Chapter 4

STRESS AND HYPOTHALAMIC–PITUITARY–ADRENAL AXIS ACTIVITY IN ADOLESCENCE AND EARLY ADULTHOOD

Emma K. Adam, Sarah Collier Villaume, Sara Thomas, Leah D. Doane, and Kathryn Grant

As early as 1904, psychologists studying adolescent development referred to it as "a period of storm and stress" (Hall, 1904). There has since been considerable critique of stress as the defining feature of adolescence, and recently researchers have focused on the many assets of adolescents and the opportunities of this developmental period (National Academies of Sciences, Engineering, and Medicine, 2019). The experience and consequences of stress do, however, represent important features of adolescence, as well as early adulthood. While complete coverage of the extensive literature on adolescent and young adult stress is not possible, we address some central questions. Why are adolescence and early adulthood stressful periods of life? Are they more stressful now than in the past? How do we best define and measure adolescent and young adult stress? What are some key sources of stress during these developmental periods? What are the major biological stress response systems of the body, and how are they impacted by stress and normative developmental change? What are the implications of stress, and biological stress responses, for adolescent and young adult health and developmental outcomes? What factors moderate the impact of stressors on stress biology and youth outcomes? How might this knowledge be leveraged by interventions to reduce adolescent and young adult stress and its impacts? While other biological stress processes are introduced, the chapter focuses on the hypothalamic–pituitary–adrenal (HPA) axis, one of the body's key stress response systems, due to its known implications for health and developmental outcomes.

ADOLESCENCE AND EARLY ADULTHOOD AS PERIODS OF CHANGE AND STRESS

The existence of widespread and co-occurring changes across adolescence and early adulthood creates a period of life that is (on average) subject to heightened stress, higher than that experienced in middle-aged and older adults (American Psychological Association, 2019, 2020). The changes of adolescence and early adulthood occur in biological, cognitive, social, and contextual domains. These changes are summarized in detail throughout the other chapters of this handbook. They include the dramatic biological changes of puberty that occur in early- to midadolescence, including changes in physical characteristics and hormonal systems, and changes in brain development that occur across adolescence and into early adulthood. There are also notable changes in circadian rhythms and sleep, with adolescents shifting to a more "owl-like" circadian rhythm that predisposes them to later bedtimes and waketimes and shorter overall sleep hours (Crowley et al., 2018), a pattern which extends into early adulthood (Park

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et al., 2019). Notable social changes also occur, in peer relations, family relationships, and romantic relationships and sexuality, which are embedded in larger contextual changes such as school transitions and increasing scholastic, work, and extracurricular demands (Steinberg & Morris, 2001). Changing cognitive abilities during adolescence occur and in turn facilitate the exploration and attainment of personal and ethnic identities, a process that continues into early adulthood (Umaña-Taylor et al., 2014). Young adults experience the added demands of culturally expected milestones such as exiting the family home, entering higher education or workforce settings, attaining financial independence, and family formation and childrearing (Barlett et al., 2020).

Each generation of adolescents and young adults also faces unique challenges associated with coming of age in specific places and time periods, characterized by varying economic conditions, changing technologies, and particular local, national, and global stressors (Lerner et al., 2019). For example, we write this chapter in 2020 and early 2021 during the global pandemic of COVID-19, which is resulting in widespread changes in social and economic conditions for adolescents and young adults. These include isolation from peers and sometimes from family, threat of sickness and death of oneself and loved ones, and highly disrupted educational and economic trajectories. We also write this chapter during times of racial protest and civil unrest, in response to the killings of George Floyd, Ahmaud Arbery, and Breonna Taylor and in response to the 2020 U.S. presidential election. Experience of these events will likely have profound impacts on the current generation of youth. Some of these impacts are already emerging, such as in increased levels of perceived stress and anger in young adults (Shanahan et al., 2020).

Adolescence is also associated with dramatic increases in depression and anxiety, particularly for girls. Existing evidence suggests that depressive symptoms and diagnoses, on average, rise throughout early adolescence, peak in mid- to late adolescence (15 and 17), and decline steadily across early adulthood (Adkins et al., 2009; Mojtabai et al., 2016). Girls, individuals of color, and low socioeconomic status (SES) youth tend to show higher depressive symptoms (Adkins et al., 2009). Externalizing symptoms also increase across adolescence, a change that is mostly normative and dissipates during early adulthood, but a subgroup with earlier and more serious problems have issues with externalizing problems into adulthood (Dodge et al., 2007). Evidence suggests that stressor exposure and biological stress responses play a role in developmental increases and disparities in depression and externalizing problems (Adam et al., 2010; Barlett et al., 2020; Grant et al., 2014). When the changes of adolescence and early adulthood accumulate within a short period of time, they are particularly associated with negative outcomes (Simmons et al., 1987), affecting both concurrent and subsequent mental and physical health (Adam et al., 2011; Raposa et al., 2014).

SECULAR TRENDS IN ADOLESCENT AND YOUNG ADULT STRESS

Anecdotal evidence (e.g., parent and media reports) suggests that adolescent and young adult stress has increased over the past 20 years, although to our knowledge, no longitudinal data exist on secular trends in perceived stress levels for these age groups. If we consider depressive symptoms and disorders to be proxy markers for stress, there is strong evidence that these have increased over recent historical time (since approximately 2011), with stronger increases for adolescents than young adults (Coley et al., 2019; Collishaw & Sellers, 2020; Keyes et al., 2019; Mojtabai et al., 2016). The sources of this secular increase are not well understood: Proposed explanations include increased social media exposure (Twenge, 2020), decreased sleep hours (Keyes et al., 2019; Patalay & Gage, 2019), and increased family economic stress or income inequality (Coley et al., 2019; Collishaw & Sellers, 2020; Kim & Hagquist, 2018). The social media explanation has been the subject of considerable challenge (Orben et al., 2019; Uhls et al., 2017). Better understanding of these trends will require repeated measurements of youth stress and its sources, informed by clear definition and strong measurement.

STRESS DEFINITION AND MEASUREMENT

Stress is a response to an internal or external challenge that consists of experiential, contextual, emotional, cognitive, and biological components. Stress has been defined as "a real or interpreted threat to the physiological or psychological integrity of an individual that results in physiological and/or behavioral responses" (McEwen, 2008, as cited in McEwen, 2010, p. 11). Most definitions of stress encompass at least two elements: (a) a demand, challenge, or perturbing force and (b) a response, consisting of cognitive, emotional, behavioral, and biological elements. Stress experts have called for a disaggregation of these two components of the stress process (Grant et al., 2003; Monroe, 2008). They argue that the word "stressor" should be used to refer to the demand or challenge eliciting a response, whereas the biological, cognitive, emotional, and behavioral responses should be referred to as the "stress response" (Grant et al., 2003). Additional stress processes include *stress mediators*, or the psychological and biological pathways by which stress exposure affects individual well-being, and *stress moderators*, which are individual and contextual factors that modify the strength and direction of the associations between stress exposure and health and developmental outcomes (Grant et al., 2003). The broader term "stress" thus refers not only to the environmental stressors themselves but also to the range of processes set in motion by exposure to environmental stressors. As a result, "stress research" refers to the body of literature that examines environmental stressors as well as reciprocal and dynamic processes among stressors, stress responses, stress mediators, and stress moderators and the health and behavioral outcomes.

Stressor Measurement Approaches in Adolescence and Early Adulthood

Even after the components of stress research are recognized and defined, key challenges associated with appropriately measuring them remain. Measures of stress exposure or stressors, typically based on self-reported life event checklists, have dominated the literature on adolescent and young adult stress. These checklists ask youth whether they have been exposed to a wide variety of circumstances and add up the number of exposures, often weighting each event equally (Grant et al., 2020). Related inventories include trauma scales, which ask youth (typically retrospectively) about exposure to severe or traumatic stressors (Finkelhor et al., 2015).

Critiques of checklist-type measures note that the impact of events may vary considerably depending on circumstances. The death of a grandmother, for example, may be extremely stressful or only slightly so depending on how involved the grandmother had been. These critiques and others led to the advent of *life stress interviews*, in which interviewers probe the context surrounding the event, giving them the ability to judge the degree to which each event is stressful for youth (Monroe, 2008). Life stress interviews also differentiate between more acute stressors and chronic, ongoing stressors (Grant et al., 2020). Life events interviews, however, are resource intensive and time consuming to conduct (Grant et al., 2020; Monroe, 2008).

Another important direction in stress measurement involves classifying the domains or dimensions of stressors or adversity, such as distinguishing between threat and deprivation events (McLaughlin et al., 2014), and considering how stressor characteristics such as novelty, unpredictability, chronicity, and developmental timing alter appraisals of and responses to stressors (Dickerson & Kemeny, 2004; Harris & McDade, 2018; Monroe, 2008).

Stressor Measurement Batteries/Inventories. In recent work, researchers have worked to construct stressor measurement batteries that are efficient while maintaining some of the advantages of intensive stressor interviews, such as rating severity and organizing stressor subtypes in ways that are theoretically meaningful (Slavich et al., 2019). For example, our system distinguishes between systemic, major, and minor stressors and examines stressor domains of threat, loss and lack, humiliation, and conflict, hypothesizing specific emotional, cognitive, physiological, and health and behavioral outcomes of each (Grant et al., 2021).

Ecological Momentary Assessment. Ecological momentary assessment (EMA) involves gathering repeated short diary self-reports of experiences and moods as individuals go about their everyday lives; it captures stressors and stress responses in naturalistic settings (Repetti et al., 2015). Individuals are prompted by a device (e.g., tablet or phone app notification), email, or text message multiple times across the day for several days to report on the occurrence of and their responses to events. EMA methods are highly suitable for adolescent and young adult populations (Heron et al., 2017). A related approach involves daily diary reporting of stress (Fuligni et al., 2009). Compared with recall-based questionnaire measures, diary measures are thought to minimize recall bias and maximize ecological validity (Shiffman et al., 2008). EMA and diary stress measures are strong correlates and prospective predictors of mood disorders (Anderson et al., 2021; Baltasar-Tello et al., 2018) and of biological stress measures in adolescents and young adults (Adam, 2006; Fuligni et al., 2009; Sladek et al., 2020).

Stress Response Measurement in Adolescence and Early Adulthood: Biological Approaches

Many research groups, including our own, approach the study of adolescent and young adult stress by measuring not only stressors but also the biological stress response, given that (a) the biological stress response is an intrinsic part of the definition and measurement of stress without which our understanding of stress processes is incomplete; (b) changes in biological stress are an important mechanism by which stressor exposure is linked to disease outcomes; (c) biological stress measures go beyond self-report to reveal stress impacts of which youth may not themselves be aware; (d) measuring how strongly various stressors affect biological stress responses helps researchers identify which stressors most impact the body and brain; (e) policy makers and interventionists find biological measures to be compelling; and (f) normative developmental changes in biological stress systems occur across adolescence and into early adulthood, with implications for changes in emotional and behavioral responding.

Multiple stress-sensitive biological stress systems have been studied during adolescence and early adulthood, including autonomic nervous system activity (Fiol-Veny et al., 2018), inflammation (Fuligni et al., 2009), and sleep processes (Adam et al., 2007). The largest literature, however, is on the HPA axis and its primary hormonal product, cortisol.

HPA Axis Activity in Adolescence and Young Adulthood: Overview of Biology

The HPA axis is an important biological stress system to study during adolescence and early adulthood because it is one of the primary biological stress response systems and is subject to developmental changes over these time periods. In addition, alterations in HPA axis activity are a plausible mechanism linking stressor exposure to behavioral, cognitive, and mental and physical health outcomes (Pagliaccio & Barch, 2016). Detailed descriptions of the neurobiology of the HPA axis are offered elsewhere (Sapolsky et al., 2000); here, we briefly describe HPA axis activity in the context of the other key biological stress response systems.

The two key arms of the mammalian stress response system are the sympathetic–adrenal–medullary (SAM) system and the HPA axis (Gunnar & Vazquez, 2015). The SAM system supports rapid mobilization and response to stressors, often described as fight-or-flight reactions. In contrast, the HPA system, through its basal activity and reactivity to stress, supports the efficacy of the SAM. It also mobilizes energy resources and counteracts or suppresses acute stress effects on the body, including its own activation (Sapolsky et al., 2000). The cascade of events in the HPA system begins with the release of corticotropin-releasing hormone (CRH) and vasopressin (VP) from the paraventricular nucleus (PVN) in the hypothalamus. CRH and VP travel through small blood vesicles to the anterior pituitary (AP), where they stimulate the production and release of adrenocorticotropic hormone (ACTH). Released into general circulation, ACTH interacts with receptors on the cortex of the adrenal glands to stimulate the production and release of glucocorticoids (cortisol in humans, corticosterone in many rodents) into circulation. The HPA

axis is under negative feedback control, such that increases in glucocorticoids result in inhibition of CRH and VP production in the PVN by way of glucocorticoid-responsive cells in the hypothalamus, hippocampus, and medial prefrontal cortex (Sapolsky et al., 2000).

Cortisol functions by interacting with two classes of receptors: mineralo- and glucocorticoid receptors (MR and GR); both receptors respond to cortisol in the brain (de Kloet et al., 1998). MRs are high-affinity receptors, binding readily to cortisol, whereas GR are low-affinity cortisol receptors, typically only binding to cortisol with MRs are already occupied. Thus, when cortisol levels are low, MRs are activated, while GRs are only activated when cortisol levels are high, at the peak of the circadian cycle or during stress. MRs tend to mediate what have been termed *permissive* effects of cortisol, including maintaining the responsiveness of neurons to their neurotransmitters, maintaining the HPA circadian rhythm, and maintaining blood pressure. GRs, on the other hand, mediate most of the effects of cortisol reactivity, including helping to promote recovery from stress, and affecting learning and memory of emotional events (Meir Drexler & Wolf, 2017). Related to MR and GR activation, both chronically low and chronically high levels of cortisol are associated with nonoptimal functioning. In contrast, moderate basal levels, a clear circadian rhythm, and rapid increases in cortisol levels in response to stress followed by a return to basal levels tend to be associated with optimal physical and behavioral health (Adam et al., 2017; de Kloet et al., 2005).

Cortisol Reactivity. In humans, short-term cortisol increases in response to acute stressors (called cortisol reactivity) can be observed in both laboratory and naturalistic settings, with cortisol levels peaking in blood approximately 15 minutes after, and in saliva approximately 20 minutes after, the onset of the stressor. Acute stress-related elevations in cortisol in blood serve key functions, mobilizing and directing energy resources, boosting immune functioning, and focusing cognition and memory, all serving to help the organism deal with the stressor at hand and be prepared for similar stressors in the future (Sapolsky et al., 2000). After stressor offset, cortisol levels take approximately 1 hour to decline to basal levels; if the stressor continues, cortisol levels remain elevated above typical basal levels.

Circadian or Diurnal Rhythm of Cortisol. The typical circadian pattern of cortisol in humans is characterized by high levels at waking, a surge in the 30 to 40 minutes after waking, a decline across the waking day to low bedtime levels, and a rise in cortisol levels overnight to return to high levels by waking the next day (Adam & Kumari, 2009). Most naturalistic human research focuses on the diurnal portion of this rhythm, measured during the waking day, for practical reasons (not wanting to interrupt sleep). For measurement purposes, the diurnal cortisol rhythm is typically decomposed into several components that are only mildly to moderately correlated and relate differentially to stressors and to health and developmental outcomes (Adam & Kumari, 2009). The rate of decline in cortisol from waking to bedtime is known as the diurnal cortisol slope; the surge in cortisol after waking is called the cortisol awakening response (CAR); and the total or average cortisol level measured by taking the area under the curve of all of the cortisol measures across the waking day is known as total diurnal cortisol or the area under the curve (AUC; Adam & Kumari, 2009).[1] While the CAR is stress responsive, it also reflects an acute response to the biological act of awakening; it is controlled by mechanisms beyond the typical HPA axis hormonal cascade (Clow et al., 2010).

Cortisol Collection Methods and Covariates

Much of the literature on cortisol levels in adolescence and young adulthood relies on measures of cortisol from small samples of saliva, with collections timed to capture the complex dynamic of acute cortisol reactivity or diurnal changes. Cortisol

[1]Other research groups have established different segmentation strategies for the diurnal cortisol rhythm; the shared aim across research groups is to best identify the components of diurnal regulation of cortisol that are most affected by stress and most related to current and subsequent health and behavioral functioning.

can also be assayed from other biological samples, including urine, plasma, and most recently, hair (Stalder et al., 2017). Measurement of hair cortisol is increasingly popular given that it: (a) only requires one sample, at any time of day, rather than repeated samples across multiple times of day and (b) provides an integrated, average level of cortisol that is thought to reflect aggregated exposure to stress over several months. This is both a strength and the primary weakness of hair cortisol measures: Hair cortisol does not allow assessment of acute stress impacts or diurnal variation in cortisol. Typically, less severe stressors will be detected through changes in diurnal cortisol rhythm more easily than they will be detected in hair cortisol. For chronic stress, however, when stressors are hypothesized to be sufficiently severe to affect average level of cortisol, hair cortisol is a good option. In meta-analytic evidence, ongoing chronic stressors are reflected in significantly elevated hair cortisol levels; more minor perceived stress and past stress were not significantly associated with hair cortisol (Stalder et al., 2017). There is also some evidence that past chronic or traumatic stress is associated with significantly lower hair cortisol levels (Stalder et al., 2017).

With both salivary and hair cortisol measurement, it is important to be aware of, measure, and statistically covary the effects of influencing and confounding variables such as sampling compliance, gender, health behaviors, body mass index (BMI), age and pubertal stage, and medication use (Adam & Kumari, 2009; Stalder et al., 2017). Important variation in cortisol also occurs by race/ethnicity, which is strongly driven by exposure of minoritized ethnic and racial groups to higher levels of stress, especially ethnic and racial discrimination (Adam et al., 2015). Next, we describe normative developmental changes in the HPA axis and then how acute and chronic stressors in adolescence and early adulthood affect the acute response and diurnal rhythm of cortisol.

Developmental Changes in HPA Axis Functioning in Adolescence and Early Adulthood

The HPA axis shows developmental changes during adolescence, with studies showing increases with age and pubertal stage in basal levels of cortisol and in cortisol reactivity to stressors (Adam, 2006; Gunnar, Wewerka, et al., 2009; Lupien et al., 2009; Stroud et al., 2009). For example, Stroud et al. (2009) observed significantly larger cortisol increases in response to lab-based stressors with increasing pubertal stage. Developmental changes have also been observed in the sensitivity of negative feedback mechanisms and other glucocorticoid-sensitive target tissues in the brain. For example, in animal models, researchers have observed increases in the density and sensitivity of glucocorticoid receptors in the brain in early adolescence, particularly in the prefrontal cortex (Lupien et al., 2009; McCormick et al., 2010).

Thus, adolescent development involves increased glucocorticoid levels and reactivity, ongoing changes to glucocorticoid-sensitive brain regions, and potentially increased impacts of glucocorticoids through increased receptor density and sensitivity. This has led researchers to conclude that "similar to the neonatal period of ontogeny, adolescence may also be a sensitive period for the programming effects of stressors on the central nervous system" (McCormick et al., 2010, p. 73). Indeed, recent research suggests that adolescence, and puberty in particular, may serve as a period for reprogramming of the effects of early (prepubertal) life stress on biology and behavior (Gunnar et al., 2019; King et al., 2017).

There is little evidence regarding developmental changes in cortisol in early adulthood; the one study we are aware of compared basal cortisol levels across age cohorts from infancy through older adulthood, finding that cortisol levels increase from age 5 through age 30 then remain stable until older adulthood, when they increase again (R. Miller et al., 2016). We are not aware of similar studies examining age-related changes in cortisol reactivity from adolescence through early adulthood. Due to ongoing maturation of prefrontal regions of the brain that help to regulate emotional reactivity in early adulthood (Kelly et al., 2009), it is reasonable to suggest that the cortisol stress response may also be more strongly regulated in early adulthood than in adolescence, but considerably more research is needed on this topic.

ACUTE AND CHRONIC STRESSORS AND HPA AXIS ACTIVITY IN ADOLESCENCE AND EARLY ADULTHOOD

A complete review of all studies linking stressors to basal cortisol and acute cortisol reactivity in adolescence and early adulthood is not possible here; instead, we summarize and organize this literature. It is helpful to note that stress–cortisol associations are observed over multiple time scales—moments, days, months, years, and over ontogeny (Adam, 2012)—and that these associations vary with stressor chronicity and the timing of measurement poststressor (e.g., acute vs. chronic stressors elicit different, sometimes opposite, cortisol responses; G. E. Miller et al., 2007). Theory and some evidence suggest that cortisol reactivity and basal cortisol shift from being elevated to being suppressed as stressors increase in chronicity and with increased time since stressor exposure (G. E. Miller et al., 2007; Trickett et al., 2010).

Acute Stress and HPA Axis Reactivity in Adolescence and Early Adulthood

As noted earlier, cortisol increases above basal levels in response to stress; cortisol reactivity to stress in adolescents and young adults has been shown in both lab-based and naturalistic settings. Lab-based studies examine cortisol increases in response to an imposed stressor (such as a public speaking task; Gunnar, Talge, & Herrera, 2009), whereas naturalistic studies examine cortisol responsivity to momentary negative affect or everyday stressors (Adam, 2006). In lab-based studies, stressors involving social-evaluative threat (fear of negative social evaluation) are a potent activator of cortisol, particularly for adolescents (Gunnar, Talge, & Herrera, 2009; Stroud et al., 2009); this stressor remains powerful in early adulthood (Dickerson & Kemeny, 2004).

Similar patterns are also seen in naturalistic studies of adolescent and young adult HPA axis reactivity, mostly using EMA or diary methods. Experiences of sadness, loneliness, and social isolation emerge as key acute activators of cortisol for youth in everyday settings (Adam, 2006; Doane & Adam, 2010; Matias et al., 2011). The prominence of perceived negative social judgement and social exclusion as activators of the HPA axis in youth should not come as a surprise, given the key importance of social (especially peer) relationships in the lives of adolescents and young adults. Youth cortisol also responds to experiences of anger (Adam, 2006) and perceived stress (Sladek et al., 2016) in daily life.

The CAR is sometimes also viewed as an acute HPA axis response, intended to prepare the individual for the demands of the day by providing a boost of energy and mental alertness calibrated to daily demands (Stalder et al., 2010). In adolescents and young adults, the CAR has been found to increase in response to prior-day stressors such as loneliness (Doane & Adam, 2010) and is higher on days with greater perceived upcoming demands (Stalder et al., 2010). Additional research in adolescents and young adults suggests the CAR may respond to social contexts and excessive demands more broadly as opposed to being tied only to stressful daily experiences (Doane et al., 2018; Sladek & Doane, 2015; Sladek et al., 2020).

Chronic Stress and HPA Axis Activity in Adolescence and Early Adulthood

A wide range of chronic stressors experienced during childhood and adolescence have been examined in relation to adolescent and young adult HPA axis activity. Here we focus on relatively severe chronic stressors, giving a bird's-eye view summary of each, primarily based on recent systematic reviews and meta-analyses (incorporating prenatal exposures is beyond the scope of this review).

Maltreatment. Studies linking maltreatment or abuse during childhood or adolescence with HPA axis activity reveal complex associations, including both hypo- and hypercortisolism and flatter diurnal cortisol rhythms. Importantly, a meta-analysis of 27 studies showed no overall effect of maltreatment on the CAR or cortisol slope but did find evidence of lower waking cortisol levels for clinic-referred samples, suggesting the presence of hypocortisolism, especially for more severe cases of maltreatment (Bernard et al., 2017). Similar conclusions were drawn from a recent study utilizing hair cortisol (White et al., 2017). In this study, maltreatment

history (especially chronic maltreatment and neglect) was associated with significantly lower hair cortisol levels for children over the age of 9.69 years, with effects growing stronger with pubertal development. An additional study found that sexual abuse in childhood was associated with an initial significant elevation of cortisol in adolescence, followed by a progressive cortisol reduction into early adulthood (Trickett et al., 2010).

Bullying. In a recent systematic review of the literature on peer victimization and cortisol in children and adolescents, peer victimization was consistently associated with blunted cortisol reactivity and a flatter diurnal cortisol slope (Kliewer et al., 2019). Flatter diurnal cortisol slopes and reduced reactivity are both signs of hypocortisolism that are evident among bullied children as young as 12 years of age (Ouellet-Morin et al., 2011). Altered HPA axis functioning associated with bullying has also been linked to poor health outcomes (Knack et al., 2011).

Low Socioeconomic Status. An early review including both adolescent and adult studies concluded that SES was not consistently associated with higher or lower cortisol but did reveal associations between low SES and flatter diurnal cortisol slopes (Dowd et al., 2009), a conclusion supported by subsequent research (Desantis et al., 2015). Low SES experienced in adolescence has also been associated with a higher CAR in adulthood, even if SES increased in adulthood, suggesting a possible adolescent sensitive period effect (Gustafsson et al., 2010).

Violence Exposure. Although acute exposure to violence in adolescence is associated with a higher CAR (Heissel, Sharkey, et al., 2018), chronic exposure to violence has been associated with lower subsequent cortisol reactivity, for boys only (Peckins et al., 2012). Similarly, chronic violence exposure in adolescence and early adulthood predicts lower cortisol reactivity in adulthood, particularly in men with low paternal support (Aiyer et al., 2014).

Discrimination. Studies of discrimination (unfair treatment according to race, gender, sexual orientation, or other group memberships) in youth have found higher discrimination to be associated with stronger acute cortisol reactivity (Doane & Zeiders, 2014), higher overall cortisol (Huynh et al., 2016; Zeiders et al., 2012), and a flatter diurnal cortisol slope (Huynh et al., 2016; Zeiders et al., 2014). In our longitudinal study, racial discrimination in early adolescence and early adulthood predicted flatter cortisol slopes and lower cortisol levels in adulthood, and racial discrimination experienced during adolescence had a stronger effect on adult cortisol than racial discrimination during early adulthood (Adam et al., 2015). At a more macrostructural level, lesbian, gay, and bisexual youth who lived between the ages of 10 and 18 in states with high levels of structural stigma (state laws and institutional practices that constrain nonheterosexual youth) evidenced blunted cortisol reactivity as young adults (Hatzenbuehler & McLaughlin, 2014).

Academic Stress. Although acute exposure to academic stress is associated with elevated cortisol, particularly when performance matters, such as during high-stakes tests (Heissel, Adam, et al., 2018), less evidence exists on whether and how chronic academic demands are associated with cortisol in adolescents and young adults. In one study of college students, hair cortisol levels were significantly higher during the academic term than the summer, and exposure to stressful events, particularly academic demands, negative evaluation, and social rejection helped to explain academic year cortisol elevations (Stetler & Guinn, 2020).

Chronic Stress and Cortisol: Unifying Themes. Across these various forms of chronic stress, several themes emerge. First, as first described in review articles (Gunnar & Vazquez, 2001; G. E. Miller et al., 2007; Susman, 2006), past chronic stress, particularly of a traumatic nature, tends to be associated with flatter diurnal cortisol rhythms, lower overall cortisol levels, and a lower CAR, whereas current chronic stress (e.g., current academic stress) tends to be associated with cortisol elevations. According to the attenuation hypothesis and related theories, a move from elevated cortisol (hypercortisolism) in the face of current and

ongoing stress to hypocortisolism (low cortisol, with a weaker diurnal rhythm and lower CAR) occurs with the passage of time with repeated and chronic exposure to stressors, remaining even after stressor offset (Adam et al., 2017; Trickett et al., 2010). Whether this shift serves a functional purpose (e.g., protecting the brain from frequently or chronically elevated glucocorticoids) or is the result of wear and tear on neuroregulatory mechanisms due to overuse (a pattern called allostatic load; McEwen, 2008) remains to be firmly established. Second, many of the chronic stressors discussed here that are found to have long-term impacts on cortisol tend to involve themes of neglect, loss, negative social evaluation, and social exclusion—all threats to the social self. Additional longitudinal studies are needed to observe the unfolding of the proposed attenuation over time and to gain a better understanding of the functional purpose served by this attenuation. Additional studies should also continue to identify the durations, severities, and psychological dimensions of stressors that relate to various patterns of HPA axis activity.

Moderators of the Effects of Stressors on HPA Axis Activity

Many factors have been found to modify (either accentuate or attenuate) the impact of stressors on adolescent and young adult HPA axis activity. These include (a) genetic polymorphisms relevant to stress perception and HPA axis functioning, such as serotonin transporter and HPA axis polymorphisms (Starr et al., 2019); (b) the presence of social (adult and peer) support (Aiyer et al., 2014; Doane & Zeiders, 2014); (c) individual coping strategies such as problem solving and engagement coping (Gilbert et al., 2017; Sladek et al., 2016); and (d) for youth of color, ethnic identity and cultural values and competencies (Gonzales et al., 2018; Sladek et al., 2019).

ADOLESCENT AND YOUNG ADULT STRESS, HPA AXIS ACTIVITY, AND DEVELOPMENTAL OUTCOMES

In comprehensive reviews of the extant stress literature, clear and consistent links have been found between increased adolescent stress exposure and a wide range of current and subsequent mental health outcomes (Grant et al., 2014), physical health outcomes (Wickrama et al., 2015), and academic performance (Lupien et al., 2007). Many studies have also established links between adolescent stress exposure and negative outcomes in early adulthood, in particular (Doom et al., 2017; Wickrama et al., 2015). Fewer studies have assessed both stress exposure and developmental outcomes during early adulthood, but there is evidence that stressors prospectively predict negative outcomes during this period (Collins et al., 2014; Ewing et al., 2019; Hatzenbuehler et al., 2014). What evidence is there that altered HPA axis activity may play a role in mediating associations between stress exposure and mental health, physical health, and academic outcomes in adolescence and early adulthood?

Stress and Mental Health Outcomes in Adolescence and Early Adulthood

Extensive cross-sectional evidence has linked increased stressor exposure (Hammen, 2005) and altered HPA axis activity to depression (Adam et al., 2017), but very few prospective longitudinal studies exist (Adam et al., 2010, 2017). In one such study, the CAR, both directly and in interaction with interpersonal life stress, was found to predict later depression and anxiety in adolescents and young adults (Adam et al., 2010, 2014). To our knowledge, however, no studies of adolescents or young adults have formally tested cortisol as a mediator of the association between stress exposure and depression (Pagliaccio & Barch, 2016). Some mediational evidence does exist for externalizing disorders: In one study mentioned earlier, the association between maltreatment and externalizing disorders was partially mediated by low cortisol levels (White et al., 2017).

Stress and Physical Health Outcomes in Adolescence and Early Adulthood

Adolescent stress has been linked to self-reported adolescent health (Slavich et al., 2019) as well as to the biological precursors of disease (e.g., elevated cholesterol, blood pressure, inflammation) in adolescence (Ehrlich et al., 2016; Fuligni et al., 2009). Adolescent stress has also been related to

self-reported general health and to specific disease outcomes in adulthood, such as cardiovascular disease and metabolic syndrome (Adam et al., 2011; Ehrlich et al., 2016; Farrell et al., 2017). In addition, alterations in HPA axis activity have been associated with a wide range of physical health outcomes. In meta-analytic research on a range of age groups including adolescents and young adults, a flatter diurnal cortisol slope was found to predict worse outcomes for five out of six types of physical health outcomes examined (Adam et al., 2017). However, very little research examines the full mediational pathway from stress exposure to HPA axis activity to health. One study in young adults did so, finding perceived stress to predict health complaints by way of alterations (an elevation and flattening) of the diurnal cortisol rhythm (Lovell et al., 2011).

Stress and Cognitive and Academic Outcomes in Adolescence and Early Adulthood

Stress is also relevant for understanding academic and other human capital outcomes in youth—evidence from both animal models and humans reveal connections between stress exposure, HPA axis activity, and cognitive and academic performance (Levy et al., 2016; Lupien et al., 2001, 2007; Shankar & Park, 2016). Generally speaking, associations between stress exposure, cortisol, and cognitive performance tend to follow an inverse U-shaped curve, with optimal performance occurring at moderate levels of stress-related arousal and moderate increases in cortisol; studies in both adolescents and young adults have demonstrated this pattern (Gabrys et al., 2019; Heissel, Adam, et al., 2018). In one policy-relevant example, students with moderate cortisol elevations on the mornings of high-stakes tests (as compared with weeks with no tests or lower stakes tests) showed the best test performance (Heissel, Adam, et al., 2018).

Evolutionary Perspectives on Stress, HPA Axis Activity, and Developmental Outcomes

In response to acute stress, short-term and moderate HPA axis activation is frequently noted as functional, contributing to individual's abilities to cope with the stressor at hand, through a combination of increased arousal, physical energy, and sharpened cognition for stress-relevant stimuli (Sapolsky et al., 2000). More chronic alterations in HPA axis activity are often framed as pathogenic in much of the HPA axis literature (Ellis & Del Giudice, 2014). By contrast, a set of theoretical models emerging from anthropology and developmental science argues that even chronic-stress-related alterations in HPA axis activity, and the behavioral and cognitive consequences thereof, represent functional adaptations that prepare the individual for their expected environment (Belsky et al., 2007; Del Giudice et al., 2011; Ellis & Boyce, 2008). These models identify different patterns of HPA axis functioning, link them to differing developmental environments and patterns of developmental growth (e.g., timing of puberty) and behavior (e.g., risk taking, sexual behavior, social withdrawal), and interpret them using evolutionary/functional frameworks.

INTERVENTIONS TO REDUCE ADOLESCENT AND YOUNG ADULT STRESS AND ITS IMPACTS ON STRESS BIOLOGY

Our growing understanding of how and in what ways environmental experiences contribute to HPA axis alterations over time has led to a small but important wave of studies in which researchers are experimentally modifying exposures to stressors or resources in order to examine impacts on youth stress biology and developmental outcomes. These studies serve two positive purposes: (a) They employ strategies that may improve the lives of adolescents and young adults, and (b) when conducted as randomized control trials, they provide causal evidence for the role of stress reduction (or improvements in resources) in the regulation of stress biology and improvements in stress-related developmental outcomes.

Several intervention studies targeting regulation of adolescent stress and stress biology have shown promising results. A preventive intervention offered following the death of a parent (Luecken et al., 2010) resulted in treated adolescents showing an increase in average cortisol levels relative to control

youth during a conflict discussion task 6 years after participation. Treatment youth also reported lower externalizing problems, suggesting lower incidence of the attenuated cortisol/elevated mental health symptoms profile that might otherwise follow from experiencing the death of a parent at a young age. In addition, a school-based behavioral-stress-education program was found to decrease cortisol levels and depressive symptomatology in adolescents making the transition to high school, with effect sizes on the order of 0.3 *SD* for youth high in anger at baseline (Lupien et al., 2013). A meditation intervention conducted with adolescents outside the school context also found lower average cortisol after 2 to 4 months of meditation intervention, with effects ranging from 0.75 *SD* to 1.25 *SD* (MacLean et al., 1997). Finally, our own group is currently examining the effects of promoting a strong ethnic identity on adolescent HPA axis activity and well-being (Adam et al., 2020).

FUTURE DIRECTIONS IN ADOLESCENT AND YOUNG ADULT STRESS RESEARCH AND CONCLUSIONS

Although a strong foundation of research exists for understanding stress and its effects in adolescence and early adulthood, additional research is needed. We argue that precise conceptualization, measurement, and modeling of both stressors and stress biology are needed to best understand the key sources and impacts of stress in adolescence and early adulthood. Also needed are both repeated cross-sectional and longitudinal research on changes in stressor exposure, perceived stress, and indicators of stress biology and stress-related disorders by age, developmental stage, and cohort; such data will allow us to better reveal the extent to which there are both developmental changes and secular trends in stressors, stress responses, and the consequences of stress. Currently, most conclusions regarding developmental trends and secular changes in stressors and stress biology are pieced together from multiple studies with varying methodologies. Research on developmental changes (or continuities) in stressor exposure and stress biology from adolescence through early adulthood is particularly lacking. Research on stressors and stress responses in early adulthood relies heavily on studies of college students; representative data on young adults are needed in order to best characterize stressor exposure and stress responses during this developmental period. Systematic reviews specifically focusing on factors affecting HPA axis activity during the early adult period are also lacking. Finally, additional intervention work that attempts to reduce adolescent or young adult stressor exposure or helps youth to better regulate their biological stress responses will help to provide additional causal evidence on how stress affects adolescent and young adult well-being.

Overall, the study of adolescent and young adult stress provides an important window on how adolescents' and young adults' ontogenetic development, as well as their multiple and interacting developmental contexts, affect biology and behavior in ways that matter for both current functioning and long-term health and well-being. As a result, this research provides important insights on where, when, and how to intervene to reduce adolescent and young adult stress exposures and experiences to appropriate levels, and how to promote the positive regulation of stress biology and help to ensure that adolescence and early adulthood are experienced as times not only of stress but also of thriving.

REFERENCES

Adam, E. K. (2006). Transactions among adolescent trait and state emotion and diurnal and momentary cortisol activity in naturalistic settings. *Psychoneuroendocrinology*, *31*(5), 664–679. https://doi.org/10.1016/j.psyneuen.2006.01.010

Adam, E. K. (2012). Emotion-cortisol transactions occur over multiple time scales in development: Implications for research on emotion and the development of emotional disorders. *Monographs of the Society for Research in Child Development*, *77*(2), 17–27. https://doi.org/10.1111/j.1540-5834.2012.00657.x

Adam, E. K., Chyu, L., Hoyt, L. T., Doane, L. D., Boisjoly, J., Duncan, G. J., Chase-Lansdale, P. L., & McDade, T. W. (2011). Adverse adolescent relationship histories and young adult health: Cumulative effects of loneliness, low parental support, relationship instability, intimate partner violence, and loss. *Journal of Adolescent Health*, *49*(3), 278–286. https://doi.org/10.1016/j.jadohealth.2010.12.012

Adam, E. K., Collier Villaume, S., & Hittner, E. (2020). Reducing stress disparities: Shining new light on pathways to equity through the study of stress biology. In L. Tach, R. Dunifon, & D. L. Miller (Eds.), *Confronting inequality: How policies and practices shape children's opportunities* (pp. 11–47). American Psychological Association. https://doi.org/10.1037/0000187-002

Adam, E. K., Doane, L. D., Zinbarg, R. E., Mineka, S., Craske, M. G., & Griffith, J. W. (2010). Prospective prediction of major depressive disorder from cortisol awakening responses in adolescence. *Psychoneuroendocrinology*, *35*(6), 921–931. https://doi.org/10.1016/j.psyneuen.2009.12.007

Adam, E. K., Heissel, J. A., Zeiders, K. H., Richeson, J. A., Ross, E. C., Ehrlich, K. B., Levy, D. J., Kemeny, M., Brodish, A. B., Malanchuk, O., Peck, S. C., Fuller-Rowell, T. E., & Eccles, J. S. (2015). Developmental histories of perceived racial discrimination and diurnal cortisol profiles in adulthood: A 20-year prospective study. *Psychoneuroendocrinology*, *62*, 279–291. https://doi.org/10.1016/j.psyneuen.2015.08.018

Adam, E. K., & Kumari, M. (2009). Assessing salivary cortisol in large-scale, epidemiological research. *Psychoneuroendocrinology*, *34*(10), 1423–1436. https://doi.org/10.1016/j.psyneuen.2009.06.011

Adam, E. K., Quinn, M. E., Tavernier, R., McQuillan, M. T., Dahlke, K. A., & Gilbert, K. E. (2017). Diurnal cortisol slopes and mental and physical health outcomes: A systematic review and meta-analysis. *Psychoneuroendocrinology*, *83*, 25–41. https://doi.org/10.1016/j.psyneuen.2017.05.018

Adam, E. K., Snell, E. K., & Pendry, P. (2007). Sleep timing and quantity in ecological and family context: A nationally representative time-diary study. *Journal of Family Psychology*, *21*(1), 4–19. https://doi.org/10.1037/0893-3200.21.1.4

Adam, E. K., Vrshek-Schallhorn, S., Kendall, A. D., Mineka, S., Zinbarg, R. E., & Craske, M. G. (2014). Prospective associations between the cortisol awakening response and first onsets of anxiety disorders over a six-year follow-up—2013 Curt Richter Award Winner. *Psychoneuroendocrinology*, *44*, 47–59. https://doi.org/10.1016/j.psyneuen.2014.02.014

Adkins, D. E., Wang, V., Dupre, M. E., van den Oord, E. J. C. G., & Elder, G. H., Jr. (2009). Structure and stress: Trajectories of depressive symptoms across adolescence and young adulthood. *Social Forces*, *88*(1), 31–60. https://doi.org/10.1353/sof.0.0238

Aiyer, S. M., Heinze, J. E., Miller, A. L., Stoddard, S. A., & Zimmerman, M. A. (2014). Exposure to violence predicting cortisol response during adolescence and early adulthood: Understanding moderating factors. *Journal of Youth and Adolescence*, *43*(7), 1066–1079. https://doi.org/10.1007/s10964-014-0097-8

American Psychological Association. (2019). *Stress in America: Stress and current events*. https://www.apa.org/news/press/releases/stress/2019/stress-america-2019.pdf

American Psychological Association. (2020). *Stress in America 2020: A national mental health crisis*. https://www.apa.org/news/press/releases/stress/2020/report-october

Anderson, S. F., Sladek, M. R., & Doane, L. D. (2021). Negative affect reactivity to stress and internalizing symptoms over the transition to college for Latinx adolescents: Buffering role of family support. *Development and Psychopathology*, *33*(4), 1322–1337. https://doi.org/10.1017/S095457942000053X

Baltasar-Tello, I., Miguélez-Fernández, C., Peñuelas-Calvo, I., & Carballo, J. J. (2018). Ecological momentary assessment and mood disorders in children and adolescents: A systematic review. *Current Psychiatry Reports*, *20*(8), 66. https://doi.org/10.1007/s11920-018-0913-z

Barlett, C. P., Barlett, N. D., & Chalk, H. M. (2020). Transitioning through emerging adulthood and physical health implications. *Emerging Adulthood*, *8*(4), 297–305. https://doi.org/10.1177/2167696818814642

Belsky, J., Bakermans-Kranenburg, M. J., & Van Ijzendoorn, M. H. (2007). For better and for worse: Differential susceptibility to environmental influences. *Current Directions in Psychological Science*, *16*(6), 300–304. https://doi.org/10.1111/j.1467-8721.2007.00525.x

Bernard, K., Frost, A., Bennett, C. B., & Lindhiem, O. (2017). Maltreatment and diurnal cortisol regulation: A meta-analysis. *Psychoneuroendocrinology*, *78*, 57–67. https://doi.org/10.1016/j.psyneuen.2017.01.005

Clow, A., Hucklebridge, F., Stalder, T., Evans, P., & Thorn, L. (2010). The cortisol awakening response: More than a measure of HPA axis function. *Neuroscience and Biobehavioral Reviews*, *35*(1), 97–103. https://doi.org/10.1016/j.neubiorev.2009.12.011

Coley, R. L., O'Brien, M., & Spielvogel, B. (2019). Secular trends in adolescent depressive symptoms: Growing disparities between advantaged and disadvantaged schools. *Journal of Youth and Adolescence*, *48*(11), 2087–2098. https://doi.org/10.1007/s10964-019-01084-1

Collins, B., Fischer, S., Stojek, M., & Becker, K. (2014). The relationship of thought suppression and recent rape to disordered eating in emerging adulthood. *Journal of Adolescence*, *37*(2), 113–121. https://doi.org/10.1016/j.adolescence.2013.11.002

Collishaw, S., & Sellers, R. (2020). Trends in child and adolescent mental health prevalence, outcomes, and inequalities. In E. Taylor, F. C. Verhulst, J. Wong, K. Yoshida, & A. Nikapota (Eds.), *Mental health and*

illness of children and adolescents (pp. 1–11). Springer Singapore.

Crowley, S. J., Wolfson, A. R., Tarokh, L., & Carskadon, M. A. (2018). An update on adolescent sleep: New evidence informing the perfect storm model. *Journal of Adolescence*, *67*, 55–65. https://doi.org/10.1016/j.adolescence.2018.06.001

de Kloet, E. R., Joëls, M., & Holsboer, F. (2005). Stress and the brain: From adaptation to disease. *Nature Reviews Neuroscience*, *6*(6), 463–475. https://doi.org/10.1038/nrn1683

de Kloet, E. R., Vreugdenhil, E., Oitzl, M. S., & Joëls, M. (1998). Brain corticosteroid receptor balance in health and disease. *Endocrine Reviews*, *19*(3), 269–301. https://doi.org/10.1210/edrv.19.3.0331

Del Giudice, M., Ellis, B. J., & Shirtcliff, E. A. (2011). The adaptive calibration model of stress responsivity. *Neuroscience and Biobehavioral Reviews*, *35*(7), 1562–1592. https://doi.org/10.1016/j.neubiorev.2010.11.007

Desantis, A. S., Kuzawa, C. W., & Adam, E. K. (2015). Developmental origins of flatter diurnal cortisol rhythms: Socioeconomic status and adult cortisol activity. *American Journal of Human Biology*, *27*(4), 458–467. https://doi.org/10.1002/ajhb.22668

Dickerson, S. S., & Kemeny, M. E. (2004). Acute stressors and cortisol responses: A theoretical integration and synthesis of laboratory research. *Psychological Bulletin*, *130*(3), 355–391. https://doi.org/10.1037/0033-2909.130.3.355

Doane, L. D., & Adam, E. K. (2010). Loneliness and cortisol: Momentary, day-to-day, and trait associations. *Psychoneuroendocrinology*, *35*(3), 430–441. https://doi.org/10.1016/j.psyneuen.2009.08.005

Doane, L. D., Sladek, M. R., Breitenstein, R. S., Park, H., Castro, S. A., & Kennedy, J. L. (2018). Cultural neurobiology and the family: Evidence from the daily lives of Latino adolescents. *Development and Psychopathology*, *30*(5), 1779–1796. https://doi.org/10.1017/S0954579418001104

Doane, L. D., & Zeiders, K. H. (2014). Contextual moderators of momentary cortisol and negative affect in adolescents' daily lives. *Journal of Adolescent Health*, *54*(5), 536–542. https://doi.org/10.1016/j.jadohealth.2013.10.007

Dodge, K. A., Coie, J. D., & Lynam, D. (2007). Aggression and antisocial behavior in youth. In W. Damon & R. M. Lerner (Eds.), *Child and adolescent development: An advanced course* (pp. 437–472). Wiley and Sons.

Doom, J. R., Mason, S. M., Suglia, S. F., & Clark, C. J. (2017). Pathways between childhood/adolescent adversity, adolescent socioeconomic status, and long-term cardiovascular disease risk in young adulthood. *Social Science & Medicine*, *188*, 166–175. https://doi.org/10.1016/j.socscimed.2017.06.044

Dowd, J. B., Simanek, A. M., & Aiello, A. E. (2009). Socio-economic status, cortisol and allostatic load: A review of the literature. *International Journal of Epidemiology*, *38*(5), 1297–1309. https://doi.org/10.1093/ije/dyp277

Ehrlich, K. B., Miller, G. E., & Chen, E. (2016). Childhood adversity and adult physical health. In D. Cicchetti (Ed.), *Developmental psychopathology: Risk, resilience, and intervention* (pp. 1–42). Wiley & Sons. https://doi.org/10.1002/9781119125556.devpsy401

Ellis, B. J., & Boyce, W. T. (2008). Biological sensitivity to context. *Development and psychopathology*, *17*(3), 183–187. https://doi.org/10.1111/j.1467-8721.2008.00571.x

Ellis, B. J., & Del Giudice, M. (2014). Beyond allostatic load: Rethinking the role of stress in regulating human development. *Development and Psychopathology*, *26*(1), 1–20. https://doi.org/10.1017/S0954579413000849

Ewing, L., Hamza, C. A., & Willoughby, T. (2019). Stressful experiences, emotion dysregulation, and nonsuicidal self-injury among university students. *Journal of Youth and Adolescence*, *48*(7), 1379–1389. https://doi.org/10.1007/s10964-019-01025-y

Farrell, A. K., Simpson, J. A., Carlson, E. A., Englund, M. M., & Sung, S. (2017). The impact of stress at different life stages on physical health and the buffering effects of maternal sensitivity. *Health Psychology*, *36*(1), 35–44. https://doi.org/10.1037/hea0000424

Finkelhor, D., Shattuck, A., Turner, H., & Hamby, S. (2015). A revised inventory of adverse childhood experiences. *Child Abuse & Neglect*, *48*, 13–21. https://doi.org/10.1016/j.chiabu.2015.07.011

Fiol-Veny, A., De La Torre-Luque, A., Balle, M., & Bornas, X. (2018). Altered heart rate regulation in adolescent girls and the vulnerability for internalizing disorders. *Frontiers in Physiology*, *9*, 852. https://doi.org/10.3389/fphys.2018.00852

Fuligni, A. J., Telzer, E. H., Bower, J., Irwin, M. R., Kiang, L., & Cole, S. W. (2009). Daily family assistance and inflammation among adolescents from Latin American and European backgrounds. *Brain, Behavior, and Immunity*, *23*(6), 803–809. https://doi.org/10.1016/j.bbi.2009.02.021

Gabrys, R. L., Howell, J. W., Cebulski, S. F., Anisman, H., & Matheson, K. (2019). Acute stressor effects on cognitive flexibility: Mediating role of stressor appraisals and cortisol. *Stress*, *22*(2), 182–189. https://doi.org/10.1080/10253890.2018.1494152

Gilbert, K., Mineka, S., Zinbarg, R. E., Craske, M. G., & Adam, E. K. (2017). Emotion regulation regulates more than emotion: Associations of momentary

emotion regulation with diurnal cortisol in current and past depression and anxiety. *Clinical Psychological Science*, *5*(1), 37–51. https://doi.org/10.1177/2167702616654437

Gonzales, N. A., Johnson, M., Shirtcliff, E. A., Tein, J.-Y., Eskenazi, B., & Deardorff, J. (2018). The role of bicultural adaptation, familism, and family conflict in Mexican American adolescents' cortisol reactivity. *Development and Psychopathology*, *30*(5), 1571–1587. https://doi.org/10.1017/S0954579418001116

Grant, K. E., Carter, J., Adam, E., & Jackson, Y. (2020). Life events. In E. Youngstrom, M. Prinstein, E. Mash, & R. Barkley (Eds.), *Assessment of disorders in childhood and adolescence* (5th ed., pp. 441–470). Guilford.

Grant, K. E., Carter, J., Marshall, H., DeCator, D., Arizaga, J., Turek, C., Chen, E., Tseng, K. Y., Rosenkranz, J. A., Achenbach, T, & Adam, E. K. (2021). *A comprehensive, empirically-based stressor classification and measurement system for adolescents: Development and use to predict mental health outcomes* [Manuscript in preparation]. Department of Psychology, DePaul University.

Grant, K. E., Compas, B. E., Stuhlmacher, A. F., Thurm, A. E., McMahon, S. D., & Halpert, J. A. (2003). Stressors and child and adolescent psychopathology: Moving from markers to mechanisms of risk. *Psychological Bulletin*, *129*(3), 447–466. https://doi.org/10.1037/0033-2909.129.3.447

Grant, K. E., McMahon, S. D., Carter, J. S., Carleton, R. A., Adam, E. K., & Chen, E. (2014). The influence of stressors on the development of psychopathology. In M. Lewis & K. D. Rudolph (Eds.), *Handbook of developmental psychopathology* (pp. 205–223). Springer. https://doi.org/10.1007/978-1-4614-9608-3_11

Gunnar, M. R., DePasquale, C. E., Reid, B. M., Donzella, B., & Miller, B. S. (2019). Pubertal stress recalibration reverses the effects of early life stress in postinstitutionalized children. *Proceedings of the National Academy of Sciences of the United States of America*, *116*(48), 23984–23988. https://doi.org/10.1073/pnas.1909699116

Gunnar, M. R., Talge, N. M., & Herrera, A. (2009). Stressor paradigms in developmental studies: What does and does not work to produce mean increases in salivary cortisol. *Psychoneuroendocrinology*, *34*(7), 953–967. https://doi.org/10.1016/j.psyneuen.2009.02.010

Gunnar, M. R., & Vazquez, D. M. (2001). Low cortisol and a flattening of the expected daytime rhythm: Potential indices of risk in human development. *Development and Psychopathology*, *13*(3), 515–538. https://doi.org/10.1017/S0954579401003066

Gunnar, M. R., & Vazquez, D. (2015). Stress neurobiology and developmental psychopathology. In D. Cicchetti & D. J. Cohen (Eds.), *Developmental psychopathology: Vol. 2. Developmental neuroscience* (2nd ed., pp. 533–577). https://doi.org/10.1002/9780470939390.ch13

Gunnar, M. R., Wewerka, S., Frenn, K., Long, J. D., & Griggs, C. (2009). Developmental changes in hypothalamus–pituitary–adrenal activity over the transition to adolescence: Normative changes and associations with puberty. *Development and Psychopathology*, *21*(1), 69–85. https://doi.org/10.1017/S0954579409000054

Gustafsson, P. E., Janlert, U., Theorell, T., & Hammarström, A. (2010). Life-course socioeconomic trajectories and diurnal cortisol regulation in adulthood. *Psychoneuroendocrinology*, *35*(4), 613–623. https://doi.org/10.1016/j.psyneuen.2009.09.019

Hall, G. S. (1904). *Adolescence: Its psychology and its relations to physiology, anthropology, sociology, sex, crime, religion and education* (Vol. I–II). D. Appleton & Company. https://doi.org/10.1037/10616-000

Hammen, C. L. (Ed.). (2005). Stress and depression. *Annual Review of Clinical Psychology*, *1*, 293–319. https://doi.org/10.1146/annurev.clinpsy.1.102803

Harris, K. M., & McDade, T. W. (2018). The biosocial approach to human development, behavior, and health across the life course. *Russell Sage Foundation Journal of the Social Sciences*, *4*(4), 2–26. https://doi.org/10.7758/RSF.2018.4.4.01

Hatzenbuehler, M. L., & McLaughlin, K. A. (2014). Structural stigma and hypothalamic–pituitary–adrenocortical axis reactivity in lesbian, gay, and bisexual young adults. *Annals of Behavioral Medicine*, *47*(1), 39–47. https://doi.org/10.1007/s12160-013-9556-9

Hatzenbuehler, M. L., Slopen, N., & McLaughlin, K. A. (2014). Stressful life events, sexual orientation, and cardiometabolic risk among young adults in the United States. *Health Psychology*, *33*(10), 1185–1194. https://doi.org/10.1037/hea0000126

Heissel, J. A., Adam, E. K., Doleac, J. L., Figlio, D. N., & Meer, J. (2018). Testing, stress, and performance: How students respond physiologically to high-stakes testing. *Education Finance and Policy*, *16*(2), 183–208. https://doi.org/10.1162/edfp_a_00306

Heissel, J. A., Sharkey, P. T., Torrats-Espinosa, G., Grant, K., & Adam, E. K. (2018). Violence and vigilance: The acute effects of community violent crime on sleep and cortisol. *Child Development*, *89*(4), e323–e331. https://doi.org/10.1111/cdev.12889

Heron, K. E., Everhart, R. S., McHale, S. M., & Smyth, J. M. (2017). Using mobile-technology-based ecological momentary assessment (EMA) methods with youth: A systematic review and recommendations. *Journal of Pediatric Psychology*, *42*(10), 1087–1107. https://doi.org/10.1093/jpepsy/jsx078

Huynh, V. W., Guan, S. A., Almeida, D. M., McCreath, H., & Fuligni, A. J. (2016). Everyday discrimination and diurnal cortisol during adolescence. *Hormones and Behavior*, *80*, 76–81. https://doi.org/10.1016/j.yhbeh.2016.01.009

Kelly, A. M. C., Di Martino, A., Uddin, L. Q., Shehzad, Z., Gee, D. G., Reiss, P. T., Margulies, D. S., Castellanos, F. X., & Milham, M. P. (2009). Development of anterior cingulate functional connectivity from late childhood to early adulthood. *Cerebral Cortex*, *19*(3), 640–657. https://doi.org/10.1093/cercor/bhn117

Keyes, K. M., Gary, D., O'Malley, P. M., Hamilton, A., & Schulenberg, J. (2019). Recent increases in depressive symptoms among US adolescents: Trends from 1991 to 2018. *Social Psychiatry and Psychiatric Epidemiology*, *54*(8), 987–996. https://doi.org/10.1007/s00127-019-01697-8

Kim, Y., & Hagquist, C. (2018). Trends in adolescent mental health during economic upturns and downturns: A multilevel analysis of Swedish data 1988–2008. *Journal of Epidemiology and Community Health*, *72*(2), 101–108. https://doi.org/10.1136/jech-2017-209784

King, L. S., Colich, N. L., LeMoult, J., Humphreys, K. L., Ordaz, S. J., Price, A. N., & Gotlib, I. H. (2017). The impact of the severity of early life stress on diurnal cortisol: The role of puberty. *Psychoneuroendocrinology*, *77*, 68–74. https://doi.org/10.1016/j.psyneuen.2016.11.024

Kliewer, W., Sosnowski, D. W., Noh, H., McGuire, K., & Wright, A. W. (2019). Peer victimization and cortisol production in children and adolescents: A systematic review. *Journal of Applied Biobehavioral Research*, *24*(4), e12172. https://doi.org/10.1111/jabr.12172

Knack, J. M., Jensen-Campbell, L. A., & Baum, A. (2011). Worse than sticks and stones? Bullying is associated with altered HPA axis functioning and poorer health. *Brain and Cognition*, *77*(2), 183–190. https://doi.org/10.1016/j.bandc.2011.06.011

Lerner, R. M., Tirrell, J. M., Dowling, E. M., Geldhof, G. J., Gestsdóttir, S., Lerner, J. V., King, P. E., Williams, K., Iraheta, G., & Sim, A. T. R. (2019). The end of the beginning: Evidence and absences studying positive youth development in a global context. *Adolescent Research Review*, *4*(1), 1–14. https://doi.org/10.1007/s40894-018-0093-4

Levy, D. J., Heissel, J. A., Richeson, J. A., & Adam, E. K. (2016). Psychological and biological responses to race-based social stress as pathways to disparities in educational outcomes. *American Psychologist*, *71*(6), 455–473. https://doi.org/10.1037/a0040322

Lovell, B., Moss, M., & Wetherell, M. A. (2011). Perceived stress, common health complaints and diurnal patterns of cortisol secretion in young, otherwise healthy individuals. *Hormones and Behavior*, *60*(3), 301–305. https://doi.org/10.1016/j.yhbeh.2011.06.007

Luecken, L. J., Hagan, M. J., Sandler, I. N., Tein, J. Y., Ayers, T. S., & Wolchik, S. A. (2010). Cortisol levels six-years after participation in the Family Bereavement Program. *Psychoneuroendocrinology*, *35*(5), 785–789. https://doi.org/10.1016/j.psyneuen.2009.11.002

Lupien, S. J., King, S., Meaney, M. J., & McEwen, B. S. (2001). Can poverty get under your skin? Basal cortisol levels and cognitive function in children from low and high socioeconomic status. *Development and Psychopathology*, *13*(3), 653–676. https://doi.org/10.1017/s0954579401003133

Lupien, S. J., Maheu, F., Tu, M., Fiocco, A., & Schramek, T. E. (2007). The effects of stress and stress hormones on human cognition: Implications for the field of brain and cognition. *Brain and Cognition*, *65*(3), 209–237. https://doi.org/10.1016/j.bandc.2007.02.007

Lupien, S. J., McEwen, B. S., Gunnar, M. R., & Heim, C. (2009). Effects of stress throughout the lifespan on the brain, behaviour and cognition. *Nature Reviews Neuroscience*, *10*(6), 434–445. https://doi.org/10.1038/nrn2639

Lupien, S. J., Ouellet-Morin, I., Trépanier, L., Juster, R. P., Marin, M. F., Francois, N., Sindi, S., Wan, N., Findlay, H., Durand, N., Cooper, L., Schramek, T., Andrews, J., Corbo, V., Dedovic, K., Lai, B., & Plusquellec, P. (2013). The DeStress for Success Program: Effects of a stress education program on cortisol levels and depressive symptomatology in adolescents making the transition to high school. *Neuroscience*, *249*, 74–87. https://doi.org/10.1016/j.neuroscience.2013.01.057

MacLean, C. R. K., Walton, K. G., Wenneberg, S. R., Levitsky, D. K., Mandarino, J. P., Waziri, R., Hillis, S. L., & Schneider, R. H. (1997). Effects of the Transcendental Meditation program on adaptive mechanisms: Changes in hormone levels and responses to stress after 4 months of practice. *Psychoneuroendocrinology*, *22*(4), 277–295. https://doi.org/10.1016/S0306-4530(97)00003-6

Matias, G. P., Nicolson, N. A., & Freire, T. (2011). Solitude and cortisol: Associations with state and trait affect in daily life. *Biological Psychology*, *86*(3), 314–319. https://doi.org/10.1016/j.biopsycho.2010.12.011

McCormick, C. M., Mathews, I. Z., Thomas, C., & Waters, P. (2010). Investigations of HPA function and the enduring consequences of stressors in adolescence in animal models. *Brain and Cognition*, *72*(1), 73–85. https://doi.org/10.1016/j.bandc.2009.06.003

McEwen, B. S. (2010). Stress: Homeostasis, rheostasis, allostasis and allostatic load. In G. Fink (Ed.), *Stress science: Neuroendocrinology* (pp. 10–14). Elsevier.

McLaughlin, K. A., Sheridan, M. A., & Lambert, H. K. (2014). Childhood adversity and neural development: Deprivation and threat as distinct dimensions of early experience. *Neuroscience and Biobehavioral Reviews*, *47*, 578–591. https://doi.org/10.1016/j.neubiorev.2014.10.012

Meir Drexler, S., & Wolf, O. T. (2017). The role of glucocorticoids in emotional memory reconsolidation. *Neurobiology of Learning and Memory*, *142*(Pt. A), 126–134. https://doi.org/10.1016/j.nlm.2016.11.008

Miller, G. E., Chen, E., & Zhou, E. S. (2007). If it goes up, must it come down? Chronic stress and the hypothalamic–pituitary–adrenocortical axis in humans. *Psychological Bulletin*, *133*(1), 25–45. https://doi.org/10.1037/0033-2909.133.1.25

Miller, R., Stalder, T., Jarczok, M., Almeida, D. M., Badrick, E., Bartels, M., Boomsma, D. I., Coe, C. L., Dekker, M. C., Donzella, B., Fischer, J. E., Gunnar, M. R., Kumari, M., Lederbogen, F., Power, C., Ryff, C. D., Subramanian, S. V., Tiemeier, H., Watamura, S. E., & Kirschbaum, C. (2016). The CIRCORT database: Reference ranges and seasonal changes in diurnal salivary cortisol derived from a meta-dataset comprised of 15 field studies. *Psychoneuroendocrinology*, *73*, 16–23. https://doi.org/10.1016/j.psyneuen.2016.07.201

Mojtabai, R., Olfson, M., & Han, B. (2016). National trends in the prevalence and treatment of depression in adolescents and young adults. *Pediatrics*, *138*(6), e20161878. https://doi.org/10.1542/peds.2016-1878

Monroe, S. M. (2008). Modern approaches to conceptualizing and measuring human life stress. *Annual Review of Clinical Psychology*, *4*(1), 33–52. https://doi.org/10.1146/annurev.clinpsy.4.022007.141207

National Academies of Sciences, Engineering, and Medicine. (2019). *The promise of adolescence: Realizing opportunity for all youth*. National Academies Press.

Orben, A., Dienlin, T., & Przybylski, A. K. (2019). Social media's enduring effect on adolescent life satisfaction. *Proceedings of the National Academy of Sciences of the United States of America*, *116*(21), 10226–10228. https://doi.org/10.1073/pnas.1902058116

Ouellet-Morin, I., Odgers, C. L., Danese, A., Bowes, L., Shakoor, S., Papadopoulos, A. S., Caspi, A., Moffitt, T. E., & Arseneault, L. (2011). Blunted cortisol responses to stress signal social and behavioral problems among maltreated/bullied 12-year-old children. *Biological Psychiatry*, *70*(11), 1016–1023. https://doi.org/10.1016/j.biopsych.2011.06.017

Pagliaccio, D., & Barch, D. M. (2016). Early life adversity and risk for depression: Alterations in cortisol and brain structure and function as mediating mechanisms. In T. Frodl (Ed.), *Systems neuroscience in depression* (pp. 29–77). Academic Press. https://doi.org/10.1016/B978-0-12-802456-0.00002-9

Park, H., Chiang, J. J., Irwin, M. R., Bower, J. E., McCreath, H., & Fuligni, A. J. (2019). Developmental trends in sleep during adolescents' transition to young adulthood. *Sleep Medicine*, *60*, 202–210. https://doi.org/10.1016/j.sleep.2019.04.007

Patalay, P., & Gage, S. H. (2019). Changes in millennial adolescent mental health and health-related behaviours over 10 years: A population cohort comparison study. *International Journal of Epidemiology*, *48*(5), 1650–1664. https://doi.org/10.1093/ije/dyz006

Peckins, M. K., Dockray, S., Eckenrode, J. L., Heaton, J., & Susman, E. J. (2012). The longitudinal impact of exposure to violence on cortisol reactivity in adolescents. *Journal of Adolescent Health*, *51*(4), 366–372. https://doi.org/10.1016/j.jadohealth.2012.01.005

Raposa, E. B., Hammen, C. L., Brennan, P. A., O'Callaghan, F., & Najman, J. M. (2014). Early adversity and health outcomes in young adulthood: The role of ongoing stress. *Health Psychology*, *33*(5), 410–418. https://doi.org/10.1037/a0032752

Repetti, R. L., Reynolds, B. M., & Sears, M. S. (2015). Families under the microscope: Repeated sampling of perceptions, experiences, biology, and behavior. *Journal of Marriage and the Family*, *77*(1), 126–146. https://doi.org/10.1111/jomf.12143

Sapolsky, R. M., Romero, L. M., & Munck, A. U. (2000). How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. *Endocrine Reviews*, *21*(1), 55–89. https://doi.org/10.1210/edrv.21.1.0389

Shanahan, L., Steinhoff, A., Bechtiger, L., Murray, A. L., Nivette, A., Hepp, U., Ribeaud, D., & Eisner, M. (2020). Emotional distress in young adults during the COVID-19 pandemic: Evidence of risk and resilience from a longitudinal cohort study. *Psychological Medicine*. Advance online publication. https://doi.org/10.1017/S003329172000241X

Shankar, N. L., & Park, C. L. (2016). Effects of stress on students' physical and mental health and academic success. *International Journal of School & Educational Psychology*, *4*(1), 5–9. https://doi.org/10.1080/21683603.2016.1130532

Shiffman, S., Stone, A. A., & Hufford, M. R. (2008). Ecological momentary assessment. *Annual Review of Clinical Psychology*, *4*(1), 1–32. https://doi.org/10.1146/annurev.clinpsy.3.022806.091415

Simmons, R. G., Burgeson, R., Carlton-Ford, S., & Blyth, D. A. (1987). The impact of cumulative change in early adolescence. *Child Development*, *58*(5), 1220–1234. https://doi.org/10.2307/1130616

Sladek, M. R., & Doane, L. D. (2015). Daily diary reports of social connection, objective sleep, and the cortisol awakening response during adolescents' first year of college. *Journal of Youth and Adolescence*, *44*(2), 298–316. https://doi.org/10.1007/s10964-014-0244-2

Sladek, M. R., Doane, L. D., & Breitenstein, R. S. (2020). Daily rumination about stress, sleep, and diurnal cortisol activity. *Cognition and Emotion*, *34*(2), 188–200. https://doi.org/10.1080/02699931.2019.1601617

Sladek, M. R., Doane, L. D., Gonzales, N. A., Grimm, K. J., & Luecken, L. J. (2019). Latino adolescents' cultural values associated with diurnal cortisol activity. *Psychoneuroendocrinology*, *109*, 104403. https://doi.org/10.1016/j.psyneuen.2019.104403

Sladek, M. R., Doane, L. D., Luecken, L. J., & Eisenberg, N. (2016). Perceived stress, coping, and cortisol reactivity in daily life: A study of adolescents during the first year of college. *Biological Psychology*, *117*, 8–15. https://doi.org/10.1016/j.biopsycho.2016.02.003

Slavich, G. M., Stewart, J. G., Esposito, E. C., Shields, G. S., & Auerbach, R. P. (2019). The Stress and Adversity Inventory for Adolescents (Adolescent STRAIN): Associations with mental and physical health, risky behaviors, and psychiatric diagnoses in youth seeking treatment. *Journal of Child Psychology and Psychiatry*, *60*(9), 998–1009. https://doi.org/10.1111/jcpp.13038

Stalder, T., Evans, P., Hucklebridge, F., & Clow, A. (2010). Associations between psychosocial state variables and the cortisol awakening response in a single case study. *Psychoneuroendocrinology*, *35*(2), 209–214. https://doi.org/10.1016/j.psyneuen.2009.06.006

Stalder, T., Steudte-Schmiedgen, S., Alexander, N., Klucken, T., Vater, A., Wichmann, S., Kirschbaum, C., & Miller, R. (2017). Stress-related and basic determinants of hair cortisol in humans: A meta-analysis. *Psychoneuroendocrinology*, *77*, 261–274. https://doi.org/10.1016/j.psyneuen.2016.12.017

Starr, L. R., Dienes, K., Li, Y. I., & Shaw, Z. A. (2019). Chronic stress exposure, diurnal cortisol slope, and implications for mood and fatigue: Moderation by multilocus HPA-Axis genetic variation. *Psychoneuroendocrinology*, *100*, 156–163. https://doi.org/10.1016/j.psyneuen.2018.10.003

Steinberg, L., & Morris, A. S. (2001). Adolescent development. *Annual Review of Psychology*, *52*(1), 83–110. https://doi.org/10.1146/annurev.psych.52.1.83

Stetler, C. A., & Guinn, V. (2020). Cumulative cortisol exposure increases during the academic term: Links to performance-related and social-evaluative stressors. *Psychoneuroendocrinology*, *114*, 104584. https://doi.org/10.1016/j.psyneuen.2020.104584

Stroud, L. R., Foster, E., Papandonatos, G. D., Handwerger, K., Granger, D. A., Kivlighan, K. T., & Niaura, R. (2009). Stress response and the adolescent transition: Performance versus peer rejection stressors. *Development and Psychopathology*, *21*(1), 47–68. https://doi.org/10.1017/S0954579409000042

Susman, E. J. (2006). Psychobiology of persistent antisocial behavior: Stress, early vulnerabilities and the attenuation hypothesis. *Neuroscience and Biobehavioral Reviews*, *30*(3), 376–389. https://doi.org/10.1016/j.neubiorev.2005.08.002

Trickett, P. K., Noll, J. G., Susman, E. J., Shenk, C. E., & Putnam, F. W. (2010). Attenuation of cortisol across development for victims of sexual abuse. *Development and Psychopathology*, *22*(1), 165–175. https://doi.org/10.1017/S0954579409990332

Twenge, J. M. (2020). Why increases in adolescent depression may be linked to the technological environment. *Current Opinion in Psychology*, *32*, 89–94. https://doi.org/10.1016/j.copsyc.2019.06.036

Uhls, Y. T., Ellison, N. B., & Subrahmanyam, K. (2017). Benefits and costs of social media in adolescence. *Pediatrics*, *140*(Suppl. 2), S67–S70. https://doi.org/10.1542/peds.2016-1758E

Umaña-Taylor, A. J., Quintana, S. M., Lee, R. M., Cross, W. E., Jr., Rivas-Drake, D., Schwartz, S. J., Syed, M., Yip, T., Seaton, E., & the Ethnic and Racial Identity in the 21st Century Study Group. (2014). Ethnic and racial identity during adolescence and into young adulthood: An integrated conceptualization. *Child Development*, *85*(1), 21–39. https://doi.org/10.1111/cdev.12196

White, L. O., Ising, M., von Klitzing, K., Sierau, S., Michel, A., Klein, A. M., Andreas, A., Keil, J., Quintero, L., Müller-Myhsok, B., Uhr, M., Gausche, R., Manly, J. T., Crowley, M. J., Kirschbaum, C., & Stalder, T. (2017). Reduced hair cortisol after maltreatment mediates externalizing symptoms in middle childhood and adolescence. *Journal of Child Psychology and Psychiatry*, *58*(9), 998–1007. https://doi.org/10.1111/jcpp.12700

Wickrama, K. A. S., Lee, T.-K., & O'Neal, C. W. (2015). Stressful life experiences in adolescence and cardiometabolic risk factors in young adulthood. *Journal of Adolescent Health*, *56*(4), 456–463. https://doi.org/10.1016/j.jadohealth.2014.12.009

Zeiders, K. H., Doane, L. D., & Roosa, M. W. (2012). Perceived discrimination and diurnal cortisol: Examining relations among Mexican American adolescents. *Hormones and Behavior*, *61*(4), 541–548. https://doi.org/10.1016/j.yhbeh.2012.01.018

Zeiders, K. H., Hoyt, L. T., & Adam, E. K. (2014). Associations between self-reported discrimination and diurnal cortisol rhythms among young adults: The moderating role of racial-ethnic minority status. *Psychoneuroendocrinology*, *50*, 280–288. https://doi.org/10.1016/j.psyneuen.2014.08.023