	3.00*	1.34	2.73*	1.40
Externalizing Problems	0.34**	0.07	0.44**	0.08
Body Mass Index	0.16	0.16	0.21	0.16
Household Income	0.18	0.39	0.13	0.41
Age ^b	0.12	0.40	0.11	0.44
Sex ^c	-3.61**	1.22	-3.55**	1.29
Pubertal Timing	2.07*	0.94	0.69	0.99
Pubertal Timing × Sex ^c	-1.49	1.27	0.33	1.34
Midday Baseline Cortisol Levels	—	—	-1.46	4.42
Cortisol Reactivity	—	—	29.41**	11.37
Cortisol Reactivity × Sex ^c	—	—	-35.54**	14.13
R ²	.22		.27	

^a 0 = no medication used, 1 = at least one medication used.

^b Age is centered at 11-year-olds.

^c 0 = girls, 1 = boys.

* $p < .05$.

** $p < .01$.