Developmental adaptation to stress: An evolutionary perspective

BEYOND DYSREGULATION: DEVELOPMENTAL PLASTICITY AND CONDITIONAL ADAPTATION

A widespread assumption in developmental science is that children raised in supportive and well-resourced environments (e.g., those who live in communities with social networks and resources for young people, who have strong ties to schools and teachers, and who benefit from nurturing and supportive parenting) tend to develop normally and express optimal trajectories and outcomes. By contrast, children raised in high-stress environments (e.g., those who experience poverty, discrimination, low neighborhood attachment, and community disorganization; who feel disconnected from teachers and schools; and who experience high levels of family conflict) are at risk for developmental dysregulation, leading to impaired functioning and problem behaviors that are destructive to themselves and others. These assumptions are powerful and pervasive, if usually implicit, and underlie prominent models of development that focus on dysregulation and pathology [e.g., models of cumulative risk (Evans et al. 2013), toxic stress (Shonkoff et al. 2012), and allostatic load (Lupien et al. 2006, McEwen & Stellar 1993)].

In this review, we survey a growing theoretical and empirical literature focused on the idea that stressful environments may prompt the development of costly but potentially adaptive strategies.[1] This evolutionary–developmental perspective suggests that at least some of the outcomes of early adversity may represent not dysfunction, but rather biologically adaptive strategies for dealing with adversity (e.g., Belsky et al. 1991, Ellis & Del Giudice 2014, Ellis et al. 2017a, Frankenhuis et al. 2016b). This emphasis on developmental adaptation to stress complements the standard emphasis on dysregulation and negative health consequences. We do not deny or downplay the costs of adaptations to adversity, which may include risk for genuine pathology and dysregulation. However, as a counterpoint to the nearly exclusive focus on pathology and dysregulation in the developmental literature, we concentrate on the potential for adaptation. Our goal is to introduce the reader to key ideas and findings, summarize the present state of knowledge, and consider some of the challenges and outstanding questions that face researchers in this area.

In the remainder of this section we review the concepts of developmental plasticity and conditional adaptation, introducing life history theory as a useful framework to conceptualize the effects of early stress across behavioral, physiological, and developmental phenotypes. Next we consider how stress response systems and related neuroendocrine processes may function as mechanisms of plasticity, collecting information about key aspects of the environment and translating it into broad patterns of life history–relevant traits. We highlight the adaptive calibration model (ACM; Del Giudice et al. 2011), a theory of adaptive individual differences in stress physiology that contrasts with disease-focused models such as allostatic load and toxic stress. The next section addresses individual differences in susceptibility to the environment. The effects of stress are moderated by individual factors, giving rise to systematic person–environment interactions. We review the main evolutionary models of differential susceptibility

[1]The term adaptive in biology refers strictly to reproductive fitness and does not imply that a trait is socially desirable or conducive to well-being; this is discussed in greater detail below.

and discuss empirical research on the genetic, physiological, and behavioral mediators of plasticity. Finally, in the section titled Beyond Fragmentation: Toward an Integrated Theory of Stress, Developmental Adaptation, and Health, we use the example of timing of pubertal maturation to illustrate how biological embedding of early adversity can both impair development and guide it in an adaptive manner by promoting survival and reproduction under more harsh and unpredictable conditions, despite the attendant costs to health and well-being. We conclude that it is necessary to understand developmental adaptations to stress—the coherent, functional changes that occur in response to adversity—to understand the costs associated with these adaptations (e.g., allostatic load and its consequences).

Developmental Plasticity and Conditional Adaptation

Theory and research in evolutionary biology have come to acknowledge that, in most species, a single best strategy for survival and reproduction is unlikely to evolve. Instead, the locally optimal strategy normally varies as a function of three overarching factors (see Ellis & Del Giudice 2014). First, the costs and benefits of different strategies depend on the physical and social parameters of an organism's environment (e.g., food availability, mortality rates, quality of parental investment, social competition). This context dependency means that a strategy that promotes success in some environmental contexts may lead to failure in others. Second, the success and failure of different strategies depends on an organism's internal condition and competitive abilities relative to other members of the population (e.g., age, body size, health, history of wins and losses in agonistic encounters). Third, an organism's sex often has important implications for the range of available strategies and their relative costs and benefits.

Because the viability of different survival and reproductive strategies is context and condition dependent, natural selection tends to favor adaptive developmental plasticity, whereby evolved mechanisms reliably guide the development of alternative phenotypes (including anatomy, physiology, and behavior) to match an organism's internal condition and external environment (see West-Eberhard 2003). Developmental plasticity involves "durable biological change in the structure or function of a tissue, organ, or biological system" (Kuzawa & Quinn 2009, p. 132). Importantly, adaptive developmental plasticity is a nonrandom process; it is the outcome of structured interplay between the organism and its environment, shaped by natural selection to increase the capacity of individuals to track both their internal condition and their external environments and, integrating this information, adjust the development of their phenotypes accordingly.

The occurrence of developmental plasticity, which is ubiquitous in the animal world, is uncontroversial (for extensive reviews, see DeWitt & Scheiner 2004, West-Eberhard 2003). For example, it is widely recognized that harsh developmental conditions, such as exposure to a suboptimal intrauterine environment, can induce durable biological changes in the phenotype (e.g., Conradt et al. 2018). The question is whether exposures to physical and psychosocial stressors simply constrain development, as assumed in dysregulation models, or guide it in an adaptive manner.

From an evolutionary perspective, developmental plasticity is critically important for enabling organisms to adapt to stressful conditions. Stress and adversity have always been part of the human experience. Indeed, almost half of children in hunter–gatherer societies—the best

model for human demographics before the agricultural revolution—die before reaching adulthood (e.g., Volk & Atkinson 2013). Thus, from an evolutionary–developmental perspective, stressful rearing conditions, even if those conditions engender sustained stress responses that must be maintained over time, should not so much impair neurobiological systems as direct or regulate them toward patterns of functioning that are adaptive under stressful conditions (Ellis & Del Giudice 2014, Ellis et al. 2012a).

Because adaptive developmental plasticity involves durable change, it is inherently forward looking; that is, it involves predicting—and preparing—for future conditions (both internal and external). Boyce & Ellis (2005, p. 290) make preparation for future environments explicit in their definition of conditional adaptation: "evolved mechanisms that detect and respond to specific features of childhood environments, features that have proven reliable over evolutionary time in predicting the nature of the social and physical world into which children will mature, and entrain developmental pathways that reliably matched those features during a species' natural selective history." A similar emphasis on forward-looking adaptation (focusing on potential later fitness advantages) is conveyed by the phrase predictive adaptive response, which is often used to describe the long-lasting effects of prenatal nutrition, exposure to maternal stress hormones, and other early environmental factors (Bateson et al. 2014). Predictive adaptive responses need to be distinguished from immediate adaptive responses, a term that refers to phenotypic responses that afford immediate adaptive benefits (as when a fetus accelerates parturition in the context of an infected uterus) (Bateson et al. 2014).

Developmental plasticity necessitates developmental trade-offs. For example, tadpoles (*Rana sylvatica*) alter their size and shape based on the presence of dragonfly larvae in their rearing environment (Van Buskirk & Relyea 1998). These alterations involve development of smaller and shorter bodies and deep tail fins. Although tadpoles that do not undergo these morphological changes are highly vulnerable to predation by dragonflies, those that do but end up inhabiting environments that are not shared with dragonflies have relatively poor developmental and survival outcomes. In short, the predator-induced phenotype is only conditionally adaptive. This process highlights the fact that, in many cases, natural selection favors a primary phenotype that yields high payoffs under favorable circumstances and a secondary phenotype that makes the best of a bad situation (West-Eberhard 2003). Adaptations to adversity often entail significant costs and drawbacks, even when they enhance an individual's survival and reproduction prospects.

A conditional adaptation perspective has been applied not only to the development of personality traits such as aggression, impulsivity, and risk taking (e.g., Belsky et al. 1991, Daly & Wilson 2005, Del Giudice 2015b, Ellis et al. 2012a), but also to cognitive abilities such as enhanced stimulus-response learning and executive function components relevant to monitoring changes in the environment (e.g., the ability to rapidly switch between tasks and update working memory) (Mittal et al. 2015, Young et al. 2018; for a review, see Ellis et al. 2017a). Such cognitive traits can be especially useful in unpredictable and fluctuating contexts.

Life History Theory as a Framework for Adaptive Plasticity

In evolutionary biology, a major framework for explaining coordinated patterns of developmental plasticity is life history theory (see Del Giudice et al. 2015, Ellis et al. 2009). Life

history theory addresses how organisms allocate their limited stocks of time and energy to the various activities (including growth, maintenance of bodily tissues, mating, and parenting) that comprise their life cycle. Since all of these activities ultimately contribute to the organism's fitness, devoting time and energy to one will typically involve both benefits and costs, engendering trade-offs between different fitness components. Natural selection favors organisms that schedule developmental activities so as to optimize resource allocation. The resulting chain of resource-allocation decisions—expressed in the development of an integrated suite of physiological and behavioral traits—constitutes the individual's life history strategy. An organism's life history strategy coordinates morphology, physiology, and behavior in ways that maximize expected fitness in a given environment (Ellis et al. 2009).

The critical decisions involved in a life history strategy can be summarized by the fundamental trade-offs between current and future reproduction, between quality and quantity of offspring, and—in sexually reproducing species—between mating and parenting effort (see Del Giudice et al. 2015). At the broadest level of analysis, life history–related traits covary along a dimension of slow versus fast life history. Variation along the slow–fast continuum is observed both between related species and between individuals of the same species (Jeschke et al. 2008, Réale et al. 2010). In humans, some individuals adopt slower strategies characterized by later reproductive development (especially in girls) and delayed sexuality, preferences for stable pair bonds and high investment in parenting, an orientation toward future outcomes, low impulsivity, and allocation of resources toward enhancing long-term survival; others display faster strategies characterized by the opposite pattern (Belsky 2012, Belsky et al. 1991, Del Giudice et al. 2015, Ellis et al. 2009, Figueredo et al. 2006). Fast life history strategies are comparatively high risk, focusing on mating opportunities (including more risky and aggressive behavior), reproducing at younger ages, and producing a greater number of offspring with more variable outcomes. Trade-offs incurred by faster strategies include reduced health, vitality, and longevity (as discussed in the section titled Beyond Fragmentation: Toward an Integrated Theory of Stress, Developmental Adaptation, and Health).

In most organisms, individual life histories are determined by a combination of genetic and environmental factors and often exhibit a remarkable degree of developmental plasticity. Key dimensions of the environment that regulate the development of life history strategies include energy availability, extrinsic morbidity–mortality, and predictability of environmental change (Del Giudice et al. 2015, Ellis et al. 2009). Energetic resources—caloric intake, energy expenditures, and related health conditions—set the baseline for many developmental processes. Energy scarcity slows growth and delays sexual maturation and reproduction, resulting in slower life history strategies. However, when bioenergetic resources are adequate to support growth and development, cues to extrinsic morbidity–mortality and unpredictability generally promote faster strategies.

Extrinsic morbidity–mortality refers to external sources of disability and death that are relatively insensitive to the adaptive decisions of the organism. Environmental cues indicating high levels of extrinsic morbidity–mortality (e.g., exposures to violence, harsh child-rearing practices, premature disability and death of other individuals in one's local ecology) cause individuals to develop faster life history strategies. Faster strategies in this context—a context that devalues future reproduction—function to reduce the risk of disability or death prior to

reproduction. Moreover, high extrinsic morbidity–mortality means that investing in parental care has quickly diminishing returns, which favors reduced parental investment and offspring quantity over quality. In research on industrialized populations, extrinsic morbidity–mortality is often operationalized in terms of socioeconomic adversity because of the relationship between poverty and higher levels of virtually all forms of morbidity and mortality. However, some studies have also collected measures of local mortality rates, developmental exposures to death and injury, or perceived danger in the environment (e.g., Chang & Lu 2018, Copping & Campbell 2015, Johns 2011).

In addition to extrinsic morbidity–mortality, environmental unpredictability also regulates development of life history strategies. In terms of evolutionary selection pressures, environmental unpredictability has been defined as variation in extrinsic morbidity–mortality (Ellis et al. 2009). In terms of adaptively calibrating developmental strategies, cues to environmental unpredictability have typically been operationalized as stochastic changes in ecological and familial conditions (e.g., Belsky et al. 2012, Simpson et al. 2012). In environments that fluctuate unpredictably, long-term investment in development of a slow life history strategy may not optimize fitness. Individuals should instead detect and respond to signals of environmental unpredictability (e.g., erratic neighborhood conditions, frequent residential changes, fluctuating economic conditions, changes in family composition) by adopting faster strategies.

Since danger and unpredictability are core defining features of stress, life history theory offers integrative principles for making predictions about how early stress shapes the development of multiple behavioral traits, as well as the associations of these traits with patterns of growth, sexual maturation, metabolism, immunity, and other life history–related systems. The life history perspective has inspired developmental research on the links between familial and ecological stress and later outcomes such as impulsivity and risk taking, pubertal maturation, sexual behavior, reproductive timing, and health (e.g., Belsky et al. 2012, 2015b; Brumbach et al. 2009; Copping & Campbell 2015; James et al. 2012; Mell et al. 2018; Sheppard et al. 2016; Simpson et al. 2012; Sung et al. 2016; Szepsenwol et al. 2015). This work has been especially important in advancing our understanding of the key distinction between childhood exposures to extrinsic morbidity–mortality cues and environmental unpredictability (Ellis et al. 2009), each of which has been found to uniquely predict the development of life history–related traits and associated health outcomes.

Outstanding Questions and Challenges

The biological concept of plasticity, when applied to human development, brings with it some important insights but also many complex problems and questions. For example, standard models of plasticity assume that early stress carries predictive information about the future state of the environment (e.g., danger and consequent high mortality). An alternative (though not incompatible) possibility is that early stress inflicts irreparable damage to the developing organism; in this view, plasticity mechanisms respond to the individual's compromised internal state and not to hypothetical cues about its future environment (Rickard et al. 2014). Distinguishing between external and internal (or somatic state–based) accounts of plasticity is going to require much careful empirical work, as well as more refined theoretical models than are currently available (see Del Giudice 2014a, Hartman et al. 2017). Other important questions

concern specific sensitive periods for the effects of early stress and their evolutionary logic. The idea that the period from conception to the end of early childhood (i.e., the first 5–7 years of life) is especially critical is widespread in the literature. However, the duration of sensitive windows may itself depend on earlier experiences (Fawcett & Frankenhuis 2015); moreover, a long-lived species like ours may be characterized by multiple windows of plasticity, including key developmental transitions such as the beginning of middle childhood and the onset of puberty (see Del Giudice 2014b, Del Giudice & Belsky 2011, Ellis 2013, Shulman et al. 2016).

Developmental research based on life history concepts faces similar challenges. There is still much that we do not know about life history strategies, especially when moving from considering evolution within a population (the standard focus of biological models) to considering development within a single individual (see Mathot & Frankenhuis 2018). Mathematical models of life history evolution also raise the possibility that some long-term outcomes of early stress are the legacy of immediate adaptive responses for infant survival, rather than adult adaptations for mating and reproduction (i.e., predictive adaptive responses; see Wells & Johnstone 2017). Within evolutionary psychology, there is a lively ongoing debate about the best way to measure life history–related behavioral traits and integrate them with demographic traits such as puberty and reproductive timing (e.g., Black et al. 2017, Richardson et al. 2017). The inferences that can be drawn from human research are also limited by the widespread lack of control for potential genetic confounding in developmental studies that correlate early environmental variables with later outcomes (see Barbaro et al. 2017). The problem of genetic confounding has been addressed in a minority of studies (e.g., Ellis et al. 2012b, Tither & Ellis 2008); fortunately, more researchers are starting to explicitly incorporate genetic information (e.g., Gaydosh et al. 2018), and the results will undoubtedly prompt revisions and refinements of current ideas.

BEYOND ALLOSTATIC LOAD: STRESS RESPONSE SYSTEMS AS MECHANISMS OF CONDITIONAL ADAPTATION

How does repeated or chronic childhood adversity shape biobehavioral development and, through it, mental and physical health? There is widespread agreement in the developmental literature that early life adversities (both prenatal and postnatal) can cause enduring changes in biological and developmental systems (i.e., biological embedding) that affect health and behavior over the life course (e.g., Hertzman 2012). Controversy exists, however, regarding the functional versus dysfunctional role of biological embedding in regulating (or dysregulating) the development of the phenotype.

In developmental models that are primarily focused on explaining dysregulation, such as models of toxic stress (Shonkoff et al. 2012) and allostatic load (Lupien et al. 2006, McEwen & Stellar 1993), biological embedding is construed negatively. These models postulate that biological responses to stress are usually beneficial in the short term (i.e., that they facilitate immediate adaptive responses), but protracted activation of stress responsive systems is maladaptive and toxic in the long term. Biological embedding of early life stress causes disruptions of brain structure and function, resulting in dysregulation of physiological mediators—autonomic, neuroendocrine, metabolic, and immune—that are "the precursors of

later impairments in learning and behavior as well as the roots of chronic, stress-related physical and mental illness" (Shonkoff et al. 2012, p. e236). As eloquently stated by Juster and colleagues (2011, p. 725), the wear and tear of toxic stress and altered stress hormone functioning "inexorably strains interconnected biomarkers that eventually collapse like domino pieces trailing toward stress-related endpoints."

Allostatic load is a term used to describe the wear and tear that results from repeated allostatic adjustments (i.e., adaptation to stressors), which expose one to adverse health consequences that increase as a person ages. According to the allostatic load model (ALM), there is an optimal level of stress responsivity, and both hyper- and hypo-activation of physiological mediators are routinely described as dysfunctional deviations from the norm, usually caused by a combination of excessive stress exposure and genetic or epigenetic vulnerability. In this framework, developmental stress exposures are regarded as risk factors for a wide array of symptoms and disorders. While some authors have argued that optimal adaptation is fostered by environments that contain moderate amounts of stressors (e.g., Rutter 1993), the underlying assumption remains that a single best environment exists, and that deviations from that optimum cause dysregulation and pathology.

Accepting these assumptions without placing them in a larger evolutionary–developmental framework has likely impeded our understanding of the role of stress response systems in adaptively regulating development (see Ellis & Del Giudice 2014). Specifically, models of allostatic load focus on the long-term costs of childhood stress and adversity—the wear and tear on multiple organ systems induced by chronic stress—but do not address the benefits of calibrating autonomic, neuroendocrine, metabolic, and immune systems to match current and future environments (i.e., predictive adaptive responses). We argue that this overemphasis on costs misses something fundamental about developmental adaptation to stress and thus weakens the conceptual power of the ALM. The result has been an imbalanced approach to research that has yielded dramatically more empirical knowledge about dysfunction than about adaptive function, making it difficult to gain a coherent big picture of the subject matter.

The Adaptive Calibration Model

A promising alternative to the ALM is provided by the ACM (Del Giudice et al. 2011), a theory of individual differences in stress responsivity that builds on the concepts of life history theory and developmental plasticity. The ACM supplements the ALM and revises some of its key assumptions, thus laying the foundation for a broad theory of individual differences (for a more extended discussion, see Ellis & Del Giudice 2014). The central tenet of the ACM is that physiological stress response systems, including the autonomic nervous system and the hypothalamic–pituitary–adrenal (HPA) axis, operate as mechanisms of conditional adaptation, with a key role in regulating the development of individual life history strategies.

In the ACM, the activation of autonomic and adrenocortical responses during childhood provides crucial information about threats and opportunities in the environment, their type, and their severity. Over time, this information becomes embedded in the parameters—recurring set points and reactivity patterns—of these physiological systems, which in turn provide the developing person with statistical summaries of key dimensions of the environment. For example, sustained activation of the HPA axis is generated by exposures to danger, unpredictable

or uncontrollable contexts, and social evaluation, as well as by energetic stress (Dickerson & Kemeny 2004); thus, the HPA axis tracks the key environmental variables involved in regulation of alternative life history strategies. In turn, individual differences in the functioning of stress response systems regulate the coordinated development of a broad cluster of life history–related physiological and psychological traits, including growth and maturation, sexual and reproductive functioning, social learning, aggression, competition and risk taking, pair bonding, and related factors (Del Giudice et al. 2011, Ellis & Del Giudice 2014). Other systems that contribute to life history regulation include the hypothalamic–pituitary–gonadal axis; the serotonergic, dopaminergic, and oxytocinergic systems; and the immune system (discussed in more detail below). Not coincidentally, all of these systems engage in extensive bidirectional cross talk with stress response systems (for reviews, see Del Giudice et al. 2011, Ellis & Del Giudice 2014).

Patterns of stress responsivity.

In contrast to the notion of a single optimal stress responsivity pattern (as per the ALM), the ACM proposes that two different adaptive patterns of stress responsivity emerge in the context of high childhood adversity. The first pattern, labeled vigilant, is characterized by heightened physiological stress reactivity (across the sympathetic nervous system and HPA axis) and is predicted to develop in dangerous or unpredictable contexts, where it enables people to cope with threats in their physical and social environment. In the ACM, the vigilant profile mediates heightened vigilance and attention to threats; it is associated with elevated levels of anxious and depressed behaviors (especially in females) and increased risk taking, agonistic social competition, and reactive aggression (especially in males), consistent with a fast life history strategy. The second pattern, labeled unemotional, is characterized by low physiological stress reactivity across autonomic and adrenocortical systems and is predicted to develop under conditions of severe, chronic stress. According to the ACM, generalized unresponsivity in this context inhibits sensitivity to social feedback and can increase risk taking by blocking information about dangers and threats in the environment (e.g., leading to low anxiety). In line with a fast life history strategy, the unemotional profile is associated with low empathy and cooperation, impulsivity, competitive risk taking, and antisocial behavior, including high levels of proactive and instrumental aggression, especially in males. The hypothesized vigilant and unemotional profiles, reflecting the emergence of both high and low stress responsivity patterns in the context of adversity, have been documented in longitudinal studies of Dutch adolescent males (Ellis et al. 2017c) and children in the United States (Laurent et al. 2014), although with some deviations from expected patterns (for a discussion, see Ellis et al. 2017b).

More generally, psychosocial stress and adversity over the course of development can either upregulate or downregulate levels of autonomic and adrenocortical reactivity. The empirical literature on this topic remains conflicted. On the one hand, many studies link stressful rearing experiences to hyper-reactivity, supporting the vigilant responsivity pattern; on the other hand, an equally impressive number of studies link stressful rearing experiences to hypo-reactivity, supporting an unemotional responsivity pattern (for reviews, see Del Giudice et al. 2011, Ellis et al. 2017b). In the ACM, we proposed that some children who grow up under high-stress conditions will first develop high stress responsivity in early childhood (vigilant profile), then shift to low responsivity during juvenility or adolescence (unemotional profile) as social competition becomes a central developmental task. We also hypothesized that this trajectory would be more common in males (Del Giudice et al. 2011). A shift from hyper- to hypo-

reactivity may help to explain an otherwise puzzling finding in the literature: that the overall association between basal cortisol and aggressive/externalizing behavior tends to be positive in preschoolers but negative starting from middle childhood (Alink et al. 2008).

The proposed developmental transition from a vigilant to an unemotional profile has been demonstrated in longitudinal studies of individuals with a history of child maltreatment. Doom et al. (2014) reported that such individuals transitioned from initially high levels of basal afternoon cortisol to blunted levels in middle childhood. Likewise, Trickett et al. (2010) found that females with a history of child sexual abuse transitioned across development from initially elevated levels of morning cortisol to attenuated levels starting in adolescence, whereas females who were not sexually abused maintained similar normative morning cortisol levels across development. Consistent with the unemotional responsivity pattern, youth exposed to maltreatment also display blunted cortisol reactivity by early adolescence, and this effect tends to be stronger in boys than in girls when contrasting maltreated and comparison groups (see Trickett et al. 2014, figure 2). A similar sex-specific effect was found in a recent study in South Africa: Adverse childhood experiences predicted blunted cortisol reactivity in boys but increased reactivity in girls (Fearon et al. 2017).

The hypothesized developmental transition from a vigilant to an unemotional profile converges with the well-established pattern of HPA responses to chronic stress: Initially, stressors tend to acutely upregulate basal cortisol levels in the time period proximal to stressor onset, but over time, severe chronic stress exposures tend to downregulate hormonal output and elicit a flat diurnal cortisol rhythm (for a meta-analysis, see Miller et al. 2007). Extending these findings on basal cortisol activation, a meta-analysis of cortisol responsivity to social stress (Bunea et al. 2017) found that early life adversity was robustly associated with blunted cortisol reactivity in adults (large effect) but not in children and adolescents (small effect). Given the focus of this meta-analysis on adverse childhood experiences that were typically chronic and severe, the results are consistent with the ACM's proposed developmental transition to an unemotional profile under high-stress conditions.

Extending the adaptive calibration model: adaptive calibration of the immune system.

Another mechanism through which childhood adversity may promote faster life history strategies is through calibration of immune system parameters. As reviewed by Nusslock & Miller (2016), childhood stress exposures sensitize cortico-amygdala neural circuitry in a manner that enhances vigilance and threat processing, and they alter the activity of immune cells in a manner that promotes and sustains inflammation. For example, greater family stress, trauma, and adversity are associated with heightened amygdala reactivity to negative emotional stimuli (e.g., Herringa et al. 2016), higher concentration of inflammation-related molecules (e.g., Baumeister et al. 2016), and profiles of gene expression consistent with a proinflammatory bias (e.g., Robles et al. 2018). Nusslock & Miller (2016, p. 25) proposed that cortico-amygdala threat circuitry and immune cells that propagate inflammation are "components of an integrated, bidirectional network that detects threats to well-being and mobilizes behavioral, physiologic, and inflammatory resources for coping." Most importantly, cross talk between these two components appears to be potentiated by early adversity. Nusslock & Miller (2016) conceptualized this enhanced cross talk as promoting immediate adaptive responses to danger, as when brain-to-immune signaling readies the immune system for pathogen eradication and tissue healing, or

when immune-to-brain signaling enhances threat vigilance. In the long run, these processes may contribute to the pathogenesis of emotional and physical health problems.

The relationship between immune functioning and life history strategies is most likely bidirectional. Like stress response systems, the immune system collects and relays information about important sources of danger and mortality, specifically the prevalence and type of pathogens in the local environment and the individual's ability to effectively cope with them. Thus, early immune activity should contribute to the development of alternative life history strategies (e.g., Hill et al. 2016, Kopp & Medzhitov 2009). At the same time, different life history strategies can be expected to entail different patterns of investment in immune defenses. For example, researchers have begun to examine the possibility that faster life history strategies may predict increased investment in innate immunity (including inflammation) at the expense of acquired immunity (Georgiev et al. 2016).

Comparing the Adaptive Calibration Model and Allostatic Load Model

The ACM and ALM diverge considerably in how they deal with cost–benefit trade-offs, individual differences, and long-term developmental changes.

Different views of cost–benefit trade-offs in development.

In an evolutionary framework, the terms adaptive and maladaptive denote the effect of a trait or behavior on biological fitness. From the standpoint of the individual organism, adaptive traits are those that enhance its expected fitness more than do potential alternatives. However, all adaptations have fitness costs as well as benefits; to be adaptive, a trait does not have to be cost free, but only to yield a positive overall contribution to fitness. This notion of adaptation and maladaptation contrasts sharply with how the same terms are usually employed in health- and disease-focused disciplines, wherein adaptive refers to traits and behaviors that are socially desirable (e.g., that promote health, safety, subjective well-being, and mutually rewarding social relations), while maladaptive refers to traits and behaviors that are socially undesirable (e.g., that have aversive or health-damaging effects).

The ALM makes no distinction between these two meanings of adaptive and maladaptive. Indeed, maladaptation is typically inferred whenever there are substantial costs to the organism. For example, if elevated cortisol levels in adolescents are associated with an undesirable outcome, such as reduced working memory, then elevated cortisol is deemed maladaptive (and classified as a biomarker of allostatic load) (see Juster et al. 2011). This reasoning ignores the crucial fact that biological processes are maintained by natural selection when their fitness benefits outweigh the costs, not when they are cost free; indeed, even large costs can be offset by large enough expected benefits. Because of the failure to distinguish between (mal)adaptive and (un)desirable outcomes, most applications of the ALM do not adequately address the trade-offs involved in the development of physiological and behavioral phenotypes; as a consequence, the ALM literature often lacks a theory of adaptive individual variation in stress responsivity. In the ALM, the focus is on optimal parameter values of stress response systems, as defined by covariation with desirable health outcomes; deviations from these optimal settings form the basis of dysregulation.

In contrast, the ACM emphasizes adaptation in context and posits that optimal stress response parameters vary as a function of environmental conditions, as illustrated by the vigilant and unemotional responsivity patterns. From this perspective, the notion of globally optimal responsivity levels is problematic. For example, consider heightened stress responsivity in dangerous, unpredictable environments (as in the vigilant pattern). In the ACM, it is hypothesized that the costs of repeated stress system activation are offset by improved management of danger (Del Giudice et al. 2011). Although the system is on a hair trigger, with a resulting increase in anxiety or aggression, few instances of actual danger will be missed. In addition, engaging in a fast, present-oriented life history strategy makes it optimal to discount the long-term health costs of chronic activation of stress response systems if the immediate benefits are large enough. In the ALM framework, the same pattern of responsivity would be treated as dysfunctional because the stress response is deployed even in the absence of true dangers (resulting, for example, in excessive responding or unnecessary triggering) (e.g., Lupien et al. 2006) and because of the associated undesirable states and health risks (e.g., anxiety, increased cardiovascular risk).

Different views of long-term adaptations to stress.

According to the ACM, childhood adaptations to stress may eventuate in long-term adaptive changes in biobehavioral systems. Herein lies the key difference between the ACM and ALM. In the ALM, energy devoted to mounting autonomic, neuroendocrine, metabolic, and immune responses to threat (immediate adaptive responses) is traded off against wear and tear on multiple organ systems. This wear and tear, according to the ALM, results in dysfunctional changes in the regulatory parameters of stress response systems (i.e., dysregulation). These biologically embedded changes are commonly viewed as indicators of allostatic load, reflecting the costs of stress-induced trade-offs; they are explicitly not viewed as predictive adaptive responses. By contrast, the ACM conceptualizes these trade-offs as decision nodes in allocation of resources. Through biological embedding, each decision node influences the next (opening up some options, foreclosing others), and thus progressively favoring one developmental trajectory over another. Predictive adaptive responses are instantiated through this chain of resource-allocation decisions, which calibrates the developing phenotype to current (and expected future) conditions. In total, the ACM shifts the emphasis from dysregulation to conditional adaptation. From this perspective, development of a fast life history strategy in dangerous and unpredictable contexts is not impairment or dysfunction; it is a coherent, organized response to stress that has been shaped by a natural selective history of recurring exposures to such contexts (for a detailed human example, see the section titled Beyond Fragmentation: Toward an Integrated Theory of Stress, Developmental Adaptation, and Health).

Outstanding Questions and Challenges

The ACM and ALM offer sharply different perspectives on the costs and benefits of adaptations to stress, particularly in regard to long-term developmental trajectories. The most urgent task for researchers is to design studies capable of distinguishing between the two models. At present, studies based on the ALM focus solely on the costs of childhood adversities (allostatic load) and do not even attempt to explore the potential benefits of the attendant physiological and behavioral changes (adaptive calibration). As an initial step in this direction, Del Giudice et al. (2011) made specific hypotheses about how different environmental conditions should give rise to adaptive profiles of stress responsivity, growth and maturation, and behavior. Some

predictions have been supported—for example, both high- and low-responsivity patterns have been identified in safe as well as harsh conditions (e.g., Del Giudice et al. 2012; Ellis et al. 2005, 2017c; Fearon et al. 2017; Gunnar et al. 2009). Other predictions (for example those concerning sex differences in high- versus low-responsivity profiles) have received mixed support, while others still are in need of revision (see Ellis et al. 2017b). This is to be expected, since moving from the general principles reviewed in this article to empirical predictions requires many additional assumptions about the functions and correlates of particular physiological variables.

As discussed above, another important task will be to extend the ACM to include metabolism and immunity, two key domains that have received considerable attention in the ALM framework. The ultimate goal should be to build a detailed map of how biologically embedded changes regulate developmental adaptations to stress, from maturation and reproductive functioning to learning and behavior. By delineating intervening functional changes that mediate the effects of early adversity on later mental and physical health problems, such a map could transform research on stress–health relations.

Finally, an adaptive calibration perspective raises methodological and statistical challenges that have yet to be adequately addressed. Notably, ACM responsivity profiles combine stress physiology with a range of other life history–related traits. Analyses that focus exclusively on the parameters of stress response systems (e.g., autonomic reactivity, cortisol levels) are unlikely to recover functionally meaningful patterns (for an example of this issue, see Peckins et al. 2015). However, properly combining behavioral, developmental, and physiological variables is a challenging task that will require sophisticated statistical approaches (see Ellis et al. 2017b,c).

BEYOND DIATHESIS STRESS: DIFFERENTIAL SUSCEPTIBILITY TO THE ENVIRONMENT

What makes developmental plasticity potentially adaptive is that it can match the organism's phenotype to its environment (or internal condition) in ways that improve the organism's capacity for survival and reproduction (West-Eberhard 2003). We note above that plasticity is rarely without costs; these include the costs and trade-offs involved in producing the appropriate phenotype (e.g., adaptations to predators in tadpoles), but also the extra time spent sampling the environment before specializing. Moreover, the cues received from the environment are usually imperfect and can lead to incorrect predictions; as a result, plastic organisms sometimes end up developing a mismatched phenotype that decreases their fitness instead of enhancing it (e.g., a predator-adapted phenotype when actual predation risk is low) (see Frankenhuis & Panchanathan 2011, Murren et al. 2015).

For all these reasons, plasticity is not always the optimal strategy for organisms. This creates the potential for the evolution of individual differences in plasticity: Within the same population, some individuals may respond strongly to their rearing conditions, while others may be barely affected (Belsky & Pluess 2009, Boyce & Ellis 2005, Ellis et al. 2011a). These differences have important implications for studying the effects of stress on development: If conditional adaptation is not a universal strategy, then the predicted correlations between early adversity and subsequent trajectories will be significantly attenuated by individual variation in plasticity.

Biological models typically assume that individual differences in plasticity are determined by differences in genotype. Another possibility is that early environmental factors also shape plasticity to later aspects of the environment; for example, prenatal exposure to maternal stress hormones may modulate the child's sensitivity to the quality of parenting and family relations (Boyce & Ellis 2005, Conradt et al. 2018, Del Giudice 2015a, Pluess & Belsky 2011). In this scenario, early stress and adversity play a dual role—they work as cues for plasticity mechanisms, but also modulate the sensitivity of the same mechanisms over time (Boyce & Ellis 2005).

The notion that some individuals are especially vulnerable to negative or stressful experiences is not new, as exemplified by the classic developmental concept of diathesis stress. However, standard vulnerability models focus exclusively on negative outcomes and lack a functional theory of individual differences that explains why such differences may evolve and persist in a population. This focus has changed with the rise of differential susceptibility models over the past 20 years (Belsky 1997, 2005; Boyce & Ellis 2005; Boyce et al. 1995; Ellis et al. 2006, 2011a). According to these models (reviewed below), many of the same factors that determine increased sensitivity to stress and adversity may also confer enhanced responsivity to the positive, supportive aspects of the environment. In other words, highly susceptible individuals respond to the quality of their environment for better and for worse (Belsky et al. 2007, Boyce et al. 1995).

Models of Differential Susceptibility

Models of differential susceptibility are based on the idea that adaptive plasticity has costs and potential drawbacks; they postulate the existence of individual differences in plasticity that give rise to systematic person–environment interactions. At the same time, different models conceptualize the costs of plasticity in somewhat different terms and propose alternative mechanisms for the development of individual differences (see Belsky & Pluess 2016, Del Giudice 2016, Ellis et al. 2011a).

Differential susceptibility theory.

According to differential susceptibility theory (Belsky 1997, 2005), the biological function of differential susceptibility is to limit the evolutionary costs of plasticity by making some individuals resistant to environmental influences, including those exerted by parents. In other words, the theory predicts the existence of differences in susceptibility as a form of insurance against developmental errors and mismatches. Indeed, mathematical models show that individual differences in plasticity among siblings spread the risk of mismatch (a pattern called bet hedging in evolutionary biology) and can be favored by natural selection in response to unpredictable fluctuations in the environment (provided that other fairly restrictive assumptions are met) (see Frankenhuis et al. 2016a). In Belsky's (1997, 2005) original formulation, plasticity was assumed to be essentially a function of genetic factors. Following biological sensitivity to context theory (see below), the model was later expanded to include both genetic and early environmental effects (such as prenatal exposure to maternal stress hormones) as factors regulating the development of differential susceptibility (Belsky & Pluess 2016, Pluess & Belsky 2011).

Biological sensitivity to context.

The biological sensitivity to context model (Boyce & Ellis 2005; Ellis et al. 2005, 2006) is rooted

in developmental research on health and adversity. Boyce and colleagues (1995) found that children high in cardiovascular and immune reactivity have worse health outcomes in stressful environments but better outcomes in positive and supportive environments. Boyce & Ellis (2005) reframed these findings in an evolutionary framework and developed the biological sensitivity to context model. According to this model, differential susceptibility to the environment is primarily mediated by individual differences in neurobiological traits, specifically variation in autonomic and adrenocortical reactivity to stress. This mechanistic focus is a key distinguishing feature of the biological sensitivity to context model (and provided the conceptual framework for the ACM responsivity patterns discussed above).

From an evolutionary standpoint, the biological sensitivity to context model links individual differences in susceptibility to the coexistence of generalist phenotypes (low biological sensitivity to context; metaphorically referred to as dandelions) and specialist phenotypes (high biological sensitivity to context; metaphorically referred to as orchids). Whereas generalists do reasonably well in most environments, specialists calibrate development to achieve high fitness in some kinds of environments (e.g., dangerous and unpredictable ones) but not in others. The most distinctive prediction of the biological sensitivity to context model is that of a U-shaped curvilinear relationship between early adversity and stress responsivity: Children growing up in very safe or very stressful conditions should develop the highest susceptibility to environmental influences (and, as a result, become specialized to their particular niche). This prediction has received some empirical support in human developmental research (e.g., Del Giudice et al. 2012; Ellis et al. 2005, 2017c; Gunnar et al. 2009). The hypothesized U-shaped curve is also consistent with simulations suggesting that, in the presence of person–environment interactions such as those postulated by differential susceptibility models, it may be optimal to express higher levels of plasticity at both ends of an environmental continuum (Del Giudice 2015a).

Patterns of person–environment interaction.

A notable contribution of differential susceptibility models has been to direct the attention of researchers to the shape of person–environment interactions. In the classic diathesis stress scenario, vulnerable and resilient individuals develop in similar ways when they are exposed to favorable conditions but diverge at increasing levels of stress and adversity. In contrast, models of differential susceptibility predict that high- and low-susceptibility individuals should diverge in both safe and stressful conditions and only become similar when they experience moderate levels of adversity (crossover interactions) (see Ellis et al. 2011a). More recently, Pluess & Belsky (2013) proposed that some individuals may exhibit vantage sensitivity, a pattern symmetrical to that of diathesis stress whereby plasticity is only expressed in safe, supportive environments. In both the diathesis stress and differential susceptibility scenarios, adaptations to stress (e.g., risk taking, heightened or blunted HPA reactivity, altered immune parameters) are expected to develop more reliably in highly susceptible individuals (so that the overall effects of stress are attenuated by individual variation in susceptibility). Under the vantage sensitivity scenario, however, adaptations to stress—to the extent that they occur—are expressed uniformly by all individuals in the population. Devising methods to reliably distinguish among these three interaction patterns has become the focus of a growing methodological literature (e.g., Belsky et al. 2013, Roisman et al. 2012).

While most research in this area has been descriptive, the possibility that person–environment interactions may fall into qualitatively different patterns raises a deeper question, namely, what conditions can be expected to favor the evolution or development of each pattern (e.g., Pluess 2015). For example, initial mathematical models indicate that interaction patterns resembling the classic diathesis stress template should evolve more frequently than patterns of vantage sensitivity, unless negative states of the environment (stress, adversity) occur much more often than positive ones (Del Giudice 2017a). The prediction that vantage sensitivity should be comparatively rare is consistent with the fact that this pattern has only been detected in a small minority of studies (for a review, see Del Giudice 2017a).

Markers of Susceptibility

What makes some individuals more susceptible than others to environmental influences, including exposure to stress and adversity? More specifically, are there traits or markers that systematically predict enhanced plasticity? To summarize the state of this very active area of research, we distinguish between three levels of analysis: genetics, physiology, and behavior (see also Belsky & Pluess 2009, 2016).

Genetic markers.

In the search for genetic markers of susceptibility, researchers have tested genotype–environment (G × E) interactions between particular genetic variants and observed environmental variables, such as parenting quality (correlational G × E), or between genetic variants and exposure to randomized conditions or treatments, such as interventions to reduce aggression (experimental G × E). Studies of single candidate genes have focused mainly on genes involved in serotonergic and dopaminergic signaling, such as the dopamine receptor 4 gene (*DRD4*) or the serotonin transporter gene (*SLC6A4*). Less often, researchers have considered genes with roles in oxytocinergic signaling [e.g., the oxytocin receptor gene (*OXTR*)], the HPA axis [e.g., the corticotropin releasing factor receptor 1 gene (*CRHR1*)], and other brain-related pathways [e.g., the brain-derived neurotrophic factor (*BDNF*)] (see Belsky & Pluess 2016, Del Giudice 2017a, Moore & Depue 2016).

The findings of individual studies in this area are highly variable (e.g., Belsky et al. 2015a) and likely inflated by a high rate of false positives, as is typical of candidate gene studies (Dick et al. 2015). So far, the most promising results come from meta-analyses of correlational G × E studies of dopaminergic and serotonergic genes (Bakermans-Kranenburg & van IJzendoorn 2011, van IJzendoorn et al. 2012) and from more recent meta-analyses of experimental G × E studies involving the same genes (Bakermans-Kranenburg & van IJzendoorn 2015, Van IJzendoorn & Bakermans-Kranenburg 2015). It remains to be seen whether these results will be consistently replicated in large samples. Another strategy to deal with the low statistical power of single-gene studies is to pool multiple variants together into a polygenic score. Several studies employing polygenic scores of serotonergic, dopaminergic, HPA-related, and other genes (such as *BDNF*) have detected significant G × E interactions, generally consistent with differential susceptibility patterns (e.g., Belsky & Beaver 2011, Cicchetti & Rogosh 2012, Feurer et al. 2017, Keers & Pluess 2017, Silveira et al. 2017).

Physiological markers.

According to the biological sensitivity to context model, a key marker of susceptibility is elevated physiological reactivity to environmental challenges, including both autonomic and HPA axis reactivity (Boyce & Ellis 2005, Ellis et al. 2005). Many empirical studies have found patterns consistent with this idea (for reviews, see Boyce 2016, Obradović 2012), although there are also contradictory findings (see Sijtsema et al. 2013). Importantly, there is emerging evidence that stress reactivity itself may be the product of G × E interactions between early adversity and plasticity-enhancing genetic variants, in line with the hypothesis that initial environmental cues modulate susceptibility to later experiences, particularly in individuals who are already genetically plastic (Allegrini et al. 2018). More recently, Del Giudice and colleagues (2018) speculated that exposure to higher levels of androgens (e.g., testosterone) during prenatal and early postnatal life should increase plasticity for the many physiological and behavioral traits that show higher variability in males. This hypothesis is still awaiting empirical testing; if supported, it would extend the range of differential susceptibility markers beyond the typical emphasis on central neurotransmitters and stress physiology.

Behavioral markers.

In the foundational papers of differential susceptibility theory, Belsky (1997, 2005) suggested that behavioral traits such as difficult temperament and negative emotionality may serve as markers of differential susceptibility in infants and children. This hypothesis has subsequently been tested in dozens of studies (see Belsky & Pluess 2016); a recent meta-analysis confirmed that difficult temperament and early negative emotionality (before 1 year of age) moderate the effects of quality of parenting on child development in a way consistent with differential susceptibility (Slagt et al. 2016). Other researchers have pointed to sensory processing sensitivity as a plausible marker of susceptibility (Boyce & Ellis 2005, Pluess 2015, Pluess et al. 2018). People high in sensory processing sensitivity show heightened awareness of sensory stimulation, susceptibility to overstimulation, elevated emotional reactivity (including both positive and negative emotionality), and behavioral inhibition in novel situations (Aron et al. 2012). From a neurobiological perspective, Moore & Depue (2016) argued that individual differences in the activity of multiple brain systems (including dopaminergic, serotonergic, and oxytocinergic pathways) contribute to a general dimension of reactivity to external stimulation, which in turn determines susceptibility. This neurobiological framework fits with the idea that susceptibility is, at least in part, a function of the individual's sensitivity to environmental stimuli, as reflected, for example, in measures of sensory processing sensitivity (Pluess 2015). Initial results support a role for sensory processing sensitivity in moderating some associations between parenting and externalizing behavior (Slagt et al. 2018); however, there is still little empirical evidence that this trait is a general marker of susceptibility, as has often been suggested in the literature (e.g., Pluess et al. 2018).

Outstanding Questions and Challenges

The study of differential susceptibility faces some formidable methodological challenges. Reliably distinguishing between different types of interaction patterns with commonly used metrics requires large samples (Del Giudice 2017b), and many correlational studies in this area (including single-gene correlational G × E studies) are seriously underpowered for the task. Exciting developments on this front include new statistical models that combine multiple genes

and multiple environmental variables into a single interaction test (Jolicoeur-Martineau et al. 2017) and indirect methods that use data from twin studies to infer the shape of the underlying interaction patterns (South et al. 2017).

Although new statistical tools and improved methodology can be expected to yield substantial benefits, we believe that the most pressing challenges in this area are theoretical in nature (see Del Giudice 2017a,b). For example, detecting an interaction that matches a diathesis stress template says little about the underlying developmental process, which may involve maladaptive vulnerability to stressors, but also adaptive phenotype–environment matching (Del Giudice 2017a). While differential susceptibility research was initially propelled by novel theoretical models and ideas, over time, the focus of most researchers has shifted to issues of measurement and data analysis. As a result, theoretical progress has been slow, and many deeper questions remain unanswered. For example, it is unclear when selection should favor domain-general plasticity mechanisms that simultaneously regulate multiple traits, versus domain-specific mechanisms that only control a particular phenotype (see Belsky & Pluess 2016). Different models of susceptibility also make different assumptions about the relationship between plasticity and specialization. In classic generalist–specialist models (Wilson & Yoshimura 1994; see also Frankenhuis et al. 2016a), generalists can fit into multiple niches owing to increased plasticity, whereas specialists develop relatively fixed phenotypes. However, a plausible alternative to this model is that plasticity supports enhanced specialization (Del Giudice 2017a, Murren et al. 2015); in fact, this scenario may be more consistent with developmentally focused differential susceptibility models because it assumes that heightened physiological and negative emotional reactivity enable plasticity during an early sensitive period (but may not operate that way later in development, after an orchid child specializes its phenotype). Other unresolved issues concern the relative strength of various sources of individual differences (e.g., direct effects of the environment versus G × E interactions), as well as the role of shared environmental factors (those that act similarly on siblings in the same family) versus nonshared factors (unique to each sibling) in the development of plasticity (Del Giudice 2016). Only through sustained theoretical effort will it be possible to address these questions and use the answers to inform empirical research.

BEYOND FRAGMENTATION: TOWARD AN INTEGRATED THEORY OF STRESS, DEVELOPMENTAL ADAPTATION, AND HEALTH

The central question addressed in this review is whether childhood exposures to adversity simply constrain development, as assumed in dysregulation models, or guide it in an adaptive manner. In this section, we use the example of pubertal development to demonstrate how both processes operate simultaneously. Early life stress exposures result in long-term, potentially permanent changes in physiological systems that both constrain development (increasing morbidity and mortality risks) and adaptively calibrate it to enhance fitness under stressful conditions. Stress-mediated development of alternative life history strategies is the key to understanding this dual process. Biological embedding of early life stress functions to calibrate life history–related traits, including timing of puberty; allostatic load and associated mental and physical impairments can be understood, in part, as costs and side effects of these adaptive processes.

Timing of Puberty: A Case Study

Pubertal maturation is a dynamic biological process—punctuated by visible changes in stature, body composition, and secondary sexual characteristics—that culminates in the transition from the prereproductive to the reproductive phase of the human life cycle (Ellis 2004). Perhaps the most striking feature of human pubertal and sexual development is its variation. Some individuals complete puberty in elementary school, while others are still relatively undeveloped when they start high school; some begin sexual activity and reproduction as teenagers, while others delay having children until decades later; some pursue short-term sexual relationships with multiple partners, while others commit to a single long-term partner for life. This variation begins with individual differences in maturation of the reproductive axis—when and how fast puberty occurs—and then feeds forward to many other reproductive characteristics.

Early timing of puberty is an important component of a fast life history strategy. Women who experience early pubertal development, compared with their later-maturing peers, tend to have higher levels of serum estradiol and lower sex hormone binding globulin concentrations that persist through 20–30 years of age; have shorter periods of adolescent subfertility (the time between menarche and attainment of fertile menstrual cycles); experience earlier ages at first sexual intercourse, first pregnancy, and first childbirth; engage in more risky sexual behavior; and display more negative implicit evaluations of men and more aggressive and delinquent behaviors as young adults (Belles et al. 2010, Najman et al. 2009; for reviews, see Baams et al. 2015, Ellis 2004, Ibitoye et al. 2017). This covariation between timing of pubertal development and other life history–related traits supports the conceptualization of puberty as a key switch point in the development of alternative life history strategies (Ellis 2013).

An Evolutionary–Developmental Theory of Pubertal Variation

Drawing on life history concepts, Belsky et al. (1991) proposed an evolutionary–developmental theory linking levels of psychosocial stress and support in and around the family to subsequent timing of puberty and related life history traits. The theory posited that (*a*) ecological conditions and family dynamics shape children's early attachment patterns and behavioral development and, through these developmental processes, subsequent pubertal development and reproductive strategy, and that (*b*) this environmentally sensitive developmental system evolved as a means of matching individuals to their environment in a manner that promotes survival and reproduction across varying ecological contexts. Over the course of our evolutionary history, individuals growing up under harsh or unpredictable family conditions may have reliably increased their reproductive success by accelerating physical maturation and beginning sexual activity and reproduction at a relatively early age (Belsky 2012, Belsky et al. 1991, Ellis 2004).

When evaluating this theory, a starting assumption is that the effects of physical and psychosocial stressors on pubertal timing are hierarchically ordered: Pubertal timing is contingent firstly on health and nutrition (see especially Kyweluk et al. 2018) and secondly, when these are adequate, on socioemotional conditions (Ellis 2004). Consistent with life history models (e.g., Belsky et al. 1991), a substantial body of literature indicates that, when energetic conditions are adequate to support growth, early exposures to childhood adversities (e.g., socioeconomic adversity, child maltreatment, lack of family warmth and supportiveness, heightened parent–child conflict, father absence) tend to predict earlier pubertal development in females (for reviews, see Belsky & Shalev 2016, Ellis 2004, Webster et al. 2014). For example,

in a large prospective study of a population-based birth cohort in Australia, extremely unfavorable socioeconomic conditions predicted a fourfold increase in boys and twofold increase in girls in rates of early puberty (Sun et al. 2017a; for convergent findings in a prospective study of a multiethnic cohort of girls in the United States, see Hiatt et al. 2017). Similar effects may occur in response to natural disasters. In a large Chinese study, exposure to the Wenchuan earthquake predicted a fourfold increase in preschool age girls (under age 7 at time of exposure) and a twofold increase in school age girls (age 7 or older at time of exposure) in rates of early menarche (Lian et al. 2018), suggesting an early sensitive period for stress-mediated acceleration of pubertal development. Although earlier puberty is associated with childhood exposure to a variety of psychosocial stressors, the most consistent psychosocial predictor of early puberty in females is a history of sexual abuse (e.g., Magnus et al. 2018, Mendle et al. 2016).

This research underscores the importance of conceptualizing pubertal development as part of a developmental continuum, whereby familial and ecological stressors in childhood may accelerate pubertal maturation, which in turn regulates important dimensions of mating and parenting effort. The results of a small number of prospective, longitudinal studies indicate that the effects of stressful family environments (e.g., harsh maternal behavior, paternal unemployment, child maltreatment) on the development of faster life history strategies in women (e.g., risky or advanced sexual behavior, intimate partner violence, early smoking, drinking, and parenthood) are partially mediated by timing of puberty (Arim et al. 2011; Belsky et al. 2010, Foster et al. 2008, James et al. 2012, Negriff et al. 2015). In sum, puberty appears to operate as an important intervening mechanism linking rearing conditions to alternative life history strategies.

Accelerated Pubertal Maturation Trades Off Against Health

Although this environmentally sensitive regulation of life history strategies is presumed be adaptive, adaptive does not mean cost free. Stress-mediated acceleration of pubertal development may induce trade-offs that compromise health and curtail the reproductive life span. A history of sexual abuse is associated not only with earlier age of menarche but also with earlier age of menopause (Magnus et al. 2018), as well as many other costs to mental and physical health (e.g., Trickett et al. 2011). Likewise, Bleil and colleagues (2012, 2013) found that psychosocial stress was associated with earlier puberty and higher antral follicle count in younger women, but with ovarian reserve depletion in older women. That stress-mediated acceleration of pubertal development results in wear and tear on the reproductive system converges with a large body of human research indicating that the development of faster life history strategies comes at the cost of increasing allostatic load (for a review, see Ellis & Del Giudice 2014). Indeed, both cross-sectional and longitudinal studies have shown that individuals who pursue faster life history strategies suffer from more mental health problems, medical ailments (e.g., thyroid disease, high blood pressure or hypertension, ulcers), and physical health symptoms (e.g., sore throat or cough, dizziness) (Brumbach et al. 2009, Figueredo et al. 2004, Gibbons et al. 2012, Hill et al. 2016, Mell et al. 2018, Sefcek & Figueredo 2010). In sum, stress-mediated regulation of life history strategies guides development along specific pathways that can be understood as predictive adaptive responses, despite substantial costs. Such trade-offs reflect the very nature of development under stress.

Consistent with the notion of trade-offs, early timing of puberty in females is associated with a broad range of mental and physical health problems, ranging from psychopathology to obesity, cardiovascular disease, and reproductive cancers (e.g., Day et al. 2015, Ellis 2004, Graber et al. 1997). Earlier sexual maturation has been linked to greater allostatic load (Allsworth et al. 2005); in that context, the links between early puberty and higher morbidity and mortality concurs with the ALM. An emerging literature has begun to test for the mediating role of pubertal timing in explaining the well-established links between childhood adversity and later mental and physical health problems. In this case, again, the results of a small number of prospective, longitudinal studies suggest that the effects of early adversity (e.g., prenatal stress, childhood trauma, child maltreatment, maternal depression, negative parenting) on behavioral problems and health (e.g., substance use, mental health symptoms, global physical health problems, cardiovascular disease risk) are mediated by early timing of puberty (Belsky et al. 2015b, Lei et al. 2018, Mendle et al., 2014; Negriff et al. 2015). In sum, earlier timing of puberty appears to mediate the effects of early adversity on faster life history strategies, on the one hand, and poor health, on the other hand. Central to the evolutionary–developmental approach presented in this review is the proposition that these dual outcomes are interconnected through developmental trade-offs.

Stress Response Systems as Mediating Mechanisms in Stress–Puberty Relations

Stress response systems may play an important role in the developmental relationships among stress, puberty, and health. As reviewed by Ellis & Del Giudice (2014), stress response systems are functionally implicated in all components of mating and parenting, beginning with sexual maturation. The autonomic nervous system, HPA axis, and hypothalamic-pituitary-gonadal (HPG) axis are connected by extensive functional cross talk (Ellis 2004; Joos et al. 2018). As reviewed by Joos et al. (2018), the HPA and HPG axes tend to operate independently prior to puberty, become positively coupled in early adolescence, and then shift toward becoming negatively coupled in later adolescence. Based on the available data, the shift toward negative coupling appears to be more robust in girls (Matchock et al., 2007; Ruttle et al., 2015), and is likely to reflect the typical adult pattern of short-term inhibition of the HPG axis by stress hormones. This developmental pattern concurs with a substantial body or research indicating that psychosocial stressors generally provoke early or accelerated development of the HPG axis in girls but suppressed ovarian functioning in adult women (for a review, see Ellis 2004). For example, in a study of Chinese elementary school children, greater chronic daily activation of the HPA axis, as indicated by hair cortisol concentrations (representing chronic stress over the 3 months preceding measurement), predicted greater testicular volume in boys and breast development in girls aged 6 to 9 years (Sun et al. 2017b). Likewise, in a longitudinal study in the United States, higher basal cortisol levels at 4 years of age partially mediated the relationship between early adversity exposures and attainment of adrenarche (the onset of adrenal androgen production) by 7 years of age (Belsky et al. 2015b). This pattern then apparently switches in later adolescence. In a separate longitudinal study in the United States, attenuated (rather than elevated) cortisol reactivity to social stress predicted faster tempo of puberty in adolescent girls (but not boys) aged 9 to 13 years (Saxbe et al. 2015).

In sum, consistent with the notion of positive coupling of the HPA and HPG axes early in adolescence followed by negative coupling later in adolescence, high pre- and peri-pubertal basal activation of the HPA axis, but attenuated HPA responsivity during puberty, were linked to accelerated sexual development—an indicator of faster life history strategy. Most interesting,

Ruttle et al. (2015) found that stressful family conditions in early childhood accelerated both the onset of positive HPA-HPG coupling (by age 11) and the transition to negative HPA-HPG coupling (by age 13) in adolescent girls. Although more empirical research is clearly needed, this early coupling could serve as a mechanism through which childhood stress promotes earlier pubertal development (Joos et al. 2018; Ruttle et al. 2015). The Wenchuan earthquake study (Lian et al. 2018) suggests that the first 5-7 years life are a sensitive period for the effects of early life stress on pubertal maturation (as originally proposed by Belsky et al. 1991). Following a history of early life stress (presumably during this sensitive period), and the resulting early elevations of basal cortisol, accelerated positive HPA-HPG coupling in early adolescence may operate as a permissive signal that hastens the onset of puberty. In turn, accelerated negative HPA-HPG coupling in later adolescence may hasten progression through puberty (given attenuated HPA functioning in children who have experienced significant early life stress; Doom et al. 2014; Trickett et al. 2010). (See earlier discussion of the transition from vigilant to unemotional patterns of stress responsivity in the section titled Beyond Allostatic Load: Stress Response Systems as a Mechanism of Conditional Adaptation.)

Importance of Differential Susceptibility in Regulation of Pubertal Timing

Despite the findings of the literature reviewed above on psychosocial antecedents of pubertal timing, the effects of childhood stress on puberty tend to be relatively small, somewhat inconsistent across studies, and could reflect gene-environment correlations (rGE) operating on a background of heritable variation in pubertal timing (e.g., Barbaro et al. 2017, Mendle et al. 2006, Rowe 2000). One should note that initial polygenic analyses have found only limited support the rGE hypothesis (Gaydosh et al. 2018). Nonetheless, theories of differential susceptibility and biological sensitivity to context suggest that the weak main effects of environmental variables on many developmental outcomes may reflect the fact that children differ in whether, how, and how much they are affected by rearing experiences. As articulated by Belsky (2012), the weak main effects of family context on pubertal timing may overestimate the impact of family environments in some children and underestimate it in others.

Consistent with this supposition, both physiological variation in autonomic and adrenocortical reactivity to stress (Ellis et al. 2011b) and genotypic variation in the estrogen receptor-α gene (*ESR1*) (Hartman et al. 2015, Manuck et al. 2011) have been found to moderate the effects of family relationships on timing of puberty in girls. This pattern of differential susceptibility enhances pubertal responses to childhood adversity in some individuals while attenuating it in others. Although the findings on *ESR1* should be considered tentative due to limited sample sizes, they converge nicely with experimental research on rodents indicating that the accelerating effects of low levels of maternal licking and grooming (a form of low parental investment) on pubertal maturation in female offspring are mediated by increased expression of estrogen receptor alpha in specific regions of the hypothalamus (for a review, see Cameron 2011). Finally, some evidence suggests that early pubertal development itself may operate as a susceptibility factor that amplifies the effects of parenting quality on aggression for better and for worse (Chen & Raine 2018). If so, susceptibility factors in middle childhood that enhance pubertal responses to early family stress (e.g., heightened autonomic and adrenocortical reactivity to stress; Ellis et al. 2011b) may set processes in motion that further potentiate susceptibility to family relationships in early adolescence.

CONCLUSION

What is the nature of developmental adaptation to stress? Does childhood adversity adaptively shape development or simply constrain it? Following the ALM and other dysregulation models, one can always make a disease-focused argument emphasizing the deleterious effects of adversity and its biological mediators (e.g., chronic low-grade inflammation, sensitized cortico-amygdala threat circuitry, abnormal HPA axis functioning). Indeed, the extensive body of research documenting the negative effects of allostatic load on health is incontrovertible. This is because development under stressful conditions necessitates trade-offs: One system is diminished so that another system can be enhanced or preserved. In the scientific literature on stress and development, however, these countervailing effects have not been equally studied; as a result, we know vastly more about the detrimental effects of childhood stress than about its benefits in context. The developmental literature on puberty and life history strategies reveals both sides of the equation. From an evolutionary perspective, stress-mediated developmental processes not only cause impairments and vulnerabilities, but also promote coherent, integrated, functional responses to childhood adversity. This includes both short-term adjustments (immediate adaptive responses) and longer-term adaptations (predictive adaptive responses) that regulate development toward faster life history strategies, which in turn promote survival and reproduction under harsh and unpredictable conditions. Mental and physical impairments or disease can be partly understood as costs and side effects of these adaptive processes. At the same time, biological sensitivity to context attenuates these effects, with some individuals responding strongly to their rearing conditions, while others are only weakly affected. In sum, natural selection may favor both developmental adaptations to stress and differential susceptibility to its effects.

The long-term focus of the ACM and other developmental programming models is critical to understanding stress–health relations because, to a great extent, allostatic load is a byproduct of the chain of resource-allocation decisions that characterize the development of faster life history strategies over the life course. In the literature reviewed above, these resource allocation decisions are mediated through earlier pubertal development and related life history traits (e.g., earlier onset of sex and reproduction, more risky and aggressive behavior, stress-adapted cognition). In the ACM, early life stress is biologically embedded in the parameters of stress response systems and other neuroendocrine processes that guide alternative developmental trajectories. Mapping out such functional biobehavioral responses to stress is critical for health risk identification and health promotion because the costs of developmental adaptations to stress (e.g., allostatic load) and the potential benefits (e.g., adaptive calibration) are inextricably linked—indeed, one cannot be understood without the other.

The evolutionary–developmental perspective presented in this review affords a big-picture view of developmental plasticity and individual differences that integrates a wide spectrum of findings on stress–health relations. From this perspective, dysregulation models—by emphasizing the pathways leading directly from adversity to dysfunction—miss something fundamental about development: the coherent, functional biobehavioral changes that occur in response to stress over time (Ellis & Del Giudice 2014). We need to understand these functional developmental changes to more fully understand dysfunction. The problem with many traditional interventions is that they ignore developmental adaptations to stress. This can result in errors of

omission (e.g., missing key intervening variables in stress–health relations) and misidentification of health risk factors (e.g., mistaking functional brain changes for dysfunction). Treatment and prevention strategies that ignore developmental adaptations to stress not only miss the opportunity to leverage these adaptations for good—working with them to enhance positive outcomes—but also risk fighting against these adaptations in an uphill battle that they are not likely to win (Ellis et al. 2012a, 2017a).

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