Psychoneuroendocrinology 88 (2018) 38–46

Contents lists available at ScienceDirect

Psychoneuroendocrinology

journal homepage: www.elsevier.com/locate/psyneuen

Infant HPA axis as a potential mechanism linking maternal mental health and infant telomere length☆

Benjamin W. Nelson[a,*], Nicholas B. Allen[a], Heidemarie Laurent[a,b]

[a] Department of Psychology, University of Oregon, Eugene, OR, USA
[b] Department of Psychology, University of Illinois Urbana-Champaign, Champaign, IL, USA

ARTICLE INFO

Keywords:
Cortisol
Depressive symptoms
Infant
Maternal mental health
Mindfulness
Telomere

ABSTRACT

Maternal depression has been suggested to be an independent risk factor for both dysregulated hypothalamic-pituitary-adrenal axis (HPA) functioning and shorter telomere length in offspring. In contrast, research suggests that individual differences in mindfulness may act as a protective factor against one's own telomere degradation. Currently, research has yet to investigate the association between longitudinal changes in maternal mental health (depressive symptoms and mindfulness) and salivary infant telomere length, and whether such changes might be mediated by alterations in infant cortisol response. In 48 mother-infant dyads, we investigated whether the changes in maternal mental health, when infants were 6–12 months of age, predicted change in infant cortisol reactivity and recovery over this period. We also investigated whether these changes in infant HPA functioning predicted subsequent infant salivary telomere length at 18 months of age. Furthermore, we investigated whether change in infant HPA functioning provided a potential pathway between changes in maternal mental health factors and infant salivary telomere length. Analyses revealed that increases in maternal depressive symptoms over that six-month period indirectly related to subsequent shorter infant telomere length through increased infant cortisol reactivity. Implications for the ways in which maternal mental health can impact offspring stress mechanisms related to aging and disease trajectories are discussed.

1. Introduction

Shorter telomere length (TL) is associated with early life stress and negative health trajectories across the lifespan (Drury et al., 2012; Shalev, 2012; Shalev et al., 2013). Therefore, it is important to identify early life factors that are associated with TL to better understand the emergence of divergent health trajectories. Indeed, the mechanistic origins of adult disease and psychopathology can often be traced back to early developmental disturbances that are both psychological and biological in nature (Shonkoff et al., 2009). Research has begun to elucidate how maternal mental health and offspring hypothalamic-pituitary-adrenal axis (HPA) stress response are independently associated with adolescent offspring TL (Gotlib et al., 2015). Importantly, questions remain as to when these divergent health trajectories begin, as well as the etiological pathways that mediate the effects of maternal mental health factors on the biological aging of infants in early life.

Telomeres are repeated nucleotide sequences (TTAGGG) at the end of eukaryotic chromosomes that protect chromosomes from deterioration and enable cellular integrity (Blackburn and Epel, 2012). During somatic cell division DNA polymerase is not able to fully replicate the 3′ end of linear DNA resulting in a progressive loss of telomeric repeats (Blackburn, 1991). TL is affected by age and genetics, indicating that telomere length is a "biological clock", which is also influenced by environmental factors, such as cumulative exposure to lifetime stressors (Aviv, 2008; Olovnikov, 1996). Shorter TL is associated with stressful life events, as well as a range of negative health outcomes (i.e., cardiovascular disease, dementia, diabetes, cancer, obesity, and early mortality; see Blackburn and Epel, 2012), while longer TL length is associated with both positive social relationships (Uchino et al., 2012) and mindfulness (Blackburn and Epel, 2012; Hoge et al., 2013; Jacobs et al., 2011). Cortisol, the end product of neuroendocrine activation, has been proposed to be one mechanism that is associated with TL and cell senescence (Shalev, 2012) as research has demonstrated that human T lymphocytes exposed to cortisol show reduced telomerase, the enzyme responsible for telomere maintenance (Choi et al., 2008), and reduced TL (Vartak et al., 2014). In addition,

Abbreviations: BMI, body mass index; CES-D, center for epidemiological studies of depression scale; HPA axis, hypothalamic pituitary adrenal axis; SES, socioeconomic status; TL, telomere length

☆ Open Science Framework Citation: osf.io/rc824

* Corresponding author: Department of Psychology, 1227 University of Oregon, Eugene, OR, 97403, USA.
E-mail address: bwn@uoregon.edu (B.W. Nelson).

https://doi.org/10.1016/j.psyneuen.2017.11.008
Received 10 June 2017; Received in revised form 13 October 2017; Accepted 15 November 2017

greater cortisol response to a laboratory stressor in young children (Kroenke et al., 2011) and adults (Tomiyama et al., 2012) is associated with shorter TL. Furthermore, adolescents of depressed mothers show both greater cortisol reactivity and shorter TL (Gotlib et al., 2015). Telomeres thus represent an important biomarker for the study of health risk and resilience processes.

1.1. Maternal mental health and infant stress response

Early relationships have implications for health outcomes across the lifespan (Shonkoff et al., 2009). Maternal psychological characteristics can serve as risk or protective factors for infant outcomes. For example, in terms of risk factors, maternal stress during pregnancy is associated with shorter infant TL (Send et al., 2017) and infants of depressed mothers tend to have greater cortisol reactivity to stress (Azar et al., 2007; Brennan et al., 2008). Furthermore, it is important to study changes across time in maternal mental health during infancy as these patterns have differential associations with infant cortisol response dynamics over the first 18 months of life (Laurent et al., 2011). Similarly, it is important to study changes in infant cortisol responses over time as research has shown that from 2 to 15 months of age infants tend to dampen their HPA responses to stressors even though they may show signs of behavioral distress (Gunnar et al., 1996). On the protective side, individual differences in mindfulness, the psychological capacity to maintain nonjudgmental awareness of the present moment (Kabat-Zinn and Hanh, 1990), may help with regulating one's own and one's infant's stress. For example, women with greater levels of dispositional mindfulness tend to have more flexible HPA axis responses (i.e., quicker post-stress cortisol recovery; see Laurent et al., 2015), and mindfulness in the parenting relationship predicts both quicker maternal cortisol recovery and lower infant cortisol levels during stress (Laurent et al., 2017). Therefore, maternal depressive symptoms and mindfulness may be hypothesized as risk and protective factors, respectively, that influence infant stress responses – with risk factors increasing cortisol reactivity and slowing recovery, and protective factors lowering cortisol reactivity and quickening recovery. Research has yet to fully elucidate how maternal mental health impacts not only the stress response of their infants, but also their infant's biological aging as reflected in TL.

1.2. HPA axis and telomere length

Research indicates that oxidative stress via dysregulated HPA axis activation may be one mechanism that connects the exposure to early life stress and later TL (Shalev, 2012). Indeed, as mentioned above, T lymphocyte exposure to cortisol is associated with reduced activity of telomerase, an enzyme responsible for maintaining TL (Choi et al., 2008), and reduced TL (Vartak et al., 2014). Research further demonstrates independent associations between early life stress and increased cortisol reactivity in infants of depressed mothers (Azar et al., 2007; Brennan et al., 2008) and shortened TL (Drury et al., 2012; Price et al., 2013). This trend seems to persist into adolescence as healthy adolescent offspring of mothers with recurrent episodes of depression are at increased risk for altered HPA axis response to stress (i.e., greater cortisol reactivity) and shorter TL (Gotlib et al., 2015). However, research has yet to investigate these connections in an infant sample and investigate whether changes in infant HPA axis activity mediate the relationship between changes in maternal mental health and later infant TL. In other words, the conceptual model of maternal depressive symptoms acting as a stressor to influence infant cortisol response, which subsequently impacts infant TL has yet to be tested.

1.3. Current study

The current study investigated whether changes in maternal mental health predict changes in infant cortisol reactivity and recovery between 6 months and 12 months of age. Moreover, we investigated whether these patterns of cortisol reactivity and recovery mediated the relationship between changes in maternal mental health (depressive symptoms and mindfulness) during this time and subsequent infant TL at 18 months of age. First, we predicted that increased maternal depressive symptoms and decreased dispositional mindfulness would be associated with increased cortisol reactivity and incomplete cortisol recovery (i.e., greater return of cortisol to baseline levels after stress exposure) in infants. Second, we hypothesized that increased infant cortisol reactivity would predict shorter TL, while more complete infant cortisol recovery would predict longer TL. Finally, we hypothesized that change in maternal depressive symptoms and/or mindfulness would indirectly relate to subsequent infant TL due to change in infant cortisol response. In particular, mothers that showed increased depressive symptoms and/or decreased mindfulness from 6 to 12 months would have infants with increased cortisol reactivity and impaired cortisol recovery, and shorter telomeres at 18 months. This study was pre-registered with Open Science Framework (osf.io/rc824).

2. Methods and materials

2.1. Participants and recruitment

Mothers were recruited from the Women Infants Children program and other community agencies serving low-income families in a mid-sized city in the pacific northwest of the United States. To be eligible, mothers had to speak English, have a $\ll$ 12-week-old infant, and anticipate remaining in the area until this target child was 18 months old. Table 1 gives demographic information about the sample at the first assessment.

Of the 91 mother-infant dyads who began the study at time 1, 48 dyads (53%) participated at all four assessment times and provided a saliva samples for telomere assay, resulting in the final sample size. Compared to non-completers, study completers tended to be older (M = 28.40 vs. 25.38, F[1,88] = 7.44, p = 0.01), in a longer-term romantic relationship (M = 3.11 years, SD = 0.88 vs. 2.19 years, SD = 0.60 F[1,38] = 15.09, $p \ll 0.001$), have more biological children (M = 2.94, SD = 0.93 vs. M = 2.55, SD = 0.83), and reported higher household income, $\chi^2(7) = 14.36$, p = 0.045. There were no differences in infant sex, racial/ethnic group identification, likelihood of being in a relationship with the target child's biological father or degree of contact with the father, education, or employment status. Of the mental health-related variables reported at time 1, the only difference that emerged was for current depressive symptoms (M = 7.68 for completers vs. 11.70 for non-completers, F(1, 86) = 5.33, p = 0.02), indicating that mothers that experienced the highest levels of depressive symptoms may have been lost in this study due to attrition. As discussed in the limitations section, this unfortunately restricts the range of depressive symptomatology in our sample to a largely non-clinical range (CES-D at T2 mean = 8.83, SD = 6.75; CES-D at T3 mean = 10.47, SD = 7.55).

2.2. Procedure

Prior to study participation, mothers gave written informed consent to all study procedures, which had been approved by the University of Oregon Institutional Review Board. Mothers completed study assessments at four times postnatally: time 1 (T1) at 3 months, time 2 (T2) at 6 months, time 3 (T3) at 12 months, and time 4 (T4) at 18 months. The rate of participation, measures collected, infant age and sex, and maternal age at each wave are outlined in Fig. 1.

At T1, participants completed a home visit that involved a diagnostic interview, and at times 2–4 participants completed laboratory sessions with their infant. Each laboratory session included a developmentally appropriate interpersonal stressor involving maternal unavailability and/or confrontation with a strange adult.

At T2, the Still Face Experiment was used, which is a procedure