Title

Mothers prenatal distress accelerates adrenal pubertal development in daughters.

Authors

Fox, Molly

Hahn, Jennifer

Sandman, Curt

et al.

Publication Date

2024-02-01

DOI

10.1016/j.psyneuen.2023.106671

Peer reviewed

HHS Public Access

Author manuscript

Psychoneuroendocrinology. Author manuscript; available in PMC 2025 February 06.

Published in final edited form as:

Psychoneuroendocrinology. 2024 February ; 160: 106671. doi:10.1016/j.psyneuen.2023.106671.

Mothers' prenatal distress accelerates adrenal pubertal development in daughters

Molly M. Fox[a,b,*,1], **Jennifer Hahn-Holbrook**[c,**,1], **Curt A. Sandman**[d], **Jessica A. Marino**[c], **Laura M. Glynn**[e], **Elysia Poggi Davis**[f,g]

[a]Department of Anthropology, University of California, Los Angeles, CA 90095, USA

[b]Department of Psychiatry and Biobehavioral Sciences, Semel Institute for Neuroscience and Human Behavior, University of California, Los Angeles, CA 90095, USA

[c]Department of Psychology, University of California, Merced, CA, 95343, USA

[d]Department of Psychiatry and Human Behavior, University of California, Irvine, CA, 92868, USA

[e]Department of Psychology, Chapman University, Orange, CA, 92866, USA

[f]Department of Psychology, University of Denver, Denver, CO, 80208, USA

[g]Department of Pediatrics, University of California, Irvine, CA, 92868, USA

Abstract

Human life history schedules vary, partly, because of adaptive, plastic responses to early-life conditions. Little is known about how prenatal conditions relate to puberty timing. We hypothesized that fetal exposure to adversity may induce an adaptive response in offspring maturational tempo. In a longitudinal study of 253 mother-child dyads followed for 15 years, we investigated if fetal exposure to maternal psychological distress related to children's adrenarche and gonadarche schedules, assessed by maternal and child report and by dehydroepiandrosterone sulfate (DHEA-S), testosterone, and estradiol levels. We found fetal exposure to elevated maternal prenatal psychological distress predicted earlier adrenarche and higher DHEA-S levels in girls, especially first-born girls, and that associations remained after covarying indices of postnatal adversity. No associations were observed for boys or for gonadarche in girls. Adrenarche orchestrates the social-behavioral transition from juvenility to adulthood; therefore, significant findings for adrenarche, but not gonadarche, suggest that prenatal maternal distress instigates an adaptive strategy in which daughters have earlier social-behavioral maturation. The stronger effect in first-borns suggests that, in adverse conditions, it is in the mother's adaptive interest for her daughter to hasten social maturation, but not necessarily sexual maturation, because it would prolong the duration of the daughter allomothering younger siblings. We postulate a novel

*Corresponding author at: Department of Anthropology, University of California, Los Angeles, CA, 90095, USA. mollyfox@ucla.edu (M.M. Fox). **Corresponding author: jhahn-holbrook@ucmerced.edu (J. Hahn-Holbrook).

[1]MMF and JHH contributed equally.

Declaration of Competing Interest

The authors have no conflicts of interest to disclose.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.psyneuen.2023.106671.

evolutionary framework that human mothers may calibrate the timing of first-born daughters' maturation in a way that optimizes their own reproductive success.

Keywords

Life history theory; Puberty; Prenatal mood; Adrenarche; DHEA-S; Fetal programming

1. Introduction

The timing of puberty is among the most flexible and consequential features of the human lifespan. Puberty involves a series of developmental processes that encompass the morphological, physiological, psychological, and behavioral shifts from the juvenile to adult phases of life. These transitions play out over several years and the rates of change in each domain are highly variable between individuals. Puberty involves both gonadal and adrenal maturation, which broadly correspond to fecundity and behavioral progressions to adulthood, respectively. Previous studies have reported that conditions encountered during sensitive periods of early-life development correlate with differential timing of pubertal maturation, but there is a paucity of studies that investigate this separately for gonadarche and adrenarche (Table 1). It is unresolved if conditions encountered during the earliest phase of life—fetal development—relate to the timing of gonadarche and adrenarche.

The adrenarche (adrenal puberty) transition involves rising levels of the adrenal androgen dehydroepiandrosterone (DHEA) and its sulfate form (DHEA-S), which initiate development of axillary hair, acne, adult body odor, skeletal maturation, a minor growth spurt (Shirtcliff et al., 2009), and brain maturation (Cumberland et al., 2021; Nguyen et al., 2017). Adrenarche typically commences in girls and boys ages 5–7 years and subsides in girls around age 20 and a few years later in boys. Gonadarche (gonadal puberty) is characterized by rising levels of sex steroids such as testosterone and estrogen that spur testicular enlargement in boys and ovarian and breast development in girls, along with vocal changes and rapid growth. Gonadarche typically begins in girls ages 9–10 and in boys 10–11 years old (Fechner, 2003).

An evolutionary perspective suggests that conditions encountered during early life shape the developing organism in ways that optimize fitness. Life history traits, i.e., growth, reproduction, and survivorship schedules, are shaped by selection to distribute time and energy allocations within an organism depending on extrinsic environmental, ecological, and demographic conditions related to risk and opportunity (Stearns, 1976). Pubertal timing has been a major focus of research on life history calibration because it represents a shift from prioritizing growth to reproduction (Gluckman and Hanson, 2006). While previous studies have reported that exposure to adversity during infancy and childhood exerts programming influences on pubertal timing, an earlier developmental phase has been overlooked. We propose that the prenatal phase is a sensitive period for programming maturational tempo.

The developmental tailoring of plastic traits based on prenatal exposure to environmental cues is known as "fetal programming." Because the fetal period in the human life cycle is unmatched by any other in growth and development, it is the stage most vulnerable to both

organizing and disorganizing influences (Barker, 2004; Sandman et al., 2012). Converging evidence supports the likelihood that fetal exposures program other aspects of hypothalamic-pituitary-adrenal (HPA) axis functionality, such as offspring stress responsivity (Davis et al., 2011), as well as other aspects of life history scheduling mechanisms, such as growth and telomere length (Stout-Oswald et al., 2022). Prenatal and postnatal adversity may be correlated, so previous studies evincing that postnatal early-life adversity is predictive of life-history scheduling (Table 1) may, actually, reflect effects that are attributable to un-measured prenatal insults. Our study controls for postnatal maternal psychological distress as well as several aspects of postnatal adversity in an attempt to determine the unique contribution of prenatal adversity.

We propose that maternal mood disturbance is a candidate prenatal cue that could program pubertal timing. While the developing fetus does not have direct access to information about the extra-maternal prenatal or postnatal environment, we propose that maternal mood disturbance may serve as a summary signal of extrinsic risk and resource availability, inducing a predictive adaptive response in offspring (Bateson et al., 2014; Hayward and Lummaa, 2013). Henceforth, we use the term “distress” to reflect our composite measurement of mood disturbances. Many possible biological pathways could connect maternal psychological distress with offspring postnatal maturational tempo. A plausible pathway is suggested by studies from our group and others, which found that prenatal psychological distress was correlated with alterations to the HPA-placental axis (Peterson et al., 2020; Sandman et al., 2012), which in turn, has been associated with children’s postnatal HPA system functionality (Irwin et al., 2021) and growth (Hahn-Holbrook et al., 2023). If our hypotheses are endorsed by data, future studies will be needed to determine the responsible biological mechanism.

Generally, previous scholarship in life history theory has posited that, in high-risk conditions, it would be adaptive to accelerate sexual debut to offset the risk of dying before reproducing. Accordingly, earlier gonadarche (menarche) has been reported for women raised in conditions of psychosocial stress and resource deprivation, such as poverty, father absence, institutionalization, and family conflict (Johnson and Gunnar, 2011; Tither and Ellis, 2008). Others found lack of evidence for accelerated menarche in response to early-life adversity, particularly father absence among non-industrialized populations, calling into question the universality of this pattern (Sear et al., 2019). Accelerated gonadarche effects either have been absent or inconsistently observed in studies of boys (Pham et al., 2022). Earlier gonadarche comes at the cost of waiting to garner more resources (somatic, social, material) before having one’s first child, so only if the benefits outweigh these costs would the strategy be enacted. In adverse circumstances, this trade-off favors earlier gonadarche for females whose accelerated mortality would dramatically curtail number of offspring. Females are biologically constrained in their pace of reproduction, so prolonging reproductive span by accelerating gonadarche is more strategic for maximizing reproductive success in females than males (Hochberg and Belsky, 2013). Males are not time-constrained in their pace of reproduction, so expanding the length of the reproductive span with an earlier start offers few benefits that could more readily be outweighed by costs. Thus, for our first hypothesis (Hypothesis 1; H1), consistent with previous studies, we predict

that the daughters of women who experience prenatal mood disturbance will exhibit early gonadarche (menarche), with no expected equivalent effect in males.

Unlike the literature on fetal programming of reproductive maturation (i.e., timing of gonadal puberty/menarche), little has been theorized or tested regarding the influence of early-life conditions on adrenarche timing. The variability in the timing of adrenarche indicates this is a plastic trait. Thus, there is opportunity for adaptive calibration to time this social-behavioral transition in a way that optimizes fitness for different environments. During adrenarche, DHEA-S contributes to the emotional and cognitive changes that instigate the psycho-behavioral transition to adulthood (Campbell, 2006; Cumberland et al., 2021). Also, DHEA-S governs development of secondary sex traits, which are key elements of social maturation because they provide a visual cue to others in the community that the adolescent is ready to take on an adult role (Thornhill and Gangestad, 1996). Contributing to the promotion of maternal caregiving may be among the neurobehavioral effects of DHEA (Apter-Levy et al., 2020), which is consistent with its role in social maturation. Therefore, for our second hypothesis (H2), we propose that, among human females, exposure to prenatal maternal mood disturbance should calibrate social-behavioral maturation to occur earlier than among those who are not exposed to prenatal maternal mood disturbance. Girls benefit from training in motherhood-related knowledge and behaviors before their own first pregnancy through allomothering, i.e., participation as a helper-at-the-nest (Hrdy, 1980; Ivey, 2000; Lancaster, 1971). Based on previous evidence that early-life adversity accelerates gonadarche (menarche), we posit it would be adaptive for allomothering interest and training, concomitantly, to begin earlier as well. While we emphasize that adrenal and gonadal puberty represent independent processes and acceleration in one domain does not necessitate the other (Grumbach, 1980), we nonetheless predict that in the unique case of adaptive early-life-adversity-accelerated gonadarche (menarche), adrenarche acceleration would also be adaptive. This line of reasoning predicts that the daughters of women who experience maternal distress during pregnancy should experience adrenarche at a younger age than those whose mothers did not experience maternal distress during pregnancy. Because boys are less frequent allomothers to their younger siblings (Helfrecht and Meehan, 2016; Valeggia, 2009; Weisner and Gallimore, 1977) we do not expect to observe this effect in sons. If results show that both girls and boys exhibit accelerated adrenarche related to prenatal mood disturbance, this would undermine our H2. An association between adrenarche and allomothering interest may be unique to girls, so a female-only effect would be consistent with our theoretical model, while an effect exhibited by both boys and girls would suggest that a different aspect of emotional or cognitive maturation could be accelerated as an adaptive strategy instigated by prenatal mood disturbance.

Allomothering starting at a younger age would benefit not only the child but also the child's mother, who benefits from her eldest daughter assisting with her younger children (Helfrecht and Meehan, 2016; Sear and Mace, 2008). We hypothesize that a pregnant woman experiencing mood disturbance may impose her own adaptive strategy on her daughters, consistent with the predictions of H2, and particularly her first-born daughter, to accelerate neurobehavioral maturation in a way that supplies herself a helper-at-the-nest as early as possible. Thus, for our third hypothesis (H3), we predict that among daughters, those who are first-borns of women who experience distress during pregnancy will exhibit

earlier adrenarche compared to first-borns who do not experience such distress and all later-born daughters.

If the prenatal period represents a sensitive window of development during which maternal mood disturbance exerts effects on pubertal developmental timing in girls, as we propose, then we would expect prenatal maternal distress to continue to be a significant predictor of pubertal timing above and beyond any contribution of postnatal maternal distress and childhood adversity (H4). This is not to say that postnatal maternal distress and childhood adversity are unimportant; these have been shown to influence parenting behavior and milk composition (Gray et al., 2013) which likely also serve as useful calibration signals for the offspring (see Table 1 "Exposure to Adversity from Age 0–5″).

Summarily, we investigate the hypotheses that maternal mood disturbance during pregnancy calibrates the tempo of gonadal (H1) and adrenal (H2) pubertal development in daughters, particularly first-born daughters (H3), above and beyond any association with indicators of postnatal maternal distress and childhood adversity (H4) (Fig. 1).

2. Methods

2.1. Cohort

Data for this study derive from a prospective, longitudinal cohort in Southern California in which 253 mother-child dyads were recruited during routine first trimester prenatal care from two obstetric clinics and followed from pregnancy through early adolescence. Detailed recruitment procedures have been described elsewhere (Glynn et al., 2018). Women with singleton pregnancies were recruited at < 16 weeks' gestation with the following eligibility criteria: English-speaking; non-smoker; age ≥ 18; no steroid medications; no self-reported use of tobacco, alcohol, or recreational drugs during the pregnancy. Also, to be included in the present analyses, mothers must have completed at least three prenatal maternal distress assessments and the child at least one of the pubertal development assessments. The race/ethnicity composition closely mirrors that of California at the time of data collection, suggesting that the sample is reasonably generalizable.

2.2. Measuring maternal psychological distress

Composite measures of pre- and postnatal psychological distress were created, as previously described (Glynn et al., 2018), combining the Perceived Stress Scale (PSS), Center for Epidemiologic Studies Depression Scale (CES-D), state form of the State-Trait Anxiety Inventory (STAI), and Pregnancy-specific Anxiety Scale (PSA, assessed prenatally only). Prenatal mood data were z-scored and then averaged across maternal assessments conducted at 15, 19, 25, 31 and 37 weeks' gestation to create the prenatal psychological distress composite scores. The postnatal distress composite uses maternal mood data deriving from assessments conducted at 2–3 months postpartum. The 10-item PSS assesses psychological stress experienced within the last month, with questions such as "how often have you felt that you were on top of things?" The 10-item PSA assesses anxiety and concerns specific to the pregnancy. Participants rate their agreement with statements such as "I am fearful regarding the health of my baby." The 9-item CES-D assesses depressive symptoms

experienced in the past week. Participants rate their agreement with statements such as "I felt lonely." The 10-item state form of the STAI assesses anxiety symptoms experienced in the past month, e.g., "Jittery." Each of these measures are validated and used widely in research involving pregnant women (Ghosh et al., 2010; Radloff, 1977; Rini et al., 1999; Spielberger, 1983). Mothers' scores on each scale were converted to *z*-scores and then averaged to create a composite; higher scores indicated more distress. Reliability analysis showed that the four scales were highly correlated (Pearson *r*'s ranged 0.523–0.783; Cronbach's α=0.891). Post-hoc, we repeated models with each of the four distress indicators separately to assess whether a particular indicator was uniquely associated with pubertal timing (Table S3). To measure postnatal distress, the same approach was implemented except that PSA was not administered postnatally or included in the postnatal distress composite.

2.3. Measuring pubertal development

We conducted three assessments when the child was 8–10, 11–12, and 13–16 years of age. Our study design measured the degree of pubertal progress at each of these three assessments, whose timing was strategically picked because, typically, pubertal development changes the most during that period. This study design captures comparatively early-developers, who would already show substantial pubertal development progress by the first assessment, and late-developers, who would still show low levels of pubertal development in the last assessment. Importantly, no child was at the maximum value on the Puberty Development Scale (PDS) for adrenal puberty at the first assessment. Thus, we maximized our ability to capture variation in adrenal and gonadal puberty progress. At each of the three child developmental assessment timepoints, both mothers and children completed the PDS. The PDS assesses the stage of development of an array of secondary sex characteristics, including body hair, skin changes (pimples), growth in height ("growth spurt"), breast development (girls only), menarche (girls only), deepening of the voice (boys only), and facial hair growth (boys only). The PDS computes two scores: an adrenal and a gonadal pubertal development score (Shirtcliff et al., 2009). Following established methods from previous studies, we used maternal PDS report before age 12 and children's reports thereafter to maximize accuracy (Terry et al., 2016). Importantly, using only mothers' or children's reports of pubertal development did not change our pattern of results (data not shown). Adrenal and gonadal PDS scores were positivity correlated in both boys (Coef. =.869, *SE* =.049, $p < .001$, 95 % CI=.772–.966) and girls (Coef. =.730, *SE* =.043, $p = .001$, 95 % CI=.646–.814). PDS scores have been shown to be moderately correlated with pubertal development assessed by physicians (Shirtcliff et al., 2009). Age of menarche was measured by child self-report.

2.4. Measuring hormones

No previous study has investigated how prenatal conditions relate to biomarkers of puberty (Table 1), thus our use of biomarkers moves this field forward. At each of the three child assessments, children provided saliva samples via passive drool for measurement of DHEA-S as a biomarker of adrenarche and testosterone (for males) and estradiol (for girls) as a biomarker of gonadarche. Saliva was aliquoted and stored at − 80 °C until assay. DHEA-S, testosterone, and estradiol were measured by enzyme-linked immunosorbent assay (ELISA;

IBL-International, Hamburg, Germany). Assays were repeated when a duplicate's CV was > 10 % if the concentration and difference between duplicates were both > 1 pg/ml. The intra- and inter- assay coefficients were, for DHEA-S, 7.8 % and 14.9 % respectively, for testosterone, 3.2 % and 4.04 % respectively, and for estradiol, 8.0 % and 3.4 %, respectively. Multilevel modeling showed that DHEA-S was positively correlated with adrenal PDS scores across all timepoints (girls: Coef. =.205, SE =.060, p = .013, 95 % CI =.086–.324; boys: Coef. =.341, SE =.055, p = .000, 95 % CI =.232–.450). Testosterone was positively correlated with gonadal PDS scores in boys (Coef. =.125, SE =.043, p = .006, 95 % CI =.038–.212) but not girls (Coef. =.047, SE =.082, p = .574, 95 % CI = −.123 to .217). Estradiol was positively correlated with gonadal PDS scores in girls (Coef. =.355, SE =.108, p = .001, 95 % CI =.141–.568); estradiol was not measured in boys. Sixteen children did not provide usable saliva samples, and so do not have available hormone data; therefore they were excluded from statistical models predicting hormone levels (N = 237 with hormone data, 111 females). In addition, one boy had a testosterone measurement that was > 3 standard deviations above the mean, so that child's one testosterone value was excluded from statistical analyses.

2.5. Measurement of demographics and birth weight

Women reported demographic information at their first prenatal assessment occurring at 15 weeks' gestation, including maternal age, education, income, household size, parity, and cohabitation with the baby's father. Income, household size and cohabitation status were assessed again in childhood at 7–9 years. Maternal and child medical records were used to determine the child's birth weight.

2.6. Operationalizing childhood adversity

Significant child life events that occurred from birth through age 5 were assessed with the Child Life Events Scale (CLES) (Coddington, 1972). The CLES is a 36-item parent report measure of a child's exposure to a range of major life events (e.g., death of a parent, parental separation). It has been widely used and has been shown to be predictive of child anxiety symptoms (Platt et al., 2016), health related quality of life (Villalonga-Olives et al., 2010), and preschool depression (Luby et al., 2006).

Childhood father absence and income-to-needs ratio were both determined from maternal report data collected when children were 7–9 years old. Income-to-needs ratio was calculated by dividing maternal report of household income by household size, adjusted for cost of living for the reported income year as determined by federal guidelines published by the Census Bureau; higher values represent higher socioeconomic status (both with prenatal and childhood assessment). Father absence was operationalized as a binary variable reflecting whether the mother was cohabitating with the child's biological father (both with prenatal and childhood assessment).

2.7. Statistical analyses

Covariates were selected in a two-step process. Firstly, we built a list of potential confounders based on our conceptual model and previous studies. The covariates considered were maternal education, parity, income-to-needs ratio, and father absence all deriving from

maternal report at 15 weeks' gestation, as well as maternal age at delivery and child birth weight. Secondly, we used traditional third variable criteria for identifying confounders, i.e., factors significantly associated ($p < 0.10$) with both the predictor of interest - prenatal distress - and at least one of the outcomes - pubertal timing metrics (Table S1). This process identified maternal age at delivery, education, and income-to-needs ratio (15 weeks' gestation) as potentially confounding variables. Therefore, these variables (z-scored) were included as covariates in all models. Analyses were conducted in SPSS version 29. Effect sizes are given in terms of standardized fixed effects for multilevel models and standardized-betas for regression models, with 95 % confidence intervals.

Multilevel linear growth curve modeling was conducted using the MIXED command. Given our sex-specific theoretical predictions, models were run separately for girls and boys. To test for intercept differences, time was centered in multilevel growth curve models at each year ages 9–16; significant intercept differences are marked in figures. When model coefficients are reported in the Tables, to ease model interpretation, models are centered at age 10, given that this was the most common (mode) age of children at visit 1 (M=9.58, SD=0.72), therefore, the continuous time variable represents changes in the outcome variable since age 10 years. Study visit was entered as a random time-varying variable in all multilevel models and unstructured covariance matrices were used to account for the shared variance between outcome variables as a function of study visit. All covariates were included as non-time varying fixed predictors.

To test H1 and H2, the prenatal maternal psychological distress composite variable ("prenatal distress") was entered at level 2 to predict gonadal (H1) and adrenal (H2) pubertal progression (entered in separate models at level 1), along with an interaction term between prenatal distress and child age over time (labeled in tables as time) to model differential changes in pubertal development indicators as a function of prenatal distress. To test H3, two-way interaction terms (first-born status*prenatal distress) tested whether first-born status moderated the effect of prenatal distress on pubertal outcomes at the intercept, along with a three-way interaction term (first-born status*prenatal distress*time) to model whether the effect of prenatal distress on pubertal development trajectories was moderated by first-born status. When there was evidence that first-born status significantly moderated the effect of prenatal distress on pubertal timing, we ran separate simple effects models in first-born and latter-born children to estimate the differential effect of prenatal distress on pubertal outcomes. To test H4, we used a step-wise multilevel modeling approach where prenatal distress alone was entered into model 1, then in model 2, we added the postnatal maternal distress composite variable ("postnatal maternal distress"), along with childhood adversity variables (childhood income-to-needs ratio and childhood father absence). If prenatal distress still significantly predicted pubertal development above and beyond the effects of postnatal maternal distress and childhood adversity in model 2, we reasoned that this supported the hypothesis that the prenatal period represents a sensitive window of development during which maternal mood disturbance exerts effects on pubertal developmental timing (H4). H4 models were tested in the subset of 226 dyads who had both prenatal and postnatal maternal distress data, and data on childhood father absence and income-to-needs ratio (108 females; 118 males;), i.e., N = 13 lacked childhood adversity data and an additional N = 14 lacked postnatal distress data.

3. Results

We tested our hypotheses in a prospective, longitudinal study in Southern California that followed 253 mother-child dyads from pregnancy through early adolescence. Mothers in this cohort were, on average 30 years old, mostly college educated, Non-Hispanic/Latinx White (45 %) or Hispanic/Latinx (30 %), about half of participants were primiparous, and children were 48 % female (Table 2).

H1: Prenatal distress predicts earlier gonadarche in girls but not boys.

Contrary to our hypothesis for girls, prenatal distress did not predict any of the gonadal pubertal development measures (Table 3). As anticipated, we observed a null result for boys.

H2: Prenatal distress predicts earlier adrenarche in girls but not boys.

Consistent with our hypothesis for girls, higher maternal prenatal distress predicted earlier adrenal pubertal development, observed for both adrenal PDS and DHEA-S (Table 3). Specifically, girls exposed to higher prenatal maternal distress had higher adrenal PDS scores at ages 9, 10, and 11 (Fig. 2a). Likewise, girls exposed to higher, compared to lower, prenatal maternal distress had significantly higher DHEA-S at ages 9–13 (Fig. 2c). Prenatal distress was not associated with girls' adrenal PDS scores after age 11 or girls' DHEA-S scores after age 13. Follow-up exploratory analyses indicated that each of the four prenatal distress indicators that comprise our composite predicted faster adrenal pubertal timing in girls with similar effect sizes (Table S3). Consistent with our anticipation of a null effect for boys, there were no associations between maternal prenatal distress and adrenal pubertal development for sons (Fig. 2b and d).

H3: Prenatal distress predicts earlier adrenarche in first-born girls.

Consistent with our hypothesis, prenatal distress was associated with adrenal PDS scores of first-born but not later-born girls (Fig. 3, Table S4). Also consistent with our prediction, first-born status did not moderate the relation between prenatal distress and adrenal pubertal status in boys (Fig. 3, Table S4). Specifically, first-born girls exposed to higher (compared to lower) prenatal maternal distress had significantly higher adrenal PDS scores at ages 9–12, and no significant differences from age 13 onwards (Fig. 3a). By contrast, prenatal maternal distress did not significantly predict adrenal PDS scores for later-born girls (Fig. 3b). Contrary to our hypothesis, first-born status did not moderate the relation between prenatal maternal distress and DHEA-S for girls (Table S4).

H4: The prenatal period as a sensitive period for programming of pubertal timing.

We tested the hypothesis that the relations we observed between prenatal maternal distress and adrenal pubertal timing in girls (H2) were driven by prenatal exposures, i.e., prenatal distress was not merely a proxy of postnatal maternal distress or childhood adversity. To test this hypothesis, we included our predictor of primary interest, prenatal maternal distress, along with 2–3 months postnatal maternal distress, adverse life events before age five, and father absence and income-to-needs ratio when the child was 7–9 years of age as predictors of adrenal pubertal timing in multilevel growth curve models (Table S5). These indicators were selected because they are the most frequent measures of early-life

adversity in this area of research (Table 1). Consistent with our prediction that the prenatal period is a sensitive window through which maternal distress influences pubertal timing in girls, prenatal maternal distress remained a significant predictor of adrenal PDS scores and DHEA-S levels in girls when postnatal maternal distress and childhood adversity were included in the model (Table S5).

4. Discussion

We found that adversity encountered during the prenatal phase of life may set the human female fetus on a path towards earlier adrenarche. Moreover, we observed this association was strongest for first-born girls. No associations were observed for adrenarche in males or for gonadarche for either sex. An evolutionary framework provides a parsimonious explanation for these patterns. We integrate the concepts of fetal programming and life history theory to situate our results in the context of other studies.

Of the small number of previous studies that examined how adversity encountered before 5 years of age correlates with the timing of puberty, only two reported on adrenal puberty, while the rest examined gonadal puberty or a composite of both processes (Table 1). A cross-sectional study of children from three small-scale societies in the Central African Republic and Ethiopia indicate the possibility of later adrenarche compared to Western norms (Helfrecht et al., 2018) and another cross-sectional study of older adolescents in Kenya found DHEA-S levels inversely associated with malaria parasite density (Leenstra et al., 2003), both studies suggestive of adaptive calibration of DHEA to environmental conditions. A substantial corpus of evidence already suggests that early-life adversity affects later-life adrenal function, e.g., cortisol reactivity (Boyce and Ellis, 2005). Additionally, it is biologically plausible that prenatal conditions influence adrenal maturation because the zona reticularis—the adrenal gland layer that grows and begins producing DHEA and DHEA-S during adrenarche—is derived from the fetal adrenal zone (Sucheston and Cannon, 1968).

Our study provides a novel, longitudinal investigation of the relation between prenatal adversity and child adrenarche timing. A previous study found that mothers' prenatal distress was associated with neither their daughters' dichotomous classifications of DHEA detectability at 7 years old nor puberty status at 11 years old (Belsky et al., 2015). Our study further advances the field by conducting longitudinal assessments with repeated measures in pregnancy and of the child from 9 to 16 years' age, a crucial developmental window for examining the process of adrenal puberty. Also, our repeated measurement of DHEA-S concentrations goes beyond the previous study's one-time dichotomous classification of DHEA detectability to provide a more detailed analysis of adrenal endocrine dynamics. Another previous study found that prenatal estriol levels were correlated with women's adulthood DHEA-S levels (Cohn and Cirillo, 2020), which further evinces the biological plausibility of prenatal conditions affecting postnatal adrenal function, although that study did not address our research question related to adaptive calibration of early-life maturational processes.

Two previously-published studies examine how prenatal conditions relate to gonadal pubertal timing; mothers' prenatal exposure to natural disaster and stressful life events,

respectively, were associated with their daughters' earlier age at menarche (Brauner et al., 2021; Duchesne et al., 2017). Contrastingly, we observed no significant associations between mothers' prenatal distress and daughters' gonadal puberty (menarche) timing. The discrepancy with previous studies could be explained by different prenatal predictors, e.g., natural disaster exposure (Duchesne et al., 2017) or adverse life events (Brauner et al., 2021). From an evolutionary perspective, the adaptive strategy of a fetus or mother may differ depending on the type of adversity encountered. Further research is needed to clarify the unique effects of various adversities on fetal programming strategies.

Maternal depression, anxiety, and stress have been associated with alterations to HPA-placental stress endocrinology during pregnancy (Peterson et al., 2020; Sandman et al., 2012), indicating a biomechanism of mother-to-fetus transmission of mood state signals. Furthermore, prenatal maternal depression, anxiety, and stress have already been associated (independent of postpartum mood) with a variety of offspring developmental outcomes (Davis et al., 2020; Glynn et al., 2018), including offspring HPA axis functionality (Davis et al., 2011). Additionally, previous studies found that postnatal early-life adversity was associated with alterations to children's pubertal development (Table 1). Our results do not contradict those observations, but we underscore the possibility that previous studies that did not account for prenatal adversity may have observed results that were actually influenced by unmeasured prenatal effects.

Controversy exists as to whether these developmental shifts reflect forecasting or response to constraints. The forecasting paradigm posits that ontogenic alterations reflect a fetal strategy to be optimally suited for the extrinsic context it is most likely to encounter during postnatal life (either just the first few years (Wells, 2012) or into adulthood (Gluckman et al., 2007)). The constraints paradigm suggests that the fetus is making compromises as a consequence of limited resources (Lea et al., 2017). The forecasting paradigm intimates that natural selection has shaped traits' degrees of phenotypic plasticity and ontogenic response to extrinsic signals in ways that prepare the organism for successful postnatal life (Bateson et al., 2014; Gluckman et al., 2007). The constraints paradigm also posits that selection promotes developmental plasticity but for a different reason, namely, to siphon resources away from non-essential towards vital functions in the face of deprivation. Accelerated maturation as a response to early-life adversity is a classic example of predictive adaptive response, but is not the expected developmental response under constraints models, so our results lend evidence to the possibility that the long-lived human species may exhibit anticipatory developmental plasticity (Lea et al., 2017; Wells, 2012).

H2 and H3 represent distinct evolutionary paths by which girls who experience prenatal maternal distress should exhibit earlier adrenarche—one primarily driven by the adaptive interests of the child, and one primarily driven by the adaptive interests of the mother. These two evolutionary paths to earlier adrenarche (H2 and H3) can be empirically distinguished by H1 results. H2 would be bolstered by H1 also being endorsed, because earlier training as an allomother would be most adaptive *for the child* if she is likely to have a relatively early first birth, i. e., earlier menarche. Then, the daughter's training through allomothering would help the daughter increase her own direct fitness by preparing her to be a successful young mother. Alternatively, H3 would be bolstered by H1 being refuted, because the child

beginning allomothering at a younger age would be most adaptive *for the mother* if the child remains an allomother for longer, delaying her own first pregnancy through later menarche.

Our pattern of results (i.e., a significant finding for adrenal puberty but not gonadal puberty) is most consistent with the idea that mothers who are experiencing psychological distress may impose their own adaptive strategy on offspring by programming daughters - particularly first-born daughters - to begin adrenarche earlier, but not menarche (non-endorsed H1), supplying themselves allomothering assistance earlier and for longer duration. A daughter's adaptive interests are partially, but not completely, aligned with her mother's, because allomothering her younger siblings enhances her inclusive fitness. However, it is important to point out that we did not test the gap between the onset of adrenal and gonadal puberty specifically, because our first measure of adrenal puberty was likely after the start of adrenal puberty for many children. We encourage future research to provide a direct test of whether prenatal distress predicts accelerated social-behavioral maturation without accelerated sexual maturation within individuals.

Alternative explanations for our results are possible. The observational nature of our study cannot rule out other causal models than the one we propose. Our results could suggest an adaptive strategy such that girls who experience prenatal mood disturbance improve their fitness by accelerating their social-behavioral transition to adulthood in order to secure extra time to garner adult-accessed resources necessary to support successful pregnancy. While our manuscript argues the most likely mature-female-specific resource is practice and training in motherhood, other mature-female-specific resources may also exist. Future studies are needed to discern these adaptive strategies.

Accelerated female adrenarche as an adaptive response to maternal prenatal adversity is not cost-free. Selection balances the benefits and costs of ontogenic adaptations, taking into account both direct and indirect fitness effects. Girls who accelerate adrenarche do so at the cost of shorter phases of early childhood, which is a phase of protection and food provisioning by parents and other adults, rapid growth, and learning through play. Across various cultures, upon the commencement of adrenarche, children transition from this safety and comfort to increasing engagement in allomothering, domestic labor, and acquiring and preparing food (Bogin, 1997). Although the prevailing view among clinicians is that early adrenarche is a risk factor for poor social functioning (Byrne et al., 2017), an evolutionary perspective implies that what has been interpreted as problematic for social relationships may, instead, reflect a set of social skills tailored for an asynchronous life phase. In other words, accelerated adrenarche may be an adaptive response to adverse conditions that promotes younger individuals thinking and behaving in ways more typically suited to older ages. The neuromaturational process of adrenarche involves reduced amygdala activation, enhanced hippocampal function, and enhanced synaptogenesis, which together, potentially promote seeking out and learning from new social experiences with unfamiliar individuals (Campbell, 2006; Spivak, 1994). This neurobehavioral profile may appear inappropriate or suboptimal when enacted at younger ages. Early adrenarche has been associated with reduced frontal white matter volume (Klauser et al., 2015) and an evolutionary perspective may suggest this reflects an alternative rather than dysfunctional neuroanatomy (Del Giudice, 2018). Additionally, adrenarche is a period of vulnerability for the onset of

obesity, type-2 diabetes (Hochberg, 2008), affective disorders, and other psychopathologies (Hochberg et al., 2011), so acceleration of its timing would, collaterally, hasten onset of these disorders.

Based on the highly-conserved nature of the HPA axis and homologous developmental sequences in chordates, it is highly probable that adrenal stimulation marks the beginning of maturational processes throughout the animal kingdom across many million years of evolution (Todd et al., 2016). The decoupling of adrenarche and gonadarche emerged later, during the evolutionary history of Great Apes, with distinctive adrenarche observed in chimpanzees and bonobos (Behringer et al., 2012; Sabbi et al., 2020). Only among humans do we see a time lag, creating an intermediate period, “middle childhood,” between adrenarche and gonadarche (Campbell, 2006). During this childhood phase, the social-behavioral transition from having a juvenile role to adult role in the community is orchestrated by adrenal maturation. Our results imply that human mothers may forecast future needs by calibrating the timing of first-born daughters’ neurobehavioral maturation (and perhaps fecundity) in a way that optimizes the mothers’ own reproductive success based on prenatal psychological distress. Psychological distress may thus reflect a crucial summary signal of conditions and resources that translates into biological, ontogenic adaptations. In this way, psychological distress may be a key human signal in the intergenerational programming of life history traits.

Strengths of this study include a longitudinal design that followed families across the prenatal and postnatal periods, from early pregnancy through the child’s assessment at 13–16 years, with multiple timepoints of data collection. Additionally, our operationalization of puberty is bolstered by combining information from maternal and child reports with biomarkers of both gonadal and adrenal maturation. Nonetheless, our results should be considered in light of several limitations. We lack data on other factors that may contribute to predicting children’s ages at gonadarche, including the mothers’ ages at menarche, potentially constraining the interpretation of gonadal results. We were limited by the timing of our data collection windows for all variables. Our analyses, although robust, could have captured more detailed information about the children’s maturational trajectories if we had pubertal assessment before age 8–10 years and more fine-grained temporal data between assessments. We also lack data on the children’s interest or participation in alloparenting as well as any stress or burden that could derive from caring for younger siblings, consequently, we can only speculate based on the hypothesized function of accelerated adrenarche. Despite this, we hope that our hypotheses and results prompt future studies examining differential interest or participation in alloparenting among first-born girls whose mothers experienced prenatal distress compared to later-born peers and those whose mothers did not experience such distress. Future studies are needed to discern the coordination of onset of adrenal and gonadal maturation alongside social-behavioral maturation using earlier childhood assessments than we had here.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors thank the families who participated in this study. We also thank the dedicated staff at the Early Human and Lifespan Development Program. This research was supported by grants from the National Institutes of Health HD-28413 (CAS), HD-40967 (LMG), HD-51852 (CAS), NS-41298 (CAS), MH-96889 (EPD, LMG, CAS), DK-105110 (MMF), DK-125524 (MMF), and AG-079093 (MMF).

References

Apter-Levy Y, Zagoory-Sharon O, Feldman R, 2020. Chronic depression alters mothers' DHEA and DHEA-to-cortisol ratio: Implications for maternal behavior and child outcomes. Front Psychiatry 11, 728. [PubMed: 32793012]

Barker D, 2004. The developmental origins of adult disease. J. Am. Coll. Nutr 23, 588S–595S. [PubMed: 15640511]

Bateson P, Gluckman P, Hanson M, 2014. The biology of developmental plasticity and the predictive adaptive response hypothesis. J. Physiol 592, 2357–2368. [PubMed: 24882817]

Behringer V, Hohmann G, Stevens JM, Weltring A, Deschner T, 2012. Adrenarche in bonobos (Pan paniscus): Evidence from ontogenetic changes in urinary dehydroepiandrosterone-sulfate levels. J. Endocrinol 214, 55. [PubMed: 22562655]

Belsky J, Houts RM, Fearon RM, 2010a. Infant attachment security and the timing of puberty: Testing an evolutionary hypothesis. Psychol. Sci 21, 1195–1201. [PubMed: 20713636]

Belsky J, Steinberg L, Houts RM, Halpern-Felsher BL, Network NECCR, 2010b. The development of reproductive strategy in females: Early maternal harshness –> earlier menarche –> increased sexual risk taking. Dev. Psychol 46, 120–128. [PubMed: 20053011]

Belsky J, Ruttle PL, Boyce WT, Armstrong JM, Essex MJ, 2015. Early adversity, elevated stress physiology, accelerated sexual maturation, and poor health in females. Dev. Psychol 51, 816–822. [PubMed: 25915592]

Bleil ME, Spieker SJ, Gregorich SE, Thomas AS, Hiatt RA, Appelhans BM, Roisman GI, Booth-LaForce C, 2021. Early life adversity and pubertal timing: Implications for cardiometabolic health. J. Pedia Psychol 46, 36–48.

Bogin B, 1997. Evolutionary hypotheses for human childhood. Am. J. Phys. Anthropol 104, 63–89.

Boyce WT, Ellis BJ, 2005. Biological sensitivity to context: I. An evolutionary–developmental theory of the origins and functions of stress reactivity. Dev. Psychopathol 17, 271–301. [PubMed: 16761546]

Brauner EV, Koch T, Juul A, Doherty DA, Hart R, Hickey M, 2021. Prenatal exposure to maternal stressful life events and earlier age at menarche: The Raine study. Hum. Reprod 36, 1959–1969. [PubMed: 33744952]

Byrne ML, Whittle S, Vijayakumar N, Dennison M, Simmons JG, Allen NB, 2017. A systematic review of adrenarche as a sensitive period in neurobiological development and mental health. Dev. Cogn. Neurosci 25, 12–28. [PubMed: 28077245]

Campbell B, 2006. Adrenarche and the evolution of human life history. Am. J. Hum. Biol 18, 569–589. [PubMed: 16917887]

Coddington RD, 1972. The significance of life events as etiologic factors in the diseases of children — II a study of a normal population. J. Psychosom. Res 16, 205–213. [PubMed: 5072914]

Cohn BA, Cirillo PM, 2020. In utero and postnatal programing of dehydroepiandrosterone sulfate (DHEAS) in young adult women. Reprod. Toxicol 92, 148–154. [PubMed: 31173873]

Cumberland AL, Hirst JJ, Badoer E, Wudy SA, Greaves RF, Zacharin M, Walker DW, 2021. The enigma of the adrenarche: Identifying the early life mechanisms and possible role in postnatal brain development. Int. J. Mol. Sci 22, 4296. [PubMed: 33919014]

Davis EP, Glynn LM, Waffarn F, Sandman CA, 2011. Prenatal maternal stress programs infant stress regulation. J. Child Psychol. Psychiatry 52, 119–129. [PubMed: 20854366]

Davis EP, Hankin BL, Glynn LM, Head K, Kim DJ, Sandman CA, 2020. Prenatal maternal stress, child cortical thickness, and adolescent depressive symptoms. Child Dev 91, e432–e450. [PubMed: 31073997]

Del Giudice M, 2018. Middle childhood: An evolutionary-developmental synthesis. In: Halfon N, Forrest CB, Lerner RM, Faustman EM (Eds.), Handbook of life course health development. CH, Cham, pp. 95–107.

DiLalla LF, Pham HT, Corley RP, Wadsworth S, Berenbaum SA, 2021. Family experiences and parent personality as antecedents of pubertal timing in girls and boys. J. Youth Adolesc 50, 1017–1033. [PubMed: 33813679]

Duchesne A, Liu A, Jones SL, Laplante DP, King S, 2017. Childhood body mass index at 5.5 years mediates the effect of prenatal maternal stress on daughters' age at menarche: Project ice storm. J. Dev. Orig. Health Dis 8, 168–177. [PubMed: 28027719]

Ellis BJ, Essex MJ, 2007. Family environments, adrenarche, and sexual maturation: A longitudinal test of a life history model. Child Dev 78, 1799–1817. [PubMed: 17988322]

Ellis BJ, McFadyen-Ketchum S, Dodge KA, Pettit GS, Bates JE, 1999. Quality of early family relationships and individual differences in the timing of pubertal maturation in girls: A longitudinal test of an evolutionary model. J. Pers. Soc. Psychol 77, 387–401. [PubMed: 10474213]

Fechner P, 2003. The biology of puberty: New developments in sex differences. In: Hayward C (Ed.), Gender differences at puberty. Cambridge University Press, Cambridge, pp. 17–28.

Gaml-Sørensen A, Brix N, Ernst A, Lunddorf LLH, Ramlau-Hansen CH, 2021. Father absence in pregnancy or during childhood and pubertal development in girls and boys: A population-based cohort study. Child Dev 92, 1494–1508. [PubMed: 33400273]

Ghosh JK, Wilhelm MH, Dunkel-Schetter C, Lombardi CA, Ritz BR, 2010. Paternal support and preterm birth, and the moderation of effects of chronic stress: A study in Los Angeles county mothers. Arch. Women'S. Ment. Health 13, 327–338. [PubMed: 20066551]

Gluckman PD, Hanson MA, 2006. Evolution, development and timing of puberty. Trends Endocrinol. Metab 17, 7–12. [PubMed: 16311040]

Gluckman PD, Hanson MA, Beedle AS, 2007. Early life events and their consequences for later disease: A life history and evolutionary perspective. Am. J. Hum. Biol 19, 1–19. [PubMed: 17160980]

Glynn LM, Howland MA, Sandman CA, Davis EP, Phelan M, Baram TZ, Stern HS, 2018. Prenatal maternal mood patterns predict child temperament and adolescent mental health. J. Affect. Disord 228, 83–90. [PubMed: 29241049]

Grey KR, Davis EP, Sandman CA, Glynn LM, 2013. Human milk cortisol is associated with infant temperament. Psychoneuroendocrinology 38, 1178–1185. [PubMed: 23265309]

Grumbach MM, 1980. The neuroendocrinology of puberty. Hosp. Pract 15, 51–60.

Hahn-Holbrook J, Davis EP, Sandman CA, Glynn LM, 2023. Maternal prenatal cortisol trajectories predict accelerated growth in infancy. Psychoneuroendocrinology 147, 105957. [PubMed: 36371954]

Hartman S, Li Z, Nettle D, Belsky J, 2017. External-environmental and internal-health early life predictors of adolescent development. Dev. Psychopathol 29, 1839–1849. [PubMed: 29162185]

Hayward AD, Lummaa V, 2013. Testing the evolutionary basis of the predictive adaptive response hypothesis in a preindustrial human population. Evol., Med., Public Health 2013, 106–117. [PubMed: 24481192]

Helfrecht C, Meehan CL, 2016. Sibling effects on nutritional status: Intersections of cooperation and competition across development. Am. J. Hum. Biol 28, 159–170. [PubMed: 26179564]

Helfrecht C, Hagen EH, DeAvila D, Bernstein RM, Dira SJ, Meehan CL, 2018. DHEAS patterning across childhood in three sub-Saharan populations: Associations with age, sex, ethnicity, and cortisol. Am. J. Hum. Biol 30, e23090.

Hochberg Z, 2008. Juvenility in the context of life history theory. Arch. Dis. Child 93, 534–539. [PubMed: 18337281]

Hochberg Z, Feil R, Constancia M, Fraga M, Junien C, Carel JC, Boileau P, Le Bouc Y, Deal CL, Lillycrop K, Scharfmann R, Sheppard A, Skinner M, Szyf M, Waterland RA, Waxman DJ, Whitelaw E, Ong K, Albertsson-Wikland K, 2011. Child health, developmental plasticity, and epigenetic programming. Endocr. Rev 32, 159–224. [PubMed: 20971919]

Hochberg ZE, Belsky J, 2013. Evo-devo of human adolescence: Beyond disease models of early puberty. BMC Med 11–24, 113.

Hrdy SB, 1980. The langurs of Abu: Female and male strategies of reproduction. Harvard University Press,.

Irwin JL, Meyering AL, Peterson G, Glynn LM, Sandman CA, Hicks LM, Davis EP, 2021. Maternal prenatal cortisol programs the infant hypothalamic–pituitary–adrenal axis. Psychoneuroendocrinology 125, 105106. [PubMed: 33340919]

Ivey PK, 2000. Cooperative reproduction in Ituri Forest hunter-gatherers: Who cares for Efe infants? Curr. Anthropol 41, 856–866.

James-Todd T, Tehranifar P, Rich-Edwards J, Titievsky L, Terry MB, 2010. The impact of socioeconomic status across early life on age at menarche among a racially diverse population of girls. Ann. Epidemiol 20, 836–842. [PubMed: 20933190]

Johnson DE, Gunnar MR, 2011. IV. Growth failure in institutionalized children. Monogr. Soc. Res. Child Dev 76, 92–126. [PubMed: 25364058]

Johnson DE, Tang A, Almas AN, Degnan KA, McLaughlin KA, Nelson CA, Fox NA, Zeanah CH, Drury SS, 2018. Caregiving disruptions affect growth and pubertal development in early adolescence in institutionalized and fostered Romanian children: A randomized clinical trial. J. Pediatr 203, 345–353 e343. [PubMed: 30172435]

Klauser P, Whittle S, Simmons JG, Byrne ML, Mundy LK, Patton GC, Fornito A, Allen NB, 2015. Reduced frontal white matter volume in children with early onset of adrenarche. Psychoneuroendocrinology 52, 111–118. [PubMed: 25459897]

Lancaster JB, 1971. Play-mothering: The relations between juvenile females and young infants among free-ranging vervet monkeys (Cercopithecus aethiops). Folia Primatol 15, 161–182.

Lea AJ, Tung J, Archie EA, Alberts SC, 2017. Developmental plasticity: Bridging research in evolution and human health. Evol. Med. Public Health 2017, 162–175. [PubMed: 29424834]

Leenstra T, ter Kuile FO, Kariuki SK, Nixon CP, Oloo AJ, Kager PA, Kurtis JD, 2003. Dehydroepiandrosterone sulfate levels associated with decreased malaria parasite density and increased hemoglobin concentration in pubertal girls from western Kenya. J. Infect. Dis 188, 297–304. [PubMed: 12854087]

Luby JL, Belden AC, Spitznagel E, 2006. Risk factors for preschool depression: The mediating role of early stressful life events. J. Child Psychol. Psychiatry 47, 1292–1298. [PubMed: 17176384]

Mendle J, Ryan RM, McKone KM, 2016. Early childhood maltreatment and pubertal development: Replication in a population-based sample. J. Res Adolesc 26, 595–602. [PubMed: 28581653]

Nguyen T-V, Wu M, Lew J, Albaugh MD, Botteron KN, Hudziak JJ, Fonov VS, Collins DL, Campbell BC, Booij L, 2017. Dehydroepiandrosterone impacts working memory by shaping cortico-hippocampal structural covariance during development. Psychoneuroendocrinology 86, 110–121. [PubMed: 28946055]

Peterson GF, Espel EV, Davis EP, Sandman CA, Glynn LM, 2020. Characterizing prenatal maternal distress with unique prenatal cortisol trajectories. Health Psychol 39, 1013. [PubMed: 32686953]

Pham HT, DiLalla LF, Corley RP, Dorn LD, Berenbaum SA, 2022. Family environmental antecedents of pubertal timing in girls and boys: A review and open questions. Horm. Behav 138, 105101. [PubMed: 35124424]

Platt R, Williams SR, Ginsburg GS, 2016. Stressful life events and child anxiety: Examining parent and child mediators. Child Psychiatry Hum. Dev 47, 23–34. [PubMed: 25772523]

Radloff, 1977. The CESD scale: A self-report depression scale for research in the general population. Appl. Psychol. Meas 1, 385–401.

Reid BM, Miller BS, Dorn LD, Desjardins C, Donzella B, Gunnar M, 2017. Early growth faltering in post-institutionalized youth and later anthropometric and pubertal development. Pediatr. Res 82, 278–284. [PubMed: 28170387]

Rini CK, Dunkel Schetter C, Wadhwa PD, Sandman CA, 1999. Psychological adaptation and birth outcomes: the role of personal resources, stress, and sociocultural context during pregnancy. Health Psychol 18, 333–345. [PubMed: 10431934]

Sabbi KH, Muller MN, Machanda ZP, Otali E, Fox SA, Wrangham RW, Emery Thompson M, 2020. Human-like adrenal development in wild chimpanzees: A longitudinal study of urinary dehydroepiandrosterone-sulfate and cortisol. Am. J. Primatol 82, e23064. [PubMed: 31709585]

Sandman CA, Davis EP, Buss C, Glynn LM, 2012. Exposure to prenatal psychobiological stress exerts programming influences on the mother and her fetus. Neuroendocrinology 95, 8–21.

Sear R, Mace R, 2008. Who keeps children alive? A review of the effects of kin on child survival. Evol. Hum. Behav 29, 1–18.

Sear R, Sheppard P, Coall DA, 2019. Cross-cultural evidence does not support universal acceleration of puberty in father-absent households. Philos. Trans. R. Soc. B: Biol. Sci 374, 20180124.

Shirtcliff EA, Dahl RE, Pollak SD, 2009. Pubertal development: Correspondence between hormonal and physical development. Child Dev 80, 327–337. [PubMed: 19466995]

Spielberger CD, 1983. State-Trait Anxiety Inventory. Mind Garden, Redwood City, CA.

Spivak CE, 1994. Desensitization and noncompetitive blockade of GABAA receptors in ventral midbrain neurons by a neurosteroid dehydroepiandrosterone sulfate. Synapse 16, 113–122. [PubMed: 7515198]

Stearns SC, 1976. Life-history tactics: A review of the ideas. Q. Rev. Biol 51, 3–47. [PubMed: 778893]

Stout-Oswald SA, Glynn LM, Bisoffi M, Demers CH, Davis EP, 2022. Prenatal exposure to maternal psychological distress and telomere length in childhood. Dev. Psychobiol 64, e22238. [PubMed: 35050506]

Sucheston ME, Cannon MS, 1968. Development of zonular patterns in the human adrenal gland. J. Morphol 126, 477–491. [PubMed: 5716437]

Sung S, Simpson JA, Griskevicius V, Kuo SI, Schlomer GL, Belsky J, 2016. Secure infant-mother attachment buffers the effect of early-life stress on age of menarche. Psychol. Sci 27, 667–674. [PubMed: 26980153]

Terry MB, Goldberg M, Schechter S, Houghton LC, White ML, O'Toole K, Chung WK, Daly MB, Keegan TH, Andrulis IL, 2016. Comparison of clinical, maternal, and self pubertal assessments: Implications for health studies. Pediatrics 138. [PubMed: 27544347]

Thornhill R, Gangestad SW, 1996. The evolution of human sexuality. Trends Ecol. Evol 11, 98–102. [PubMed: 21237770]

Tither JM, Ellis BJ, 2008. Impact of fathers on daughters' age at menarche: A genetically and environmentally controlled sibling study. Dev. Psychol 44, 1409–1420. [PubMed: 18793072]

Todd EV, Liu H, Muncaster S, Gemmell NJ, 2016. Bending genders: The biology of natural sex change in fish. Sex. Dev 10, 223–241. [PubMed: 27820936]

Valeggia CR, 2009. Felixble caretakers: Responses of Toba families in transition. In: Bently G, Mace R (Eds.), Substitute parents: Biological and social perspectives on alloparenting in human societies. Berhahn Books, Oxford.

Villalonga-Olives E, Rojas-Farreras S, Vilagut G, Palacio-Vieira JA, Valderas JM, Herdman M, Ferrer M, Rajmil L, Alonso J, 2010. Impact of recent life events on the health related quality of life of adolescents and youths: The role of gender and life events typologies in a follow-up study. Health Qual. Life Outcomes 8, 71. [PubMed: 20642830]

Weisner TS, Gallimore R, 1977. My brother's keeper: Child and sibling caretaking. Curr. Anthropol 18, 169–190.

Wells JC, 2012. A critical appraisal of the predictive adaptive response hypothesis. Int. J. Epidemiol 41, 229–235. [PubMed: 22422458]

Zhang L, Zhang D, Sun Y, 2019. Adverse childhood experiences and early pubertal timing among girls: A meta-analysis. Int. J. Environ. Res. Public Health 16. [PubMed: 31861365]

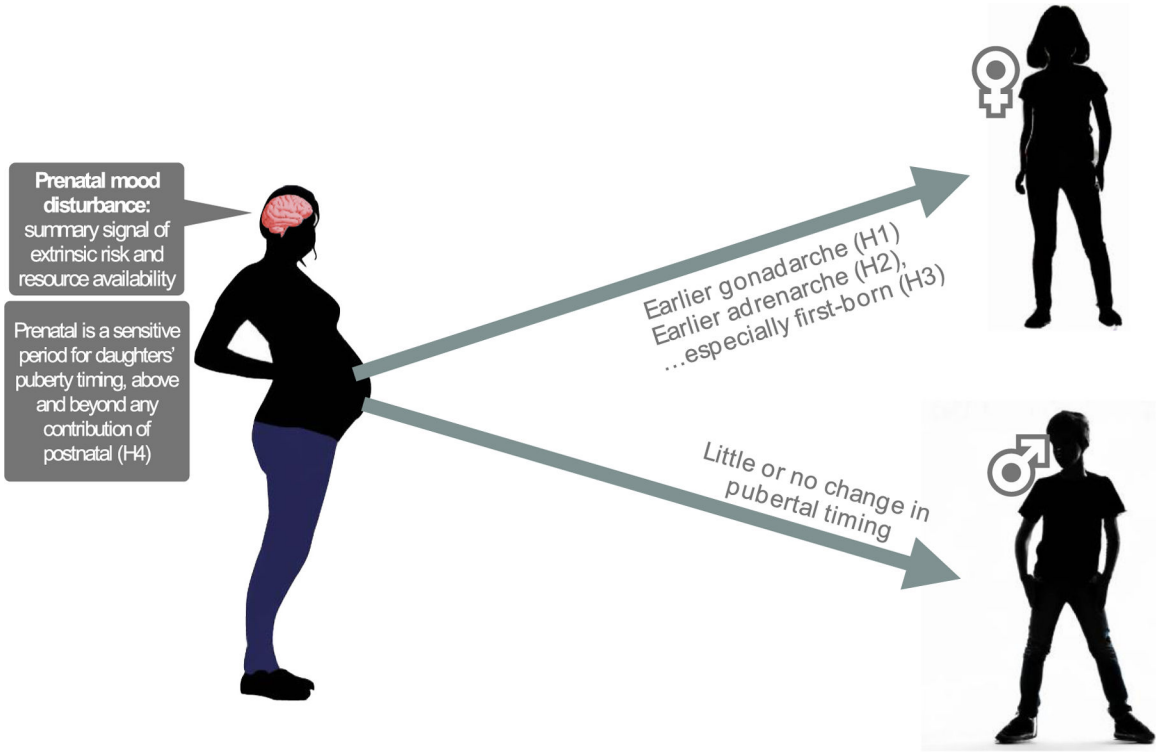

Fig. 1.

Conceptual diagram of hypotheses. We hypothesize that daughters' pubertal timing may be, partly, calibrated in response to their mothers' prenatal mood.

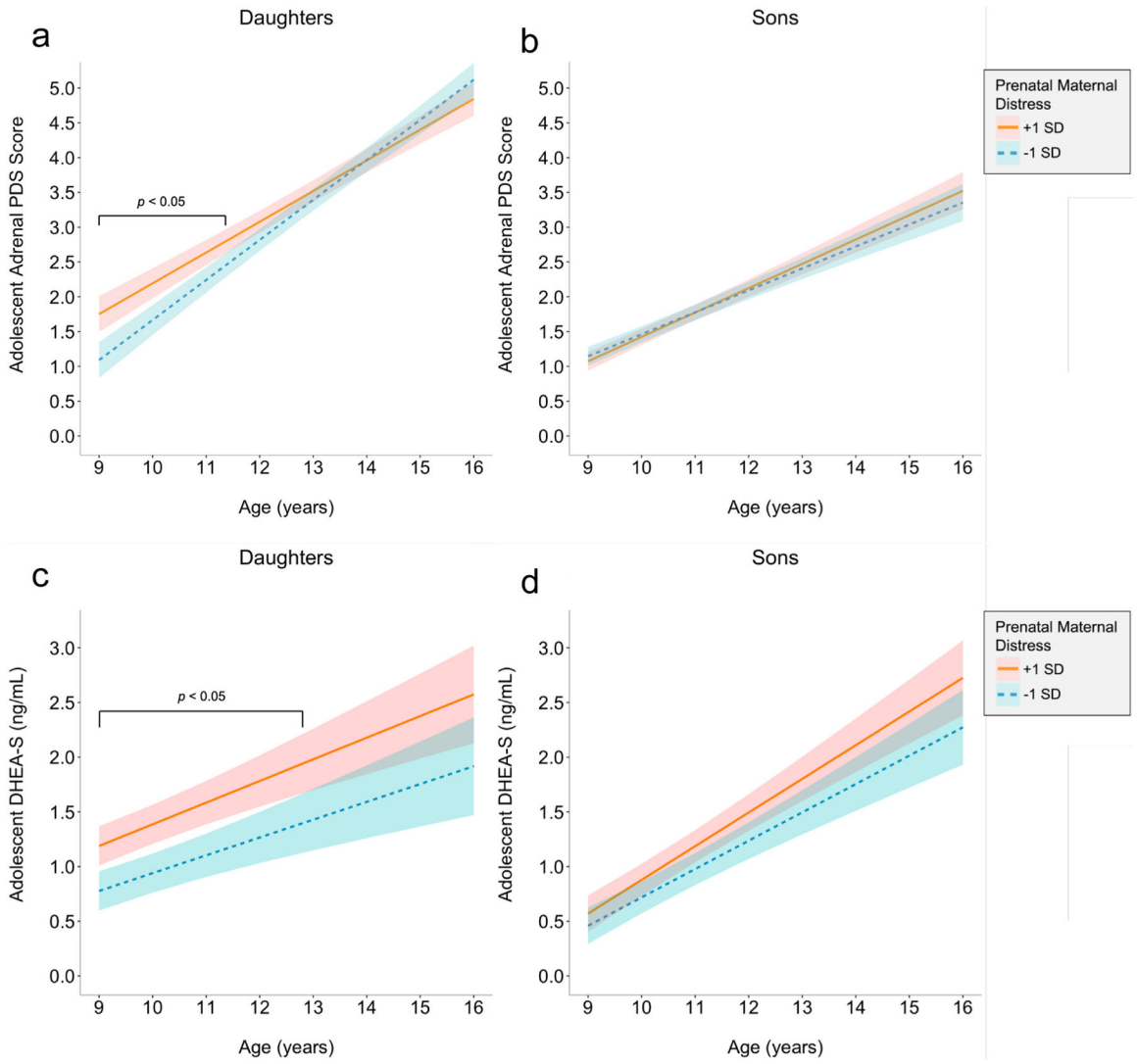

Fig. 2.

Association between prenatal distress and adrenal pubertal timing in daughters and sons. Here, although data were analyzed continuously, we plotted the adrenal puberty outcomes for girls and boys exposed to high and low levels of prenatal distress (at one standard deviation above and below the mean) for the purpose of visualization. In first-born girls, higher (compared to lower) levels of prenatal distress predicted more advanced adrenal PDS scores at the assessments occurring at ages 9 through 11 (panel a) and higher DHEA-S levels at ages 9 through 13 (panel c). No effect of prenatal distress on either adrenal pubertal outcome was observed for boys (panels b and d). Graphs show 95% confidence intervals and all models are statistically adjusted for maternal age at delivery, maternal education, and prenatal income-to-needs ratio (all z-scored).

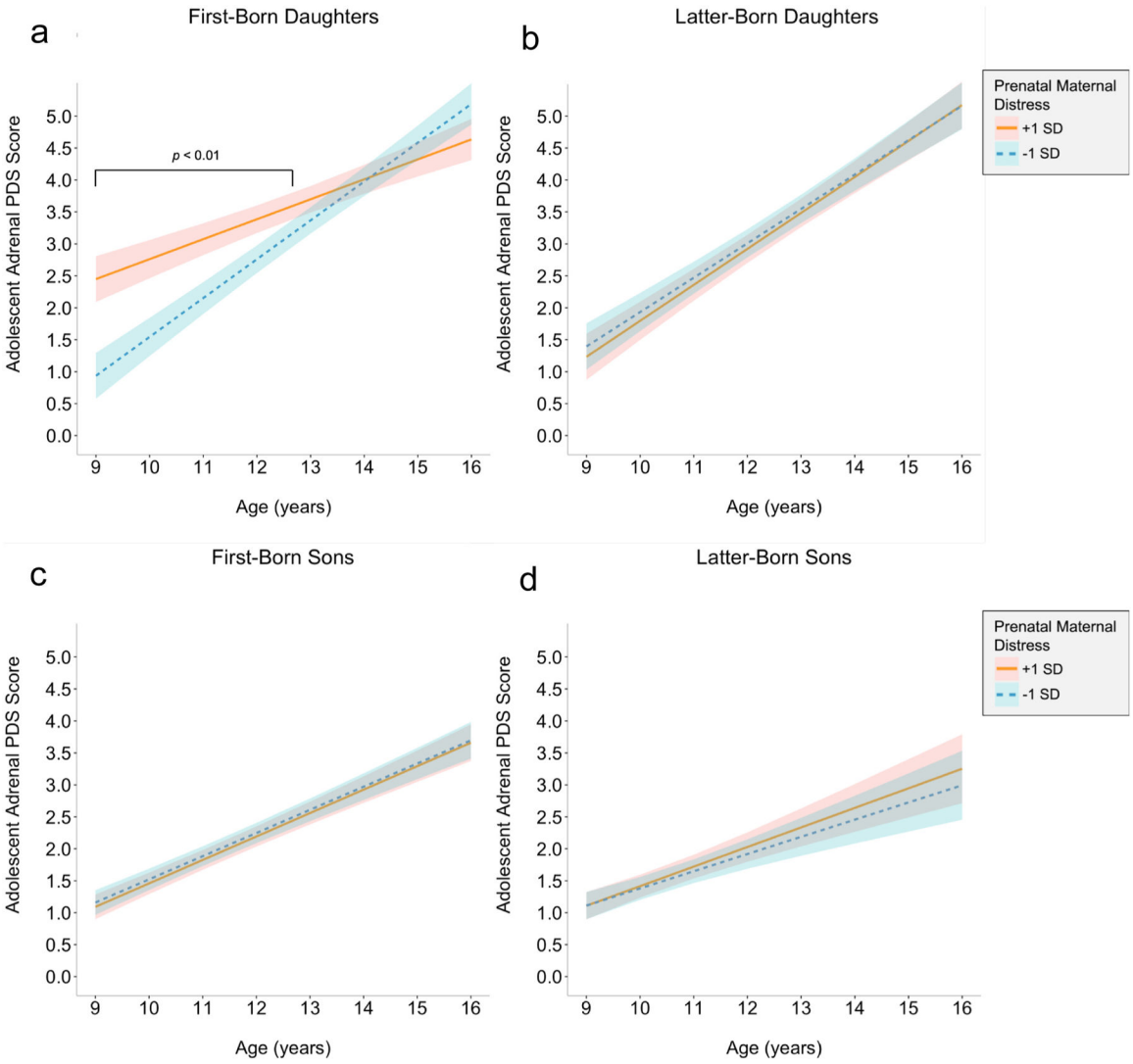

Fig. 3.

Interaction between prenatal distress and first-born status on adrenal pubertal timing in daughters and sons. Here, we plotted the adrenal Pubertal Development Scores (PDS) for first-born and latter-born children exposed to high and low levels of prenatal distress (at one standard deviation above and below the mean), dichotomized for the purpose of visualization. In first-born girls, higher (compared to lower) levels of prenatal distress predicted more advanced adrenal PDS scores at ages 9 through 12 (panel a), but no effect was found for latter-born girls (panel b). No effect of prenatal distress was observed for first-born or latter-born boys (panels c and d). Graphs show 95 % confidence intervals and all models are statistically adjusted for maternal age at delivery, maternal education, and prenatal income-to-needs ratio (all z-scored).

Table 1

Literature review of studies that assess how exposure to adversity during pregnancy and birth to age five years relates to pubertal timing.

Author and Year	Sample	Measure of Adversity	Measure(s) of Puberty	Adrenal	Gonadal	Aggregate	Results
Exposure to Adversity in Prenatal Period							
(Belsky et al., 2015)	73 girls	Maternal prenatal distress (maternal depression symptoms, marital conflict, and financial stress)	Salivary DHEA after social challenge at mean age of 7.3 years and categorized as preadrenarcheal or adrenarcheal; Tanner staging or maternal PDS at age 11 years	X			No detected relations between prenatal distress and adrenarche
(Brauner et al., 2021)	753 girls	Maternal prenatal stressful life events	AAM assessed at ages 8, 10, 14, 17 years		X		U-shaped relation between prenatal stressful life events and AAM. One exposure predicted ~4 months' earlier AAM while 2 or more exposures predicted ~2 months' earlier AAM.
(Duchesne et al., 2017)	31 girls	Natural disaster during prenatal period	AAM assessed at ages 13.5 and 15.5 years		X		Prenatal exposure to natural disaster predicted earlier AAM.
Exposure to Adversity from Age 0–5							
(Belsky et al., 2010a)	373 girls	Insecure mother-infant attachment at 15-months	AAM and physician physical examination of breast and pubic hair development at ages 9.5, 10.6, 11.6, 12.6, 13.6, 14.6, 15.6 years		X		Insecure mother-infant attachment predicted earlier initiation and completion of breast growth and pubic hair development and earlier AAM.
(Belsky et al., 2010b)	526 girls	Maternal harshness at age 4.5 years	AAM assessed at age 9.5 years and every year until age 15		X		Maternal harshness at 4.5 years predicted earlier AAM.
(Bleil et al., 2021)	426 girls	Composite of socio-economic status (SES; parental education attainment and family income-to-needs ratio), maternal sensitivity, mother–child attachment, and negative life events occurring between birth and age 4.5 years	AAM and physician physical examination of breast and pubic hair development at age 9.5 years and every year until 15.5		X		Higher SES directly predicted later AAM; secure mother-child attachment indirectly predicted later AAM via higher pre-pubertal BMI, and did not predict other puberty measures.
(DiLalla et al., 2021)	733 girls	Family context (divorce, SES, harsh parenting, warmth and cohesion, conflict) at ages 1–3 and 4–5 years	AAM and PDS at age 9 years and every year until age 15		X	X	Harsher home environment at age 4–5 predicted earlier AAM and puberty
(Ellis and Essex, 2007)	73 girls 47 boys	Family environment composite (parental depression, family negativity, marital conflict, parental insecurity, parental negativity, warmth/positivity, parenting style) averaged across ages 3.5 and 4.5 years	Salivary DHEA concentrations collected after social challenge at mean age of 7.3 years and categorized as pre-adrenarcheal or adrenarcheal; self-report pubic hair at age 11 years	X			Higher quality parental supportiveness (component derives from PCA) and less father-reported marital conflict/ depression were associated with later adrenarche.
(Ellis et al., 1999)	173 girls	Early family relationships (family stressors, SES, father absence, family life stress, quality of family relationships, family conflict, parent support, father support in childcare) at age 4–5 years	Subset of PDS items: occurrence of menarche, breast development, body hair at age 12–13 years			X	Fathers' presence, greater fathers' presence, greater supportiveness in the parental dyad, more father-daughter affection, and more mother-daughter affection each predicted later pubertal timing.

Author and Year	Sample	Measure of Adversity	Measure(s) of Puberty	Adrenal	Gonadal	Aggregate	Results
(Gaml-Sørensen et al., 2021)	8123 girls 7696 boys	Father absence (separation or had never lived together) during pregnancy, between ages 0–5 and ages 6–10 years	AAM and self-reported first ejaculation, breast, pubic hair, and axillary hair development, and acne at age 11 years and every 6 months until age 15			X	Father absence during pregnancy and early childhood were associated with earlier puberty in girls; father absence in pregnancy, early, and late childhood did not predict boys' pubertal status.
(Hartman et al., 2017)	659 girls 705 boys	Composite of maternal sensitivity, maternal harshness, unpredictability, and income harshness measured between birth and 4.5 years	AAM assessed at age 15 years		X		Environmental adversity indirectly predicted AAM via childhood health.
(James-Todd et al., 2010)	262 girls	SES (family income, paternal occupation, and education) measured at birth and age 7 years	AAM assessed at age 35–40 years		X		Reductions in SES from birth to age 7 years predicted earlier AAM.
(Johnson et al., 2018)	114 children	Random assignment to foster care or institutional care from ages 2–12 years	AAM and self-reported breast and pubic hair development at ages 12 and 14 years		X		Boys' gonadarche was later at age 12 years, not age 14, in the institutionalized group compared to foster care group.
(Mendle et al., 2016)	6273 girls	Maltreatment (including sexual and physical abuse, neglect, harshness, father absence) that occurred prior to age 6 years assessed at mean age 28.7 years	AAM assessed at ages 15.8 and 16.1 years; self-reported breast development and curviness at age 15.8 years		X		Only sexual abuse predicted earlier AAM and puberty gonadarche
(Reid et al., 2017)	165 girls 118 boys	Compared institutionalized youth who were adopted prior to age 5 years versus non-adopted	Nurse physical examination of breast development, pubic hair, genital development, and PDS across ages 7–14 years		X	X	No significant effects of adoption prior to age 5 years on puberty measures.
(Sung et al., 2016)	492 girls	Environmental harshness, unpredictability, infant-mother attachment from birth to 5 years	AAM assessed at age 9 years and every year until age 15		X		Exposure to harshness, but not unpredictability, predicted earlier AAM.
(Zhang et al., 2019)	45 datasets	Adverse Childhood Experience scale (ACEs)	Studies with AAM, Tanner staging scores, overall PDS, and relative puberty item *			X	Meta-analysis finds total ACEs are not associated with early pubertal timing; father absence, sexual abuse, and family dysfunction were associated with early puberty in girls.

Caption: Literature search was restricted to studies with a predictor of early-life adversity or stress that occurred prior to age 5 (the average age of commencement of adrenal puberty) and an outcome measure of pubertal development: gonadal, adrenal, or both.

* Relative puberty item compares perceived development to same-age peers: "How advanced is your physical development compared to other [girls/boys] your age?"

AAM = Age at Menarche, PDS = Pubertal Development Scale; DHEA = Dehydroepiandrosterone

Table 2

Cohort descriptive statistics.

Variable	*M* (*SD*)/ *N* (%)
Maternal age at delivery	30.49 (5.61)
Maternal education (years)	15.73 (2.39)
Primiparous	128 (49.8)
Prenatal income-to-needs ratio	451.17 (251.54)
Childhood income-to-needs ratio	418.32 (378.92)
Prenatal father absence	33 (12.94)
Childhood father absence	51 (18.82)
Maternal race/ethnicity	
Non-Hispanic/Latinx White	117 (45.35)
Hispanic/Latinx	74 (28.68)
Asian	28 (10.85)
Multi-ethnic/racial	24 (9.30)
African American/Black	14 (5.43)
Child birth weight (grams)	3440.38 (531.36)
Child gestational age at delivery (weeks)	39.28 (1.65)
Child sex at birth (female)	123 (47.7)
Child age at 8–10 year old assessment (years)	9.58 (0.72)
Child age at 11–12 year old assessment (years)	11.89 (0.86)
Child age at 13–16 year old assessment (years)	14.47 (1.29)

Caption: Continuous variables are described as mean and standard error. Categorical variables are described as *N* and percent of cohort. Total cohort is *N* = 253 mother-child dyads, but note that 10 dyads were missing childhood father absence and childhood income-to-needs ratio data. Maternal ethnicity, education, prenatal father absence, prenatal income-to-needs ratio, and primiparity were reported at 15 weeks' gestational age. Maternal age at delivery, child birth weight, and child gestational age at delivery were abstracted from medical records. Childhood father absence and childhood income-to-needs ratio were reported when children were 7–9 years old. "Primiparous" reflects mothers for whom the focal child in this study was their first live birth.

M=Mean; *SD*=standard deviation of the mean.

Psychoneuroendocrinology. Author manuscript; available in PMC 2025 February 06.

Table 3

Association between maternal prenatal psychological distress and adrenal and gonadal pubertal development.

Variable	Adrenal Pubertal Development				Gonadal Pubertal Development				
	Adrenal development		*DHEA-S*		*Gonadal development*		*Gonadal Hormones*		*Age of Menarche*
	Boys Coef. (95 % CI)	Girls Coef. (95 % CI)	Boys Coef. (95 % CI)	Girls Coef. (95 % CI)	Boys Coef. (95 % CI)	Girls Coef. (95 % CI)	Boys Testosterone Coef. (95 % CI)	Girls Estradiol Coef. (95 % CI)	Girls Only Coef. (95 % CI)
Intercept	1.44 * ** (1.32; 1.56)	1.93 * ** (1.73; 2.13)	0.80 * ** (.65;.94)	1.16 * ** (1.00; 1.33)	1.67 * ** (1.53; 1.81)	2.25 * ** (2.04; 2.46)	10.99 * ** (8.76; 13.21)	2.42 * * (2.12–2.72)	11.96 * ** (11.56; 12.37)
Time	0.33 * ** (.29;.38)	0.51 * ** (.45;.56)	.28 * ** (.23;.34)	.18 * ** (.11;.25)	0.38 * ** (.32;.44)	0.49 * ** (.44;.54)	5.46 * ** (3.96; 6.95)	0.23 * * (0.07)	n/a
Prenatal distress	−0.02 (−.13;.10)	0.26 * (.05;.48)	.08 (−.07;.23)	0.22 * (.05;.40)	0.05 (−.09;.18)	0.12 (−.11;.34)	−0.67 (−3.38; 2.04)	0.25 (−.07 to .59)	0.01 (−.47;.50)
Prenatal distress*Time	0.02 (−.03;.06)	−0.07 * (−.12; −.01)	0.02 (−.03;.08)	0.02 (−.05;.08)	0.01 (−.05;.06)	−0.04 (−.10;.02)	−0.06 (−1.87; 1.73)	−.007 (−.15 to .14)	n/a

Caption: Multilevel linear growth curve modeling was used for all analyses, except for age of menarche, in which linear regression was used. All multilevel models were centered at age 10, thus, intercept coefficients for prenatal distress represent differences in the outcome at age 10 as a function of prenatal distress (z-scored). Time is included in the model as child's age (in years) since age 10 (first child visit) and models the linear change in the outcome from age 10 until age 16 (the last adolescent visit). All coefficients are statistically adjusted for maternal age at delivery, education, and prenatal income-to-needs ratio. DHEA-S is dehydroepiandrosterone sulfate. p values < .05 = *; p < .01 = ** ; p < .001 = ** *