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Authors

Beijers, Roseriet

Hartman, Sarah

Shalev, Idan

et al.

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Testing Three Hypotheses About Effects of Sensitive–Insensitive Parenting on Telomeres

Roseriet Beijers,
Radboud University and Radboud University Medical Center

Sarah Hartman,
University of California, Davis

Idan Shalev,
Penn State University

Waylon Hastings,
Penn State University

Brooke C. Mattern,
Penn State University

Carolina de Weerth,
Radboud University Medical Center

Jay Belsky
University of California, Davis

Abstract

Telomeres are the protective DNA-protein sequences appearing at the ends of chromosomes; they shorten with each cell division and are considered a biomarker of aging. Shorter telomere length and greater erosion have been associated with compromised physical and mental health and are hypothesized to be affected by early life stress. In the latter case, most work has relied on retrospective measures of early life stressors. The Dutch research (n = 193) presented herein tested 3 hypotheses prospectively regarding effects of sensitive–insensitive parenting during the first 2.5 years on telomere length at age 6, when first measured, and change over the following 4 years. It was predicted that (1) less sensitive parenting would predict shorter telomeres and greater erosion and that such effects would be most pronounced in children (2) exposed to prenatal stress and/or (3) who were highly negatively emotional as infants. Results revealed, only, that prenatal stress amplified parenting effects on telomere change—in a differential-susceptibility-related manner: Prenatally stressed children displayed more erosion when they experienced insensitive parenting

Correspondence concerning this article should be addressed to Roseriet Beijers, Department of Social Development, Behavioural Science Institute, Radboud University, Montesorrilaan 3, 6525 HR Nijmegen, the Netherlands., r.beijers@psych.ru.nl.
Roseriet Beijers, Department of Social Development, Behaioural Science Institute, Radboud University, and Department of Cognitive Neuroscience, Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Center; Sarah Hartman, Department of Human Development and Family Studies, University of California, Davis; Idan Shalev, Waylon Hastings, and Brooke C. Mattern, Department of Biobehavioral Health, Penn State University; Carolina de Weerth, Department of Cognitive Neuroscience, Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Center; Jay Belsky, Department of Human Development and Family Studies, University of California, Davis.

and less erosion when they experienced sensitive parenting. Mechanisms that might initiate greater postnatal plasticity as a result of prenatal stress are highlighted and future work outlined.

Keywords

telomeres; maternal caregiving quality; prenatal stress; infant negativity; differential susceptibility

Whereas there was a time when developmental scientists interested in early experience effects focused principally on psychological and behavioral development, widely appreciated today is that mind and body are interconnected, leading many scholars to ask questions about effects of early life experiences on physical health and biological functioning (e.g., Belsky, 2019; Belsky, Ruttle, Boyce, Armstrong, & Essex, 2015; Repetti, Taylor, & Seeman, 2002). Perhaps the best evidence of this comes in the form of longitudinal research inspired, at least in part, by the initially retrospective study of Adverse Childhood Experiences and their relation to several risk factors for premature death in later life (Chen, Turiano, Mroczek, & Miller, 2016; Felitti et al., 1998). The fact that extensive prospective evidence now links adversity in childhood and/or adolescence with compromised health later in life (e.g., Danese et al., 2009) has stimulated interest in physiological mechanisms that initiate—or biomarkers that might statistically mediate—these long-term effects. Telomeres, the focus of this article, are one such biomarker that is receiving increased attention.

Telomeres play a critical role in the maintenance of chromosomal integrity. They consist of repeated DNA sequences and proteins that cap and protect eukaryotic chromosomes. With each cell division, telomeres shorten, eventually reaching a critical length, which itself results in cellular senescence or apoptosis (Bojesen, 2013). With increasing age, then, telomeres shorten substantially, leading many to regard telomere length as a biomarker of cellular aging and as one of the hallmarks of aging (López-Otín, Blasco, Partridge, Serrano, & Kroemer, 2013). Telomere shortening appears to be accelerated by stress-inducing developmental experiences (Belsky, 2019; Belsky & Shalev, 2016; Monaghan, 2014), and this acceleration of telomeric loss is already observable in children after exposure to adversity (Coimbra, Carvalho, Moretti, Mello, & Belangero, 2017; Lang et al., 2019).

Moreover, extensive evidence in adults indicates that shorter telomeres are associated with greater mortality (e.g., Kimura et al., 2008; Rode, Nordestgaard, & Bojesen, 2015; Wang, Zhan, Pedersen, Fang, & Hägg, 2018), and morbidity, with the latter including psychological disorders, such as depression (e.g., Gillis et al., 2019; Lindqvist et al., 2015), as well as physical ones, such as cardiovascular disease, specific types of cancer and diabetes (e.g., Desai et al., 2018; D'Mello et al., 2015; Haycock et al., 2014; Ma et al., 2011; Smith et al., 2019; Wentzensen, Mirabello, Pfeiffer, & Savage, 2011). Even though effect sizes vary across outcomes (e.g., high: gastric cancer; moderate: diabetes; low: depression; see also Smith et al., 2019), an inferential case can be made that telomere length and shortening are important to study because they predict health risk in adulthood and may provide mechanistic understanding of the link between early adversity and poor mental and physical health in later life.

In light of these observations, the research presented herein tested three-interrelated hypotheses about the accelerating effect of adversity on telomere-indexed cellular aging, drawing on longitudinal data collected across the first decade of life: (1) greater exposure to insensitive caregiving among family reared children across the first 2.5 years of life will predict shorter telomeres at age 6 (when first measured) and greater telomere shortening across the next 4 years. (2) This accelerating effect of insensitive care will be most pronounced in the case of children exposed to prenatal stress and/or (3) those who are highly negatively emotional early in life. The empirical basis for each of these hypotheses is outlined in the following text.

Rather than predicting, in line with diathesis-stress thinking, that prenatal stress and infant temperament will function exclusively as additive "vulnerability" factors, amplifying susceptibility to the negative effects of postnatal contextual adversity (i.e., insensitive parenting), we predict that they will operate in a multiplicative differential-susceptibility-related manner. Thus, operating as more general "plasticity" factors, prenatal stress and infant negativity will make children especially susceptible to effects of both supportive and unsupportive care (Belsky & Pluess, 2009, 2013). Notably, we test this alternative-model prediction using a competitive and confirmatory model-testing approach developed for this very purpose (Belsky, Pluess, & Widaman, 2013; Belsky & Widaman, 2018; Widaman, Helm, Castro-Schilo, Pluess, Stallings, & Belsky, 2012).

Hypothesis 1: Effects of Adversity on Telomeres

Initial cross-sectional studies of telomeres linked their length to physical health (e.g., D'Mello et al., 2015, for meta-analysis of cardio-metabolic outcomes); and given emerging ideas about effects of adversity on health, it was not long before the relation between childhood adversity and the length of telomeres and their shortening emerged. Such an empirical focus was based on the proposition that telomere erosion might be a mechanism mediating effects of the early life adversity on later physical and mental health (Belsky & Shalev, 2016). Although it is clear that telomere length is substantially heritable, perhaps accounting for as much as 70% of the variance in telomere length (Broer et al., 2013; Hjelmborg et al., 2015), such estimates clearly leave room for environmental effects. In fact, despite substantial genetic influence on telomere length before birth, twin studies indicate that environmental factors are the dominant source of influence across the life span (Bakaysa et al., 2007), a finding consistent with a recent meta-analysis linking exposure to stress and adversity with shorter telomeres (Pepper, Bateson, & Nettle, 2018).

Although the exact mechanisms leading from stress to shorter telomere length are not well understood, stress can cause system-wide changes, including increased cortisol, proinflammatory cytokines and oxidative stress, that can permeate cells and affect telomere length (Borthakur, Butryee, Stacewicz-Sapuntzakis, & Bowen, 2008; Houtepen et al., 2016; Kroenke et al., 2011). In fact, early life adversity would appear to affect other biomarkers of accelerated aging, not just telomeres, including hormonal coupling of cortisol and testosterone, epigenetic methylation and perhaps even brain development (Belsky, 2019). Investigations of stressful life events in adulthood were first to document effects of stress on shorter telomere length (Epel et al., 2004; Schiavone, Colaianna, & Curtis, 2015). But those

most important to consider herein—given the focus of the current report on adversity in the first few years of life—come from studies showing that prenatal stress predicts shorter telomeres at birth (Entringer et al., 2013; Marchetto et al., 2016; Send et al., 2017); that prenatal tobacco exposure predicts shorter telomeres in children 4–14 years of age (Theall, McKasson, Mabile, Dunaway, & Drury, 2013a); that exposure to violence in middle childhood forecasts accelerated telomere erosion (Shalev et al., 2013; see also Drury et al., 2014); and that residence during childhood and adolescence in neighborhoods with high rates of domestic violence and violent crime also are associated with shorter telomeres during these developmental periods (Theall, Shirtcliff, Dismukes, Wallace, & Drury, 2017; see also Theall, Brett, Shirtcliff, Dunn, & Drury, 2013b).

Given theory and evidence that developmental plasticity—that is, susceptibility to environmental influences—is especially pronounced in the opening years of life, it is somewhat surprising that the experience of adversity during the infant and toddler years has not yet been examined in telomere research other than in (1) Wojcicki and associates (2016) recent pilot study linking greater exposure to sugar-sweetened beverages at age 2 years with shorter telomere length at this age and (2) in Drury and associates' (2012; see also Humphreys et al., 2016) work linking early life exposure to severe deprivation in the form of institutional care in Romania with shorter telomere length across middle childhood and adolescence. Although there are many reasons why institutional care early in life may accelerate cellular aging, the fact that such rearing environments are severely understaffed calls attention, as does so much other developmental research, to the role that insensitive, unresponsive, and neglectful caregiving may play in accounting for institutional-care effects on telomere length.

According to the early life stress model, the lack or loss of sensitive and responsive parental caregiving is among the most potent stressors early in life (Loman & Gunnar, 2010). What remains to be determined, then, is whether variation in the normal—not severely deprived—range of sensitive–insensitive care during a presumed highly sensitive period of life is related to telomere length and/or shortening. Theory and evidence suggest the rate of telomere shortening will be more pronounced in the opening years of life (Frenck, Blackburn, & Shannon, 1998; Rufer et al., 1999; Zeichner et al., 1999). We thus first test the proposition that insensitive caregiving among family reared children in the first 2.5 years of life will predict shorter telomeres at age 6, when first measured, and greater telomere erosion over the next 4 years of life (i.e., from age 6 to 10 years).

Hypotheses 2 and 3: The Amplifying Effect of Prenatal Stress and Infant Negativity

Extensive evidence indicates that prenatal stress is a risk factor for a variety of detrimental physical and mental health outcomes (for review, see Van den Bergh et al., 2017; Zijlmans, Riksen-Walraven, & de Weerth, 2015), with the same being true of heightened infant negative emotionality or difficult temperament (for review, see Rothbart & Bates, 2006; Zentner & Shiner, 2015). Although the former evidence suggests that prenatal stress disrupts "optimal" development, Belsky and Pluess (2009) advanced a radically different

interpretation. Based on research with human infants showing (1) that prenatal stress is associated with heightened negative emotionality and (2) that this phenotype is itself associated with increased susceptibility to both positive and negative developmental experiences and environmental exposures, they hypothesized that prenatal stress programs postnatal plasticity, making prenatally stressed infants especially susceptible to effects of both positive and negative rearing.

Most significant for the present article, then, is evidence linking prenatal stress with infant negative emotionality and the latter with enhanced developmental plasticity—in a manner consistent with differential susceptibility models of Person × Environment interaction (Belsky & Pluess, 2009). Consider, first, research showing that prenatal stress is linked to increased displays of sadness, frustration, and fear, as well as a stable disposition of (negative) emotional reactivity (Gartstein & Rothbart, 2003; Glover, 2011). Consider, too, that maternal psychological stress during pregnancy is also associated with increased behavioral reactivity of 4-month-old infants (Davis et al., 2004), higher levels of restless and disruptive temperament of 27-month-old children (Gutteling et al., 2005), and heightened inhibition and negative emotionality of 5-year-old children (Martin, Noyes, Wisenbaker, & Huttunen, 1999). Just as noteworthy is evidence that elevated levels of cortisol in pregnant women forecast greater infant negativity at 7 weeks (de Weerth, van Hees, & Buitelaar, 2003) and 2 months of age (Davis et al., 2007).

These findings linking prenatal stress—measured psychologically and physiologically—with heightened negative emotionality in young children become especially intriguing when juxtaposed to independent work showing that highly negatively emotional (and physiologically reactive) children are not only more adversely affected than others by negative environmental exposures (e.g., poverty) and developmental experiences (e.g., harsh parenting), as long appreciated (Rothbart & Bates, 2006) but also benefit more than others from supportive contextual conditions (e.g., sensitive-responsive parenting; Belsky & Pluess, 2009, 2013; Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2007). In fact, a recent meta-analysis of results of observational studies found that negative emotionality in infancy moderates effects of parenting in infancy on a range of child-adjustment outcomes (e.g., social competence, cognitive development; Slagt, Dubas, Deković, & van Aken, 2016) in just such a “for-better-and-for-worse,” differential-susceptibility-related manner (Belsky et al., 2007). Even more compelling, perhaps, are evaluations of experimental interventions showing that more negatively emotional children benefit more, sometimes exclusively, from such efforts than do other children (for review, see Belsky & Pluess, 2013). Especially notable may be a recent animal study which experimentally manipulated both prenatal-stress exposure and quality of postnatal rearing (via cross fostering), finding that variation in postnatal rearing conditions only affected prairie voles (*Microtus ochragaster*) that had been prenatally stressed (Hartman, Freeman, Bales, & Belsky, 2018)—and in a for-better-and-for-worse, differential-susceptibility-related manner (Belsky et al., 2007).

Collectively, the findings summarized in this subsection are the basis of our second and third predictions—that is that infants exposed to prenatal stress (2) or who show heightened negative emotionality in early infancy (3) are most likely to have shorter telomeres at age 6 years and/or greater telomere shortening from age 6 to 10 years if they experience

insensitive maternal care, but just the opposite (i.e., longer telomeres, less erosion) if they experience sensitive mothering. Evidence that characteristics of individuality can moderate environmental effects on telomeres in just such a manner can be found in recent gene–environment–interaction research. Mitchell and associates (2014) observed that a polygenic score based on serotonergic and, separately, dopaminergic "sensitizing" genotypes conditioned the effects of family disadvantage on the telomere lengths of 9-year-old boys growing up in high-risk communities—and in a differential-susceptibility-related manner. Greater family disadvantage predicted boys' shorter telomeres, whereas less disadvantage predicted longer telomeres, but only for those boys carrying more sensitizing genes. No such contextual effects on telomere length emerged in the case of children carrying few such genes. In seeking to extend such work, here we evaluate whether similar differential-susceptibility-related results emerge when the focus is on sensitive–insensitive mothering and the moderating effects of infant negativity and/or prenatal-stress exposure. Beyond the primary tests of our three hypotheses, we planned to evaluate whether any telomere measurement predicted in the course of testing the hypotheses would itself prove related to children's behavior at age 10 years and physical health from age 10 to 11 years.

Method

Participants

Participants were part of an ongoing prospective study in which mothers and children were followed from late pregnancy onward (see Beijers, Jansen, Riksen-Walraven, & de Weerth, 2010, 2011). Dutch participants were recruited through midwife practices in the cities of Nijmegen and Arnhem. Inclusion criteria were singleton pregnancy, no drug use during pregnancy, no current severe physical and/or mental health problems, and a clear understanding of the Dutch language. Of the 220 mother–infant dyads that enrolled in the study, eight were excluded for medical reasons (e.g., prematurity), and another 19 discontinued their involvement during the child's first 3 months of life for personal reasons (e.g., too busy). This resulted in a final analysis sample of 193 mothers and their infants (see Table 1 for sample descriptives). No measured demographic factors distinguished families that took part in the study and the 19 that dropped out. The ethical committee from the Faculty of Social Sciences of Radboud University approved the (Basal Influences on Baby Development - in Dutch: Basale Invloeden op de Baby Ontwikkeling [BIBO]) study (#ECG300107), and all mothers provided written informed consent.

Design

At 37 weeks of gestational age, mothers filled out questionnaires on general and pregnancy-specific stress and anxiety. During the infant's first years of life, maternal caregiving was observed three times, at ages 5 weeks, 12 months, and 30 months. At 3 and 6 months of age, infant temperament was assessed. Finally, telomere length was measured at 6 and 10 years.

Measures

Because of the desire to reduce the total number of analyses conducted, and thus the risk of chance findings (i.e., Type I errors), it was our a priori plan to create composite scores of the parenting predictor and the prenatal-stress and infant-negativity moderators. This strategy

was guided by two considerations: Epstein's (1980, 1983) classic analysis of the benefit of compositing measurements presumed to tap into the same construct, and cumulative-contextual-risk work underscoring the utility of such compositing even when indicators are not highly correlated (e.g., Evans, 2003; Evans & Kim, 2007; Liu, Shelton, Eldred-Skemp, Goldsmith, & Suglia, 2019). The chosen approach of "lumping" rather than "splitting" seemed especially sound as we lacked a strong basis for anticipating that a particular parenting measure at a particular age would be more predictive than any others, or that one prenatal-stress or negative-emotionality indicator would be a stronger moderator than any other.

Parenting: Quality of maternal caregiving—Two measures of maternal caregiving quality were obtained at three different times of measurement; each pair was averaged, then standardized, and then averaged across three time points to create a single grand composite of caregiving quality as long as no more than one measurement occasion was missing. If more than one measurement occasion was missing, the grand composite was not calculated for that specific individual and considered missing. Correlations among the measurement occasions range between .0 and .15.

During the 5-week home visit (M = 35 days, SD = 4 days), mothers were videotaped while bathing their infant (i.e., undressing, bathing, and dressing). Videotapes were rated by at least two independent observers for *maternal sensitivity* (i.e., the extent to which the mother timely and adequately responds to the infant's needs and signals) and *cooperation* (i.e., the extent to which the mother adjusts her behavior to the infant and does not interfere with the infant's ongoing activity) using nine-point rating scales (Ainsworth, Blehar, Waters, & Wall, 1978). Interobserver reliability (intraclass correlations) exceeded .90 for both constructs which were themselves highly and positively correlated (r = .83, p < .05). Of the mothers, 16.1% received averaged ratings of three or lower, reflecting low to inadequate care (Helmerhorst, Riksen-Walraven, Fukkink, Tavecchio, & Gevers Deynoot-Schaub, 2017).

During a visit to the lab at 12 months of age (M = 53 weeks and 6 days, SD = 19 days), mothers were instructed to play with their infants using four toys (e.g., puzzle, books, hand puppets), for 3 min each. The videotaped interactions were rated by at least two independent observers (using seven-point rating scales) for *supportive presence* (i.e., the extent to which the mother provides emotional support and confidence, intraclass coefficient [IC] = .95) and *respect for the child's autonomy* (i.e., the extent to which the mother respects the validity of the child's individuality, motives, and perspectives, IC = .70; Erickson, Sroufe, & Egeland, 1985). The two measures were highly and positively correlated (r = .61, p < .05). Of the mothers, 21.7% received averaged ratings of three or lower, indicating low to inadequate care (Helmerhorst et al., 2017).

During a home visit at 30 months of age (M = 30 months and 5 days, SD = 19 days), mothers were instructed to play with their children using three toys (e.g., puzzle, blocks), for 4 min each. The videotaped interactions were rated by at least two independent observers (using seven-point rating scales) for supportive presence (IC = .91) and respect for the child's autonomy (IC = .70; Erickson et al., 1985). The two constructs were moderately,

positively correlated ($r = .44$, $p < .05$). Of the mothers, 5.8% received averaged ratings of three or lower, indicating low to inadequate care (Helmerhorst et al., 2017).

Maternal prenatal psychosocial stress—Maternal psychosocial stress can be defined as demanding conditions, including stressful life events and antenatal anxiety, experienced by the mother that exceed her psychological and behavioral resources (Beijers, Buitelaar, & de Weerth, 2014). Expectant mothers were thus administered four questionnaires related to general, as well as pregnancy-related stress and anxiety. Resultant stress scores from each were standardized and then averaged to create a single grand composite when no more than one questionnaire was missing. Correlations among the questionnaires range from .09 to .36.

Daily hassles were measured using the 49-item Alledaagse Problemen Lijst (APL; Vingerhoets, Jeninga, & Menges, 1989). Each item describes one event. Mothers indicated whether each event had occurred in the last 2 months and, if so, rated how much it had bothered them on a four-point scale. A mean intensity rating was calculated by dividing the sum of these ratings by the number of reported events. Higher values reflect more negative experiences.

State anxiety was measured using the 20-item state subscale of the State–Trait Anxiety Inventory (Cronbach's $\alpha = .93$; Van der Ploeg, Defares, & Spielberger, 1981). Mothers rated how much each item applied to them at the current time on a 4-point scale. Higher values reflect higher anxiety.

Pregnancy-specific anxiety was measured using two subscales of the Pregnancy-Related Anxiety Questionnaire–Revised (Huizink, de Medina, Mulder, Visser, & Buitelaar, 2003). These subscales measure fear of giving birth (Cronbach's $\alpha = .70$) and fear of bearing a handicapped child (Cronbach's $\alpha = .83$). Items were rated on a five-point scale. Higher scores reflect higher levels of anxiety.

Pregnancy-specific daily hassles were measured using the 43-item Pregnancy Experience Scale (Cronbach's $\alpha = .87$; DiPietro, Ghera, Costigan, & Hawkins, 2004). Each item describes a pregnancy-specific experience (e.g., morning sickness). Mothers rated the degree to which each item resulted in a positive or negative experience on a four-point scale. The ratio of negative to positive experiences was calculated. Higher scores reflect a more negative emotional valence toward pregnancy.

Infant negative emotionality—To assess infant negative emotionality, mothers completed the Infant Behavior Questionnaire–Revised (191 items; Gartstein & Rothbart, 2003) when infants were 3 and 6 months of age. Negative affectivity at each age reflected the average of subscales assessing sadness, distress to limitations, fear, and falling reactivity (reversed; Cronbach's αs of .71 and .91, respectively). These age-specific average scores were then themselves averaged to create a single grand composite; if only one measurement was available, this was used. Correlation between the two measurements is .52.

Child telomere length and erosion—At 6 ($M = 6$ years and 20 days, $SD = 67$ days) and 10 years of age ($M = 10$ years and 19 days, $SD = 122$ days), buccal epithelial cells were

collected using buccal swabs. Due to ethical considerations associated with obtaining repeated blood samples from children, most studies have used saliva or buccal swabs instead of the peripheral blood cells. Notably, prior research indicates telomere length to be modestly to highly correlated across somatic tissues (Daniali et al., 2013; Friedrich, Griese, Schwab, Fritz, Thon, & Klotz, 2000; Gadalla, Cawthon, Giri, Alter, & Savage, 2010; Lin, Smith, Esteves, & Drury, 2019), and that stress-induced changes in telomere length can be detected in buccal cell DNA (Essex, Boyce, Hertzman, Lam, Armstrong, Neumann, & Kobor, 2013; Non et al., 2016; Shalev et al., 2013). DNA was extracted using QIAamp DNA Mini Kit (Qiagen, Hilden, Germany), and quantified using Quant-iT PicoGreen reagent (Thermo Fisher Scientific, Qiagen). DNA was stored at −80°C until telomere length assays.

Telomere length assays were performed using a quantitative PCR protocol adapted from Cawthon (2002). Briefly, telomere length is expressed as a ratio of telomeric content (T) to a single-copy housekeeping gene (S). The single copy gene used in the assay is *36B4*. Separate PCR reactions using DNA from the same sample were conducted to quantify telomeric DNA content and *36B4* content. The cycling profile consists of denaturing at 95°C for 15 s and annealing/extending at 60°C for 1 min followed by fluorescence reading, 45 cycles. The final reaction mix for the telomeric DNA contains 1x SYBR Green Master Mix (Qiagen, Hilden, Germany), 0.2U Uracil Glycosylase (Thermo Fisher Scientific, Qiagen), 0.1uM forward primer and 0.1uM reverse primer (Integrated DNA Technologies), and 3 ng DNA in a 20uL reaction. The reaction mix for *36B4* contains 1x SYBR Green Master Mix, 0.2U Uracil Glycosylase, 0.3uM forward primer, 0.5uM reverse primer, and 3 ng DNA in a 20uL reaction. The telomere primer sequences are as follows: forward primer 5′CGGTTTGTTTGGGTTTGGGT-TTGGGTTTGGGTTTGGGTT3′; reverse primer 5′GGCTTGCCTTACCCTTACCCTTAC-CCTTACCCTTACCCT3′. The *36B4* primer sequences are as follows: forward primer 5′CAGCAAGTGG-GAAGGTGTAATCC3′; reverse primer 5′CCCATTCTATCATCAACGGGTACAA3′. PCR amplifications used a robotic pipettor (QIAgility, Qiagen, Hilden, Germany) to ensure maximum pipetting accuracy, and real-time qPCR was performed with a unique rotary design machine for sensitive and accurate optical performance (Qiagen's Rotor-Gene Q, Qiagen, Hilden, Germany), which reduces well position effects.

The T/S ratio was calculated using the formula $\frac{T}{S} = \frac{2^{Ct36B4}}{2^{CtTelo}}$, where *Ct* is the cycle at which the sample crosses a critical threshold of detection for the *36B4* and telomere reactions respectively. The same threshold was used for all assays (*36B4* and telomere). Samples were run in triplicate and the mean *Ct* across replicates was used for calculating the T/S ratio. When the *Ct* of one replicate deviated from the mean *Ct* by more than 15% it was considered an outlier and the mean *Ct* was recalculated using two replicates.

To control for interassay variability, controls samples were run on each plate. Five control samples were run on plates for 6-year samples. To control for time-dependent batch effects, these same five controls, plus three additional controls, were run on plates for 10-year samples. For each plate, the Ct value of each control DNA was divided by the average *Ct* value for the same DNA across all runs to get a normalizing factor for that sample on a given plate. This was done for all controls to get an average normalizing factor for that plate. In

this manner the average intraassay coefficient of variation (CV) across all samples was less than 1% and the average interassay CV was 1.1%.

Missing Data

Of the 193 mothers and children comprising the analysis sample, the following data were missing: grand composite score maternal caregiving quality ($N = 0$), grand composite score prenatal psychosocial stress ($N = 19$), grand composite score infant negativity ($N = 2$), and buccal swabs for telomere length at ages 6 ($N = 46$) and 10 ($N = 33$). Missing value analysis showed that data were missing completely at random ($p = .370$). The expectation-maximization algorithm was used to impute missing values in the dataset, as described by Dempster, Laird, and Rubin (1977).

Statistical Analysis

Only one outlier of all measurements—defined as greater than three standard deviations above the mean—was detected, for telomere length at age 6; it was winsorized (i.e., replaced with $M + 3\ SD$). Measures of telomere length at age 6 and age 10 were each adjusted to control for variation in child age when buccal cells were collected. Specifically, we created the telomere length variables by using standardized residuals derived from regressing telomere length at age 6 and age 10 on the child's age (in months) when buccal cells were collected. Using these age-adjusted indices, we created a measure of telomere erosion by adjusting the residualized age-10 index of telomere length for its counterpart at age 6. In view of some prior evidence that telomere length and/or change varies by sex (Barrett & Richardson, 2011), body mass index (BMI; Gielen et al., 2018), and maternal age (Broer et al., 2013), we evaluated sex, BMI, and maternal age-at-delivery differences in all telomere measurements (i.e., length, erosion) prior to proceeding with the main analyses. Because none were discerned (see Table 1), we proceeded with analyses without consideration of child sex, BMI, and maternal age at delivery.

For the first of our three hypotheses (i.e., more insensitive parenting predicts shorter telomere length at age 6 and greater telomere erosion from 6 to 10 years of age), quality of caregiving was correlated with telomere length at age 6 and erosion from 6 to 10.

To test the second and third hypotheses, we used the competitive–confirmatory model-fitting approach developed by Widaman and colleagues (2012; Belsky & Pluess, 2013) to determine whether a Person × Environment interaction proved more consistent with differential susceptibility of diathesis stress models. This procedure was implemented to evaluate the interaction between (1) parenting and prenatal stress (Hypothesis 2) and (2) parenting and negative emotionality (Hypothesis 3).

The first step in the competitive and confirmatory model-testing approach involves a traditional and exploratory regression analysis which affords comparison of a main effects-only model with a model that includes main effects plus the interaction term. Only if the F ratio of the interaction term exceeds 1.0 does one proceed to confirmatory analyses (Belsky & Widaman, 2018), which evaluates the form of the interaction. This involves F comparison tests and consideration of Akaike information criterion (AIC; Akaike, 1987), the Bayesian information criterion (BIC; Schwartz, 1978), and variance explained using the R^2 statistic.

Under diathesis-stress theorizing, the predicted interaction should be ordinal in form. That is, in the most positive environments, all children should display similar telomere scores regardless of prenatal stress exposure or negative emotionality. But as the quality of parenting decreases, these scores should diverge due to differences in vulnerability to adversity. Specifically, putatively less-vulnerable children (i.e., little exposure to prenatal stress or low negative emotionality) should be relatively unaffected by the quality of mothering, whereas more vulnerable children (i.e., high negative emotionality or high exposure to prenatal stress) should exhibit shorter telomeres (at age 6) and/or greater telomere erosion over the next 4 years as maternal quality decreases. In consequence, the crossover point of the linear functions should fall at or be greater than the most positive value of sensitive parenting.

Differential susceptibility leads to a contrasting prediction regarding the form of the interaction (and thus the crossover point). Those children considered least developmentally plastic (for better and for worse)—namely, those not exposed to high levels of prenatal stress and/or scoring low in negative emotionality—should exhibit a weak or nonexistent effect of parenting, (as in the diathesis stress model). In contrast, those children considered most developmentally plastic—namely, those exposed to high levels of prenatal stress and/or scoring high on negative emotionality—should display greater telomere length and/or less erosion when sensitively reared and shorter telomeres and greater erosion when exposed to insensitive parenting. In consequence, the crossover point of the linear functions should be within the range of the parenting variable and, ideally, near its midpoint.

Notably, strong and weak versions of differential susceptibility and diathesis stress models can be distinguished and evaluated using the Widaman et al. (2012) method. In the case of strong models, some individuals (i.e., least susceptible) are totally unaffected by the contextual conditions under investigation (i.e., zero-order association between environmental predictor and developmental outcome), whereas in the case of weak models, the effect of the environmental predictor is greater for some than others, but all are affected.

The analytic plan also included a more exploratory-analysis phase: Should evidence from the primary analyses emerge in support of any of the three core hypotheses, secondary analyses would be conducted to determine which parenting quality predictor—measured at age 5 weeks, 12 months, and 30 months of infant age—contributed to the interaction effect involving the composite parenting index, and whether the predicted telomere outcome itself was related to children's behavior at age 10 years and physical health from age 10 to 11 years.

Results

Primary Analyses: Testing Three Hypotheses

Table 2 shows the correlations among the study variables. As expected, telomeres eroded significantly between age 6 and age 10 (M age 6 = 1.11, SD = .55; M age 10 = .61, SD = 33, p > .001). Independent samples t tests failed to document any significant sex differences in either of the telomere outcomes (i.e., length: p = .61; erosion: p = .58). Nor did any significant association emerge among BMI at age 6 and telomere length (r = −.09) or erosion

(r = .09) or among maternal age and telomere length (r = .06) or erosion (r = −.12). For these reasons, these potentially confounding factors were not included in the statistical analyses.

Hypothesis 1 was not confirmed because correlational analyses revealed that parenting quality did not predict telomere length at age 6 (r = .12, *ns*) or telomere erosion (r = −.02, *ns*). Regarding Hypotheses 2 and 3, the four initial regression analyses indicated that the F ratio of the interaction term only exceeded 1.0 for the interaction involving prenatal stress and parenting in predicting telomere erosion (see Model 2 in Table 3). Thus, we proceeded to confirmatory model testing only in the case of this specific interaction and telomere outcome.

Inspection of Table 3 reveals that although strong and weak differential-susceptibility models fit the data better than the strong and weak diathesis-stress models in terms of variance accounted for, the two differential-susceptibility models were indistinguishable with respect to this index. More informative, then, was the evidence indicating that the crossover point of the Prenatal Stress × Parenting interaction in predicting telomere erosion was within the range and toward the midpoint of the environmental predictor (c = 0.43, SE = 0.25), consistent with the differential-susceptibility model (see Figure 1). The fact that the strong differential-susceptibility model also had the lowest AIC and BIC values revealed it to be the best fitting model according to Widaman et al. (2012; Belsky et al., 2013) criteria. Notably, we also reexamined the form of the interaction using somewhat different criteria for distinguishing the two models advanced by Roisman et al. (2012). The fact that the proportion of the interaction was .71 and the proportion affected was .67 also proved consistent with differential susceptibility (Del Giudice, 2017).

Secondary Analyses

These results led us to undertake two secondary analyses. The first pertained to the components of the parenting composite and the second to the relation between the successfully predicted outcome, telomere erosion, and children's mental and physical health.

Decomposing the Composite Parenting Predictor

Given the primary interaction results, we investigated whether any of the components of our parenting composite was more or less responsible for the significant Prenatal Stress × Parenting interaction that predicted telomere erosion. This led to rerunning the same interaction to predict the same outcome three times, once for each of the parenting components. Results revealed interactions just like the one detected using the parenting composite in the case of both the 12- and 30-month parenting variable, but not for the 5-week one (see Tables S1 and S2 in the online supplemental material). Figures S1 and S2 in the online supplemental material display the two significant interactions, both of which, in concert with the Widaman et al. (2012) critieria (i.e., variance accounted for, BIC, and AIC values), proved most consistent with strong differential susceptibility.

Effects on Health and Behavior

Given evidence that prenatal stress moderated the effect of parenting on telomere erosion, it became of interest to determine whether telomere erosion itself predicted child behavior and

health. To evaluate the former, we relied on both parent- and child-reported problem behavior, measured via the Strengths and Difficulties Questionnaire (Goodman, 1997; Goodman, Lamping, & Ploubidis, 2010), at age 10 years. To assess physical health, mothers were queried, when the child was 11 years of age, about the child's health over the last year (i.e., from age 10 to 11), with illnesses classified following the International Classification of Primary Care (Lamberts & Wood, 1987; see also Beijers et al., 2010).

Simple correlation analysis revealed that although greater telomere erosion proved unrelated (r range = −.02–.08, ps > .244) internalizing and externalizing behavior measured at age 10, it did predict more general illnesses (including fever and chicken pox: $r = .15$, $p < .05$), even if not more digestive ones (including diarrhea and obstipation: $r = .05$, $p > .05$), respiratory (including having a cold and respiratory tract infections: $r = -.03$, $p > .05$), or skin illnesses (including eczema and impetigo: $r = -.08$, $p > .05$). Because of the little variation, the correlation between telomere erosion and antibiotic use was not tested.

Discussion

Empirical evidence pertaining to the developmental origins of health and disease stimulated us to examine effects of insensitive versus sensitive parenting in the first 2.5 years of life on telomere length at age 6, when first measured, and change over the following 4 years. Indeed, we set out to test three distinct hypotheses based on prior work linking a variety of adverse experiences and exposures with shorter telomeres or accelerated telomere erosion (e.g., Epel et al., 2004; Shalev et al., 2013) and nontelomere work indicating that children exposed to prenatal stress (Belsky & Pluess, 2009) or who are highly negatively emotional (Belsky & Pluess, 2009, 2013; Ellis, Boyce, Belsky, Bakermans-Kranenburg & van Ijzendorn, 2011) are especially susceptible to both positive and negative environmental influences. It was predicted that both telomere outcomes would be related to observed parenting, but that parenting effects would be most pronounced in the case of children exposed to prenatal stress (based on the prenatal programming of postnatal plasticity hypothesis) and that the same would be true of highly negatively emotional infants (based on the differential-susceptibility hypothesis).

Predicted Interactions

Perhaps somewhat surprisingly, we could discern no simple association between quality of parenting and telomere length at 6 years. Nor did we detect any evidence—in the case of the 6-year telomere outcome—that children who experienced prenatal stress (Hypothesis 2) or who were temperamentally highly negatively emotional (Hypothesis 3) were more susceptible to effects of parenting quality. Such null results could well have been due to the fact that children naturally vary in telomere length due to genetic factors (Broer et al., 2013) and effects of prenatal stress (e.g., Entringer et al., 2013)–and that such initial differences, if still evident at age 6, could thus obscure any potential rearing influence, should there be one. Of course, this explanation could not account for the failure of parenting quality—by itself or in interaction with infant negative emotionality—to predict telomere erosion because our adjustment of age-10 telomere length for age-6 length discounted any differences that may have existed at age 6.

It thus becomes especially notable that children exposed to greater prenatal stress proved more susceptible to effects of parenting quality when predicting telomere erosion, consistent with the claim that prenatal stress fosters postnatal plasticity (Hartman & Belsky, 2018a; Pluess & Belsky, 2011). This seemed especially so when parenting was measured later in infancy (12 months) and early childhood (30 months) rather than very early in postnatal life (5 weeks). Because we did not advance any hypotheses about these timing-related results, it will be important to see if they can be replicated before breathing too much meaning into them.

What would seem most important about the Prenatal Stress × Parenting findings in the prediction of telomere erosion is that they proved more in line with the differential-susceptibility than diathesis-stress models of Person × Environment interaction. Recall that it was not just that more insensitive rearing forecast accelerated telomere shortening, but that more sensitive rearing was also associated with less telomere erosion from age 6 to 10 (see Figure 1). There was even evidence that strong differential susceptibility characterized the interaction under consideration in that only children highly stressed prenatally appeared affected, for better and for worse, by their rearing experiences. Had those unstressed or just less-stressed children been affected to a significant extent by the care they received, but to a lesser degree than prenatally stressed children, evidence would have been more in line with the weak model of differential susceptibility (Belsky et al., 2013; Widaman et al., 2012).

Exactly why prenatally stressed infants should prove especially susceptible to rearing effects on telomere length remains to be determined. Elsewhere, we have highlighted several possible mechanisms that may contribute to enhanced postnatal plasticity in response to prenatal stress (Hartman & Belsky, 2018a). In short, prenatal stress involves, among others, a cascade of complex and diverse endocrine actions and stable epigenetic modifications, including changes in cortisol, serotonin, oxytocin, and vasopressin, that might affect fetal neural and physiological development and, in turn, several infant outcomes, including increased infant physiological reactivity of the hypothalamic–pituitary–adrenal (HPA) axis, and altered intestinal microbiota (Beijers et al., 2014; Hartman & Belsky, 2018a; de Weerth, 2017). There is even suggestive evidence that prenatal stress may influence postnatal plasticity by affecting the microbiome (Hartman & Belsky, 2018b). Notably, some of these factors are themselves thought to play a role in the postnatal regulation of telomere length and erosion (Belsky & Shalev, 2016). For example, several human studies document significant associations between stress-related HPA-axis indices and shorter telomere length, including research on children (e.g., Tomiyama et al., 2012; Kroenke et al., 2011). Future work should thus seek to extend the current inquiry by seeking to illuminate processes instantiating the prenatal-stress effects chronicled in this article.

Additional Findings

Beyond the primary foci of the research reported herein, the analyses provided additional information of potential interest. First, although the telomere erosion measure—itself predicted by the interaction of prenatal stress and parenting—did not predict problem behavior at age 10, nor digestive, respiratory or skin illnesses, greater telomere erosion from age 6 to 10 did forecast more general illnesses in the subsequent 1-year period. To our

knowledge, this is the first such finding to be reported using longitudinal data in childhood. It is important to note that causality cannot be assumed based on our research design and that the association might be bidirectional or a function of some unmeasured third variable. Telomeres that are shortened past a critical length become senescent and can exert harmful effects, including an increase in proinflammatory cytokines (Davalos, Coppe, Campisi, & Desprez, 2010). However, as our study did not include an earlier measure of health, it is also possible that inflammation due to illnesses triggers cell division, one known cause of telomere shortening (Zhang et al., 2016). Future prospective studies are needed to replicate our erosion-health finding and disentangle the direction of the association between these constructs. Regarding our failure to discern any relation between telomere erosion and problem behavior at age 10, it may take more time for telomere erosion to influence behavior later in life, should such effects exist. Thus, we encourage longer follow-up studies than we were able to implement. In any event, readers should recall that “the absence of evidence is not evidence of absence,” so simple acceptance of the null findings is inadvisable.

Also of note is that no sex differences in telomere length at age 6 or erosion from age 6 to age 10 emerged. As men tend to have shorter telomeres than females, indicating that male telomeres shorten faster (for reviews, see Barrett & Richardson, 2011; Gardner et al. (2014)), this raises some questions about these null results. To be appreciated, however, is that most work chronicling such sex differences has focused on adults; and the few studies at younger ages, especially at birth, present conflicting results (Barrett & Richardson, 2011; Gardner et al., 2014; Wojcicki et al., 2016). It seems notable that mechanisms proposed to account for sex differences in telomere length include differences in sex steroid hormones, which emerge during pubertal transition (Aviv, Shay, Christensen, & Wright, 2005; Barrett & Richardson, 2011; Patton & Viner, 2007).

Even though we failed to detect main effects of sex on telomere length or erosion, the possibility remains that sex might have further moderated the prenatal-stress interaction that emerged in this inquiry. Unfortunately, we were not well positioned to test this possibility, given limited power to detect a three-way interaction given our sample size. In consequence, we encourage future investigators working with larger samples to consider such empirical complexities.

Another finding of interest that should be highlighted was that greater negative emotionality in infancy proved related to shorter telomeres at age 6. To our knowledge, this is the first prospective, longitudinal study to chronicle such a link. Intriguingly, this could be an early reflection of the inverse relation documented at later ages between trait *neuroticism* (i.e., the tendency to experience negative emotions, especially when confronted with threat, frustration or loss) and shorter telomeres in adulthood (Brody, Yu, & Shalev, 2017; Conklin et al., 2018; Van Ockenburg, de Jonge, van der Harst, Ormel, & Rosmalen, 2014). It will be interesting to see future work replicate this unanticipated relation that links early temperament and telomere measurements.

Returning to the general issue of effects of early life conditions, including parenting, it will also be important to evaluate whether telomere length or erosion, considered by many to

index cellular aging (e.g., López-Otín et al., 2013), actually mediates such effects of stressful and adverse experiences, including insensitive parenting, on poor health later in life. Even if this proves to be the case, it will be important to remain sensitive to the limits of observational evidence, even if longitudinal in character. After all, telomeres could statistically mediate an early life-experience effect on health either because it plays a truly causal role in producing such effects or because it is correlated with another process that does so. It will thus take observational studies that measure multiple plausible mediators—like oxidative stress and inflammation, to name just two—in order to discount effects of such alternative explanatory factors before stronger causal inferences can be drawn about any true influence of telomeres on health. Clearly, then, the present inquiry represents only a single brick in a complex developmental edifice which requires a great deal more work before it is fully assembled.

Limitations

Our work was not without limitations, despite its substantial strengths, including reliance on composited measurements of prenatal stress parenting quality, and infant temperament, a focus on telomere erosion and not just length, and a reasonably sized, even if not very large, sample. The fact that we did not measure telomere length at birth is perhaps the major weakness of the current work, in that doing so would have allowed us to focus on telomere erosion across the first 6 years of life rather than trying to predict telomere length at age 6 without being able to take into account initial differences between children. Additionally, an added measure of telomere length at age 2.5 (at the end of the infancy period in which parenting quality was repeatedly observed) would have enabled us to shed light upon the question of whether early caregiving experiences lead to shorter telomere length at age 2.5 and/or ongoing declines in telomere length.

The fact that we had to rely on buccal cells when measuring telomere length raises the question of whether similar findings would emerge if other cell types were the source of telomere measurements (e.g., blood). This would seem especially important because the pathway from stress (or support) to buccal cell telomere length and erosion remains unclear; in contrast, in the case of immune cell telomere length (i.e., leukocytes), there exists a hypothesized pathway (via oxidative stress and inflammation, e.g., Borthakur et al., 2008; Houtepen et al., 2016; Kroenke et al., 2011). Nevertheless, previous studies suggest that the variance in telomere length shared between tissue types ranges between 50% and 80% (Daniali et al., 2013; Friedrich et al., 2000; Gadalla et al., 2010; Lin et al., 2019), raising the possibility that our results can be translated to telomere length in peripheral blood cells. Such a possibility should not be treated as an established fact. Nevertheless, it needs to be appreciated that even though the exact mechanisms leading from stress to shorter buccal telomere length remain unknown, stress can cause system-wide changes that can permeate to buccal mucosa cells, including increased cortisol, proinflammatory cytokines and oxidative stress (Borthakur et al., 2008; Houtepen et al., 2016; Kroenke et al., 2011). Apparently, stress-induced telomere length alterations are not restricted to the brain or blood; they can be detected in buccal cell DNA as well (Essex et al., 2013; Non et al., 2016; Shalev et al., 2013).

In view of evidence chronicling the stability of maternal sensitivity over even long periods of time (Dallaire & Weinraub, 2005; Else-Quest, Clark, & Tresch Owen, 2011; Hall, Hoffenkamp, Tooten, Braeken, Vingerhoets, & van Bakel, 2015), additional measures of parenting at age 6 and 10 would have enabled us to investigate the potential determinants of change in parenting quality from infancy through the first decade of childhood. Another limitation of our research was that we needed to rely on multiple imputation due to substantial missing data. Also, almost all mothers were highly educated and lived together with their partner. Whereas the prenatal stress and parenting quality variables showed considerable variability, with at least 20% of the mothers providing insensitive care at 12 months of infant age, one can question the generalizability of the findings. Indeed, we are forced to wonder whether effects would be larger in a less privileged and more at-risk sample. This includes, of course, the very interaction detected between prenatal stress and parental sensitivity. We are also led to wonder whether the timing of pregnancy-stress measurements might matter. After all, we only assessed prenatal stress at 37 weeks.

Conclusion

This study did not reveal a simple association between parenting quality and telomere length, nor provide support for the hypothesized moderation of such a parenting–telomere relation as a function of infant negative emotionality. Results indicated that prenatal stress amplified the association between insensitive parenting and telomeres in a manner consistent with differential susceptibility theorizing when change in telomere length was the focus of inquiry. Thus, the more insensitive parenting experienced by children exposed to prenatal stress, the more their telomeres shortened from age 6 to 10, with the reverse being true the more sensitive parenting proved to be; just as notably, no such relation between parenting and telomeres emerged for children not prenatally stressed. If future studies provide converging evidence, this body of research could encourage interventions to increase the quality of parenting to delay child telomere shortening, especially in mothers who suffered from prenatal stress. Should such results emerge, it would be critical to determine whether such slowing of cellular aging proved related to health later in life.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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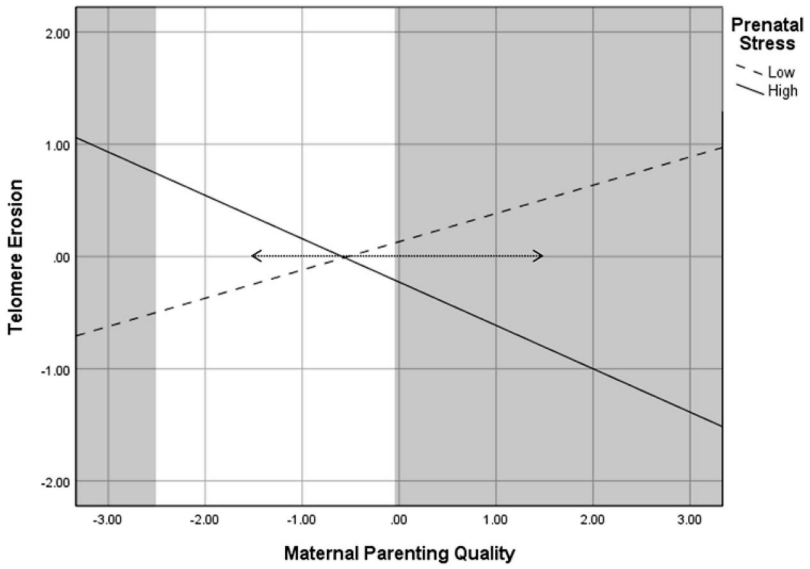

Figure 1.

Interaction between maternal parenting quality and prenatal stress (mean split) in predicting telomere erosion (erosion operationalized as [age-adjusted] telomere length at age 10 controlling for [age-adjusted] telomere length at age 6). For the prenatally stressed group, exposure to more parental sensitivity led to less telomere erosion while experiencing less parental sensitivity predicted greater telomere erosion (β = −.29, p = .01). For the low-prenatal-stress group, parental sensitivity did not significantly predict telomere erosion (β = .13, p = .19). Shaded areas represent the regions of significance for maternal parenting quality (−2.47, −0.12) with observed data ranging from −1.49 to 1.41 (see arrowed line).

Table 1

Descriptive Statistics

Characteristic	*M*	*SD*	Range
Infant birth weight	3616.97	465.32	2645.0–4730.0
Maternal age	32.46	3.79	21.1–42.9
Maternal marital status (wedlock or living together, %)	97.9		
Maternal educational level (%)			
Primary education	3.8		
Secondary education	20.4		
College/university	75.8		
Child sex (%)			
Girls	47.2		
Firstborn (%)	41.0		
Maternal caregiving quality			
At 5 weeks of age	5.49	2.06	1.0–9.0
At 12 months of age	4.33	1.29	1.0–7.0
At 30 months of age	5.29	.70	3.0–6.5
Prenatal stress			
Daily hassles	1.14	.46	0–2.5
State anxiety	32.16	8.88	20.0–64.0
Fear of giving birth	5.36	2.48	3.0–15.0
Fear of bearing a handicapped child	8.53	2.80	4.0–18.0
Pregnancy-specific daily hassles	.33	.23	.0–1.4
Infant negative emotionality			
At 3 months	2.55	.57	1.38–4.67
At 6 months	2.48	.53	1.33–4.19

Table 2

Correlations Among the Study Variables

Variable	Maternal caregiving quality	Prenatal stress	Infant negative emotionality	Telomere length age 6[a]	Telomere erosion[b]
Maternal caregiving quality	—				
Prenatal stress	−.08	—			
Infant negativity	−.14*	.18*	—		
Telomere length age 6[a]	.12	−.07	−.16*	—	
Telomere erosion[b]	−.02	−.14	.05	.00	—

[a]Telomere length adjusted for actual age at buccal-swab collection.

[b]Erosion operationalized as (age-adjusted) telomere length at age 10, controlling for (age-adjusted) telomere length at age 6.

*$p = .05$.

Table 3

Results of Alternate Regression Models for Parenting and Prenatal Stress Predicting Telomere Erosion

Standard parameterization			Reparameterized regression equation				
				Differential susceptibility		Diathesis–Stress	
Parameter	Main effects: Model 1	Main effects and interaction: Model 2	Parameter	Strong: Model 3A	Weak: Model 3B	Strong: Model 3C	Weak: Model 3D[a]
Intercept (B_0)	−.00 (.07)	−.02 (.07)	B_0	−.02 (.07)	−.02 (.09)	.00 (.07)	−.07 (.19)
Parental sensitivity (B_1)	−.06 (.12)	−.00 (.12)	B_1	0 (–)	−.00 (.12)	0 (–)	−.05 (.13)
Prenatal stress (B_2)	−.24 (.12)	−.25 (.12)	C	−.43 (.25)	−.43 (.25)	1.41 (–)	1.41 (–)
Parental Sensitivity × Prenatal Stress (B_3)		−.58 (.20)	B_3	−.57 (.20)	−.57 (.20)	.05 (.08)	.06 (.08)
R^2	.02	.06	R^2	.062	.062	.003	.003
F	2.02	4.14	*F*	6.24	4.14	.48	.32
df	2,190	3,189	*df*	2,190	3,189	1,191	2,190
p	.14	.007	*p*	.002	.007	.49	.73
F vs. 1		8.163	*F* vs. 3B	.83		5.82	11.63
df		1,189	*df*	1,189		2,190	1,189
p		.005	*p*	.36		.02	.00
			AIC	538	541	548	550
			BIC	552	557	558	563

Note. Values in the table are parameter estimates, with standard errors in parentheses (except if the parameter is fixed). *F* vs. 1 = *F* test of the difference in R^2 for Model 2 versus that for Model 1; *F* vs. 3B = *F* tests of the difference in R^2 for a given model versus that for Model 3B; AIC = Akaike information criterion; BIC = Bayesian information criterion.

[a]Erosion was operationalized as (age-adjusted) telomere length at age 10, controlling for (age-adjusted) telomere length at age 6.