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Childhood adversity and pubertal timing: Understanding the origins of adulthood cardiovascular risk☆

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ABSTRACT

Objective: To determine whether greater childhood adversity relates to younger menarcheal age; whether younger menarcheal age relates to increased CVD risk; and whether greater childhood adversity relates to increased CVD risk, directly or indirectly (mediated by menarcheal age).
Methods: Among 650 pre-menopausal women (ages 25–45; $M = 34.9[5.6]$), SEM was performed to estimate relations between childhood adversity, menarcheal age, and CVD risk.
Results: Results supported a covariate-adjusted model (RMSEA = 0.035; CFI = 0.983) in which greater childhood adversity was related to younger menarcheal age ($\beta = -.13$, $p < .01$) and younger menarcheal age was related to greater CVD risk ($\beta = -.18$, $p < .05$). Direct and indirect effects of childhood adversity on CVD risk were non-significant. Re-evaluation of the same model with additional covariate-adjustment for adulthood body composition showed the relation between menarcheal age and CVD risk attenuated ($\beta = -.03$, $p = .376$).
Conclusions: Cross-sectional evidence suggests family-related adversity experiences in childhood confer risk for earlier menarche which, in turn, relates to increased CVD risk in adulthood, possibly via post-pubertal body size.

Associations between childhood adversity and earlier onset puberty have been reported in the developmental literature with an emphasis on the problematic psychosocial (e.g., depression, disordered eating behavior, increased substance use (Mendle et al., 2007)) and reproductive (e.g., earlier age at sexual debut, teenage pregnancy, increased risk for sexually-transmitted infections (Fisher et al., 1991; Deardorff et al., 2005; Dunbar et al., 2008)) outcomes that commonly occur among early-maturing adolescent girls. Separately, associations between earlier menarcheal age and increases in cardiovascular disease (CVD) risk factors, incident CVD-related events, CVD-specific mortality, and all-cause mortality have been reported in the epidemiological literature (Cooper et al., 1999; Frontini et al., 2003; Remsberg et al., 2005; Jacobsen et al., 2007, 2009; Feng et al., 2008; Kivimaki et al., 2008; Lakshman et al., 2009), suggesting such early-maturing girls may go on to suffer additional health problems in adolescence and adulthood. There is a paucity of research relating these literatures, however, limiting our ability to develop more comprehensive models by which links between childhood adversity, pubertal timing, and disease risk trajectories may be investigated. This gap is particularly notable given the modifiable nature of many of the psychosocial risk factors for earlier onset puberty that have been identified (e.g., negative parenting practices) which, if ameliorated, could plausibly improve the life-course trajectories of disease risk in vulnerable girls.

The timing and rate of progression of puberty, influenced both by genetic and environmental factors (Mustanski et al., 2004), is highly variable (Marshall and Tanner, 1969). Age at menarche, although occurring late in pubertal development, is a commonly used indicator of pubertal timing that has been shown to correlate ($r = .53$) with pubertal onset as measured by medical provider

Abbreviations: BMI, body mass index; CVD, cardiovascular disease; FES, Family Environment Scale; HDL, high density lipoprotein; LDL, low density lipoprotein; SEM, structural equation modeling; SES, socioeconomic status.

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reports of Tanner stages (Belsky et al., 2007), a well-established system for identifying stages of sexual maturation (Marshall and Tanner, 1969). In addition to childhood nutrition and body size (Ahmed et al., 2009), contextual factors reflecting childhood adversity experiences have also been shown to explain variability in pubertal timing. In longitudinal investigations, factors indexing problematic early environments such as marital conflict, father absence, negative parenting practices, parent–child relationship difficulties, lower socioeconomic status (SES), and fewer positive parenting/family interactions all predicted earlier onset puberty as well as younger menarcheal age (Moffitt et al., 1992; Wierson et al., 1993; Campbell and Udry, 1995; Graber et al., 1995; Ellis et al., 1999; Ellis and Garber, 2000; Belsky et al., 2007; Ellis and Essex, 2007; Saxbe and Repetti, 2009). Life history models have proposed that early life (ages 0–7) is a period of increased sensitivity to environmental cues which shape an adolescent girl's reproductive strategy, biasing her toward more accelerated reproductive development when the environment threatens her reproductive lifespan via signals that its resources (i.e., parental investment) are limited and/or unpredictably available (Belsky et al., 1991; Ellis, 2004).

In addition to associations with negative psychosocial and reproductive outcomes, earlier menarcheal age has been linked prospectively to more problematic CVD risk factor profiles in adolescence and in adulthood (Frontini et al., 2003; Remsberg et al., 2005; Feng et al., 2008; Kivimaki et al., 2008; Lakshman et al., 2009) as well as a worsening of these profiles over time (Frontini et al., 2003; Remsberg et al., 2005). A similar pattern has also been shown when CVD-related non-fatal and fatal incident events were examined. In Lakshman et al. (Lakshman et al., 2009), the prospective examination of 15,807 women over a median follow-up period of 10.6 years showed earlier menarcheal age predicted higher incident CVD, incident coronary heart disease, and all-cause mortality. In two large cohort studies, earlier menarcheal age was also related to risk for all-cause mortality (Jacobsen et al., 2007, 2009) as well as ischemic heart disease- and stroke-specific mortality (Jacobsen et al., 2009). To date, findings are mixed, however, with respect to whether obesity may account for observed relations between menarcheal age and CVD outcomes. For example, following statistical adjustment for indicators of body composition, studies have shown menarcheal age to continue to predict CVD risk (Cooper et al., 1999; Frontini et al., 2003; Remsberg et al., 2005), whereas in other studies, effects of earlier menarcheal age on CVD outcomes attenuated fully (Kivimaki et al., 2008) or partially (Jacobsen et al., 2009; Lakshman et al., 2009), leaving open questions regarding the mechanisms by which earlier menarcheal age and CVD risk are linked.

In the current study, we evaluated associations between childhood adversity, menarcheal age, and CVD risk in a multi-ethnic sample of 650 pre-menopausal women ages 25–45. First, we evaluated covariate-adjusted associations between individual markers of childhood adversity and menarcheal age as well as menarcheal age and individual markers of CVD risk. Next, we utilized a modeling framework to assess an integrated covariate-adjusted model in which associations between childhood adversity, menarcheal age, and CVD risk were estimated simultaneously. Specifically, a model was fit (1) to determine whether greater childhood adversity related to younger menarcheal age which, in turn, related to increased CVD risk; and (2) to determine whether childhood adversity related to CVD risk either directly or indirectly (mediated by menarcheal age). In addition, evaluation of the same model was repeated but included additional covariate-adjustment for waist circumference, waist-to-hip ratio (WHR), and body mass index (BMI) to determine whether the relation between menarcheal age and CVD risk (if observed) would persistent independently of statistical control for adulthood body composition. Childhood adversity was modeled as a latent construct using 5 indicators (family conflict, family expressiveness, family cohesion, family disruption events, and abuse events) derived from self-report questionnaires and CVD risk was modeled as a latent construct using 8 indicators (total cholesterol, total:high-density lipoprotein [HDL], HDL, low-density lipoprotein [LDL], triglycerides, glucose, insulin, and hypertension).

1. Methods

1.1. Participants

The current sample was derived from the Ovarian Aging (OVA) Study, an investigation of reproductive aging, including women belonging to Kaiser Permanente (KP) of Northern California, a large, integrated health care delivery system that provides medical care to approximately one third of the population of Northern California. Comparisons of the KP membership with the population of Northern California indicate that the KP membership is generally representative in its socio-demographic and health-related characteristics, particularly if the comparison is limited to those with health insurance (Gordon, 2006). Selection criteria for the OVA Study included that participants be between ages 25–45, have regular menses, and have their uterus and both ovaries intact. All participants self-identified as one of five race/ethnicities: white, African-American, Latina, Chinese, or Filipina and spoke/read English, Spanish, or Cantonese. Women were excluded if they reported a major medical illness, were on medications affecting the menstrual cycle within the 3 months prior to study participation, or were pregnant or breastfeeding.

The OVA Study protocol required women to participate in an in-person interview, trans-vaginal ultrasound, anthropometric assessment, and blood draw. Participants also completed a questionnaire packet of self-report measures that was added to the study protocol after its initiation. Of the 1019 women who completed the OVA Study, 879 women participated in the study in the timeframe in which the questionnaire packet was added to the study protocol. Of these women, 650 were retained for analysis in the current study. Of the 229 women who were excluded, 37 Filipina women were excluded due to their small numbers, 163 women were excluded because they did not return the questionnaire packet, and 29 women were excluded due to missing data on a variable of primary interest. The 29 women with missing data included 4 women who could not recall their age at menarche and 25 women missing information on a question pertaining to the educational attainment of their parents (10 did not have a mother or father-figure, 4 refused/did not know the information, and 11 left the question blank). The study protocol was approved by the University of California San Francisco Committee on Human Research as well as the KP of Northern California Institutional Review Board. Informed, written consent was obtained from all study participants.

1.2. Measures

Family environment. The Relationship subscales of the Family Environment Scale (FES) (Moos and Moos, 1994) were used to measure participants' perceptions of their family life during childhood. On a 5-point scale, response choices indicated the level of agreement ("strongly disagree" scored 1 to "strongly agree" scored 5) with each of 27 statements (Plomin et al., 1988). Items were then summed to produce three 9-item Relationship subscale scores for dimensions of Family Conflict, Family Expressiveness, and Family Cohesion. For the current study, scores were reversed so that higher values reflected more family conflict, less family expressiveness, and less family cohesion. Internal consistency (0.61–0.78) and test-retest (0.52–0.91) reliabilities for the FES are adequate (Moos and Moos, 1994) and validity of the FES is supported by studies showing the FES to discriminate between distressed and non-distressed families (Moos and Moos, 1994). In the current sample, internal consistency reliabilities for the relationship subscales of the FES were all high: conflict ($\alpha = 0.85$), expressiveness ($\alpha = 0.73$), and cohesion ($\alpha = 0.84$).

Stressful life events. The original Life Events Checklist (Tennant and Andrews, 1977) was adapted to include 26 items pertaining both to conventional life events (e.g., parental divorce) as well as traumatic life events (e.g., sexual abuse). For each item, participants indicated whether they experienced the event and their age(s) at the time the event occurred. For each of the 10 items relevant to early childhood, participants were assigned one point if they endorsed experiencing the event between the ages of birth to 7 years old. This timeframe was chosen to be consistent with life history theories suggesting this age range to be a time of increased sensitivity to environmental influences on pubertal timing (Belsky et al., 1991). Two subscale scores were computed reflecting dimensions of family disruption and abuse history. The family disruption subscale (score range = 0–7) consisted of 7 items pertaining to death of a parent/caregiver; separation or divorce of parents/caregivers; serious marital/relationship problems of parents/caregivers; witnessing physical fights between parents/caregivers; witnessing frequent arguments between parents/caregivers; living with a relative who has a serious drinking or drug problem; and living with a relative who has a psychiatric illness. The abuse history subscale (score range = 0–3) consisted of 3 items pertaining to physical abuse; sexual abuse; and severe neglect.

Menarcheal age. In a structured medical history interview, women were asked to report the age of their first menstrual period. The reliability of retrospective reports