Early stress and human behavioral development: Emerging evolutionary perspectives

Early Stress and Human Behavioral Development: Emerging Evolutionary Perspectives

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Abstract

Stress experienced early in life exerts a powerful, lasting influence on development. Converging empirical findings show that stressful experiences become deeply embedded in the child's neurobiology, with an astonishing range of long-term effects on cognition, emotion, and behavior. In contrast with the prevailing view that such effects are the maladaptive outcomes of "toxic" stress, adaptive models regard them as manifestations of evolved developmental plasticity. In this paper, I offer a brief introduction to adaptive models of early stress and human behavioral development, with emphasis on recent theoretical contributions and emerging concepts in the field. I begin by contrasting dysregulation models of early stress with their adaptive counterparts; I then introduce life history theory as a unifying framework, and review recent work on predictive adaptive responses in human life history development. In particular, I discuss the distinction between forecasting the future state of the environment (external prediction) and forecasting the future state of the organism (internal prediction). Next, I present the adaptive calibration model (ACM), an integrative model of individual differences in stress responsivity based on life history concepts. I conclude by examining how maternal-fetal conflict may shape the physiology of prenatal stress and its adaptive and maladaptive effects on postnatal development. In total, I aim to show how theoretical work from evolutionary biology is reshaping the way we think about the role of stress in human development, and provide researchers with an up-to-date conceptual map of this fascinating and rapidly evolving field.

Keywords

Developmental plasticity, early stress, life history, parent-offspring conflict, prenatal stress.

Stress experienced early in life exerts a powerful, lasting influence on development. Already during gestation maternal stress is transmitted to the fetus via stress-related hormones such as glucocorticoids and catecholamines. Later on, the developing child faces many potential sources of stress, ranging from physical danger and material deprivation to psychosocial stressors such as family conflict, harsh or neglectful parenting, and peer rejection or hostility. Converging empirical findings show that early stress becomes deeply embedded in the child's neurobiology, with an astonishing range of long-term effects on cognition, emotion, and behavior.[1-10] Most dramatically, stress exposure during early life stages has been linked to increased risk for psychopathology, from depression and conduct disorders to autism and schizophrenia.[2,11]

Why does stress play such a central role in behavioral development? What biological mechanisms mediate the long-term effects of early stress? Are those effects entirely maladaptive, or do they reflect a more complex balance of costs and benefits? The implications are far-reaching, not only for basic research but also for prevention and treatment. In this paper, I show how theoretical work from evolutionary biology is providing new answers to these questions, potentially reshaping the way we think about the role of stress in human development. Indeed, the field is undergoing a conceptual revolution, as traditional approaches founded on notions of "toxic stress"[12] are revised in light of the potential of early stress to shift the developing organism along alternative adaptive trajectories. Even more recently, researchers have broadened their view beyond the individual organism, and have started to explore the role of genetic conflict between mother and fetus in the regulation of prenatal stress.

The goal of this paper is to offer a brief introduction to the evolutionary literature on early stress and behavioral development, with emphasis on recent theoretical contributions and emerging concepts in the field. Instead of attempting a detailed analysis of the neurobiological and genetic mechanisms involved in stress physiology and behavioral development, I will aim for the "big picture" and focus on the key conceptual issues in this area of research. The functional approach I emphasize here is meant to provide conceptual grounding for the mechanistic analysis of neurobiological and endocrine processes. While some of the biological principles I discuss apply to a broad range of organisms, this paper will specifically deal with human behavior and human-centered models of early stress.

From Dysregulation to Adaptive Plasticity

Stress and Allostasis

Stressors can be defined as *unpredictable and/or uncontrollable events* that challenge an organism's ability to maintain self-regulation and achieve key biological goals.[13] Coping with stressors requires organisms to alter their physiological and psychological parameters so as to adapt to the changing demands of the environment, a process called *allostasis* ("stability through change") to differentiate its dynamic quality from the static regulatory scope of homeostasis.[14,15]

Allostatic responding is orchestrated by the *stress response system* (henceforth SRS). The SRS is an integrated, hierarchically organized system that comprises the hypothalamic-pituitary-adrenal (HPA) axis, the sympathetic and parasympathetic autonomic branches, and various

limbic structures including the amygdala.[16-19] Through the SRS, the brain coordinates whole-body reactions to stressors and other challenges, with both short- and long-term effects on cardiovascular functioning, metabolism, immune regulation, attention, memory, and so forth.[1,16,20,21] The long-term effects of SRS activation are thought to be largely mediated by epigenetic modifications induced by stress-related hormones, with adrenal glucocorticoids (cortisol in humans) playing a prominent role.[22,23] It is important to note that the SRS does not only respond to stressors as defined above; instead, it activates in response to all sorts of events that require organismal readiness, including potential opportunities such as the presence of an attractive sexual partner.[9,24,25]

There is no question in the literature that allostasis is a fundamentally adaptive process. The short-term changes in physiology and behavior mediated by the SRS are designed to increase the organism's ability to survive and reproduce—despite the metabolic, immune, and psychological costs of SRS activity. However, theoretical models diverge considerably in how they address the long-term effects of sustained, chronic SRS activation.

Dysregulation Models of Early Stress

The prevailing view in psychology and medicine is that while allostatic responses are usually adaptive in the short term, protracted SRS activation is maladaptive and toxic in the long term. In addition, gestation is such a critical period for development that even a comparatively brief exposure to elevated maternal stress hormones—in the order of weeks or months—can have disruptive effects on brain development, resulting in maladaptive outcomes that may last into adulthood. In total, early stress tends to impair behavioral development, leading to dysregulation of multiple neurobiological systems and subsequent maladaptation.[4,5,7,11,12,26-28] The logic of dysregulation models of early stress is outlined in Figure 1a. The leading example of this approach is the *allostatic load model* (ALM).[4,15,26] Allostatic load can be defined as the cost of allostasis—the "wear and tear" of biological systems that results from repeated adaptation to stressors. According to the ALM, chronic stress and the resulting allostatic load may lead to both hyper- and hypo-responsive profiles of SRS functioning;[29] protracted exposure to cortisol negatively affects the development of critical brain structures such as the hippocampus, amygdala, and prefrontal cortex,[4] with a range of maladaptive behavioral correlates.

On the face of it, the evidence consistent with dysregulation models is impressive. Early exposure to chronic stress and/or elevated maternal stress hormones has been linked to reduced cognitive ability, impaired attention and memory, rigid learning strategies, and higher levels of anxiety, fearfulness, impulsivity, aggression, and risk-taking. Early stress also increases the risk for conduct and personality disorders, attention deficit-hyperactivity disorder, depression, autism, and schizophrenia.[2,7,10,11,30-33] While chronic stress in childhood has been linked to both hyper- and hypo-responsive profiles of SRS activity,[4,5,8] prenatal exposure to glucocorticoids appears to specifically predict *increased* SRS responsivity and behavioral vigilance, at least in infancy and early childhood.[34-37] While a recent study by O'Connor and colleagues[38] found a blunted HPA response to separation in infants exposed to higher levels of prenatal cortisol, the data also showed higher pre-separation cortisol levels in the same infants, which may indicate a stronger anticipatory response rather than attenuated responsivity.[39]

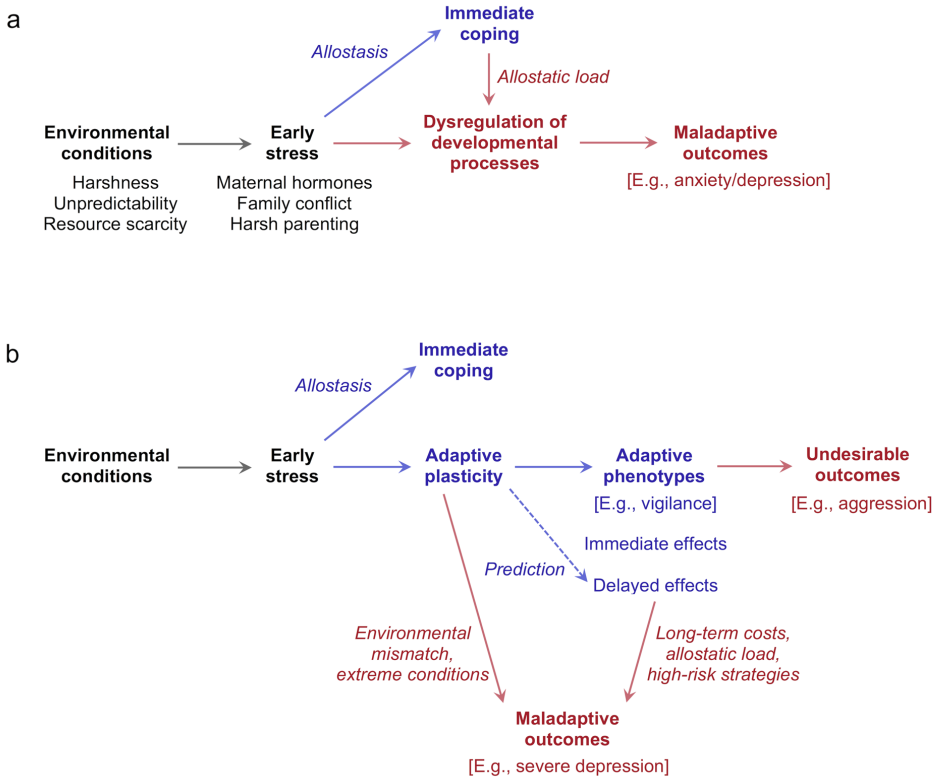

Figure 1. Schematic representation of (a) dysregulation models and (b) adaptive models of early stress and behavioral development. Adaptive processes and outcomes are shown in blue; maladaptive and/or undesirable processes and outcomes are shown in red.

Adaptive Models of Early Stress

Dysregulation models postulate the existence of a single optimal level of stress and a corresponding optimal trajectory of behavioral development. Depending on the model, the optimum may be found either at minimal levels of stress (the lower the better) or at some intermediate level—high enough to build up resilience but not so high as to become toxic.[40,41] In contrast with this view, converging theoretical and empirical findings in evolutionary biology have brought about the realization that natural selection is unlikely to favor a single optimal strategy for survival and reproduction.[42,43] What constitutes the optimal strategy in a given environment may prove detrimental to fitness in a different set of ecological circumstances. As a result, selection tends to favor *adaptive phenotypic plasticity*, the capacity of a single genotype to support a range of phenotypes in response to ecological conditions that recurrently influenced survival and reproduction during a species' evolutionary history.[44-46] The development of alternative phenotypes is often guided by environmental cues found in the organism's early environment—for example cues to the presence of predators, the intensity of social competition,

or the local mortality rate—and leads to durable or even irreversible changes in the individual's morphology, physiology, and behavior (*developmental plasticity*).

Building on the concept of developmental plasticity, researchers have been increasingly advancing alternative models in which early stress does not primarily impair or dysregulate children's developmental trajectories, but rather shifts them toward behavioral strategies that have proven biologically adaptive in harsh or unpredictable conditions.[1,2,8,9,16,31,47-49] In evolutionary biology, adaptive traits are those that promote fitness and are thus favored by natural selection. An individual's fitness is a function of its own reproductive success and that of genetically related individuals, with the latter discounted by a coefficient of relatedness (the concept of *inclusive fitness*).[50-52] Adaptive traits may or may not improve happiness, well-being, or health, and often carry substantial costs for the individual along with their reproductive benefits. The distinction between (biologically) *maladaptive* and (psychologically and/or socially) *undesirable* outcomes is a fundamental concept in the evolutionary study of human health and development.[53,54]

The logic of adaptive models of early stress is summarized in Figure 1b. Exposure to stress works as a *cue* to local environmental conditions, and feeds into plasticity mechanisms that coordinate the development of alternative phenotypes. As shown in Figure 1b, the effects of early stress can be either immediate or delayed—sometimes becoming manifest after years or even decades. When a plastic phenotype is induced by early cues but its benefits are only accrued at a later phase of the life cycle, the process can be described as a *predictive adaptive response* (PAR).[55,56] In predictive adaptive responses, early cues are employed to forecast the future state of the environment, and developmental trajectories are adjusted from the start to match the individual's expected needs. In the literature, the term "programming" is often used to describe the long-term effects of early stress;[10] while the programming metaphor might suggest an inflexible and deterministic process, developmental trajectories often show considerable openness to later environmental inputs.[55,56]

In this perspective, many putative maladaptive traits such as anxiety, aggression, and impulsivity can be reframed as costly but adaptive phenotypes that improve an individual's survival and reproduction prospects in hostile, unpredictable contexts. For example, increased vigilance and anxiety can be regarded as defensive reactions to potential threats, whereas aggression and impulsivity can be effective competitive strategies in harsh, unstable social environments.[2,8,31,47,48,57] Furthermore, there is evidence that high levels of physiological and emotional reactivity increase an individual's sensitivity to context, making him/her more open to both negative and positive social influences.[16,24,42,57] Of course, some of these adaptive traits are going to have undesirable consequences for the individual and/or the social group, and may even be diagnosed as symptoms of psychopathology (e.g., conduct disorders). According to adaptive models, children exposed to early stress should exhibit patterns of impaired cognitive and emotional functioning when tested in safe, stress-free contexts and/or with tasks that mimic the demands of those contexts; but they should often perform *better* than their peers on tasks that reproduce key features of the dangerous, unpredictable environments they are adapted to. The initial evidence suggests that this may be the case.[20,48]

Adaptation or Maladaptation?

While adaptive models emphasize the biological value of stress-related traits, they do not negate the possibility of genuinely maladaptive outcomes. For example, maladaptive outcomes may result from phenotype-environment *mismatches*—both at the individual level when the actual environmental state does not match the predicted one, and at the population level when the broader environment changes so that previously adaptive traits become maladaptive.[59,60] Other causes of maladaptation include exposure to extreme environments (for example conditions of severe sensory and affective deprivation) that exceed the evolved plasticity range of an organism; high-risk behavioral strategies that trade potential fitness benefits against the risk of severely maladaptive outcomes; and dysregulation of adaptive processes due to genetic and/or environmental causes, including deleterious mutations and the long-term effects of allostatic load.[53,59,61,62]

In short, adaptive models incorporate the key insights of dysregulation models, as they acknowledge both the short-term benefits and the long-term costs of early stress (compare Figures 1a and 1b).[4] However, adaptive models give center stage to the long-term *benefits* of stress exposure as a determinant of developmental plasticity.[9] Within this general approach, specific models differ in the hypothesized balance between adaptation and maladaptation.[10] Some theorists have speculated that the outcomes of early stress may be almost always beneficial, either for the individual or for the broader social group;[2] others have explicitly discussed various pathways to genuine maladaptation.[9,34] Teasing apart adaptation and maladaptation in human development will require a great deal of empirical work, and a thorough understanding of the evolved function of psychological and physiological mechanisms.

Life History Theory: An Integrative Framework

The logic of adaptive plasticity outlined in the previous section can be applied separately to various psychological traits such as anxiety, aggression, and self-regulation. However, these behavioral traits cluster together in a way that suggests a high degree of functional coordination; moreover, they show reliable associations with individual differences in other domains including physical and sexual maturation, metabolism, and immune function.[4,8,9,55]

In evolutionary biology, a major framework for explaining coordinated patterns of developmental plasticity is *life history theory*.[63-66] Life history theory deals with the way organisms allocate time and energy to the various activities—including growth, bodily maintenance, mating, and parenting—that comprise their life cycle. Since all these activities 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. For example, there is a trade-off between growth and reproduction because both require substantial energetic investment, and thus producing offspring reduces somatic growth. Natural selection favors organisms that schedule developmental tasks and activities so as to optimize resource allocation; this chain of resource-allocation decisions—expressed in the development of a coherent, integrated suite of physiological and behavioral traits—constitutes the individual's *life history strategy*.

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.[64,67,68] In humans, some individuals adopt slower strategies characterized by later reproductive development and behavior, a preference toward 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.[45,64,69,70] 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 (of self and offspring). 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. In general, dangerous and unpredictable environments tend to entrain fast life history strategies, whereas safe and predictable environments favor slower strategies.[64,71,73]

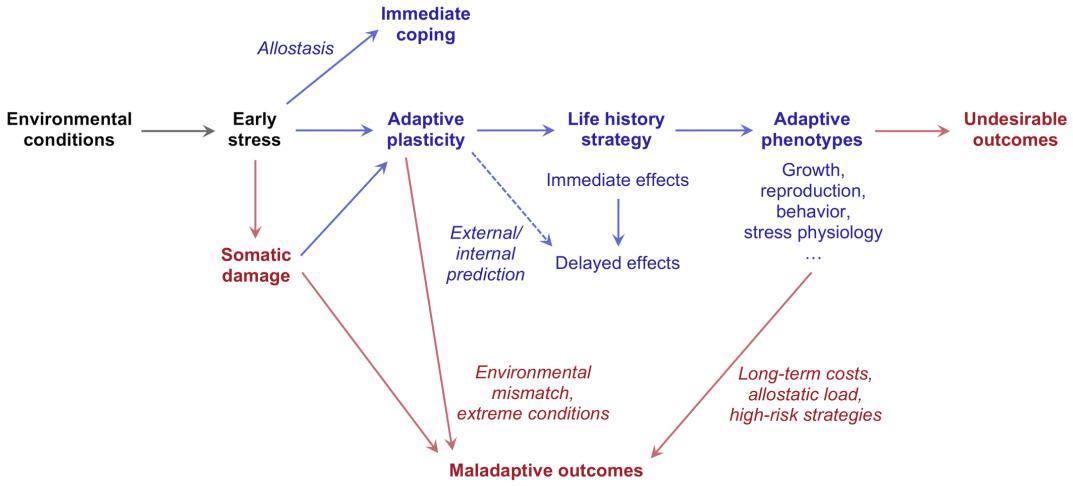

Figure 2. An integrative life history perspective on early stress. Adaptive processes and outcomes are shown in blue; maladaptive and/or undesirable processes and outcomes are shown in red.

Over the years, a number of authors have employed the concepts of life history theory to explain the long-term effects of early stress on development.[8,16,31,47] The central idea of these models is that early stress exposure—especially during the first 5-7 years of life—conveys predictive information about life history-relevant parameters of the environment (in particular *danger* and *unpredictability*), thus promoting the development of alternative life history strategies (Figure 2). Higher levels of stress are predicted to entrain faster strategies, characterized by earlier sexual maturation (especially in females), impulsivity, and higher levels

of both externalizing (aggression, attention-seeking) and internalizing symptoms (anxiety, depression). This perspective offers an elegant way to explain the coordination among stress-related behavioral traits and their associations with patterns of growth, maturation, metabolism, and so forth.[9,56,74]

Internal vs. External Prediction

In life history models, the delayed effects of early stress—for example on the timing of sexual maturation—are usually interpreted as predictive-adaptive responses based on the anticipated state of the external environment ("external" PARs). In order to be adaptive, external PARs require a sufficient level of environmental stability between childhood and adulthood. In a recent paper, Nettle and colleagues[75] argued that early stress may influence life history development by a different route. If early stress causes permanent damage to the organism and thus reliably reduces life expectancy, it may be adaptive for individuals exposed to stress early in life to engage in faster strategies even if the environment improves later on. Such "internal" PARs do not require environmental stability and seem likely to evolve under a wider range of conditions.[76] In a nutshell, external PARs forecast the future state of the environment, whereas internal PARs forecast the future state of the *organism*.

Internal and external PARs are not mutually exclusive and may coexist in human development. Further elaborations of Nettle et al.'s model indicate that the degree of environmental stability required for the evolution of external PARs is likely to be lower than initially suggested (i.e., annual autocorrelations in the order of .80-.85 instead of .95), thus broadening the scope for adaptive external prediction.[76] The concept of internal PARs is theoretically intriguing because it suggests that the adaptive and maladaptive effects of early stress may be inextricably linked (see Figure 2), as somatic damage (a maladaptive effect) contributes to inform and direct life history development (an adaptive effect). For this reason, internal prediction also raises new challenges for empirical research, by questioning the standard distinction between adaptive and maladaptive hypotheses on the developmental role of stress.

The Adaptive Calibration Model

My colleagues and I recently advanced an integrative evolutionary-developmental model of stress responsivity based on life history theory, the *adaptive calibration model* (ACM).[8,9,77] The ACM synthesizes and extends previous models of early stress, and makes a host of detailed predictions about adaptive patterns of SRS functioning in different environments, their behavioral correlates, and their relations with individual variation in other neurobiological systems—including dopaminergic and serotonergic pathways and the hypothalamic-pituitary-gonadal (HPG) axis. A simplified diagram of predicted responsivity patterns in the ACM is shown in Figure 3. *Sensitive* patterns are hypothesized to develop in safe, predictable conditions and warm family environments. High stress responsivity in sensitive individuals increases their openness to the social and physical environment. Sensitive individuals are reflective, self- and other-conscious, and high in inhibitory control; collectively, these traits promote sustained learning and long-term cooperation in the context of slow life history strategies. *Buffered* patterns are predicted to develop preferentially in conditions of moderate environmental stress, where

they strike a balance between the costs and benefits of responsivity. Buffered responsivity is predicted to arise primarily through moderate, repeated activation of the stress response system during the first years of life. Buffered individuals are predicted to be comparatively low in anxiety and aggression and moderately sensitive to social feedback, making intermediate exposure to stress look like a "protective factor" in the development of psychopathology.[40,41]

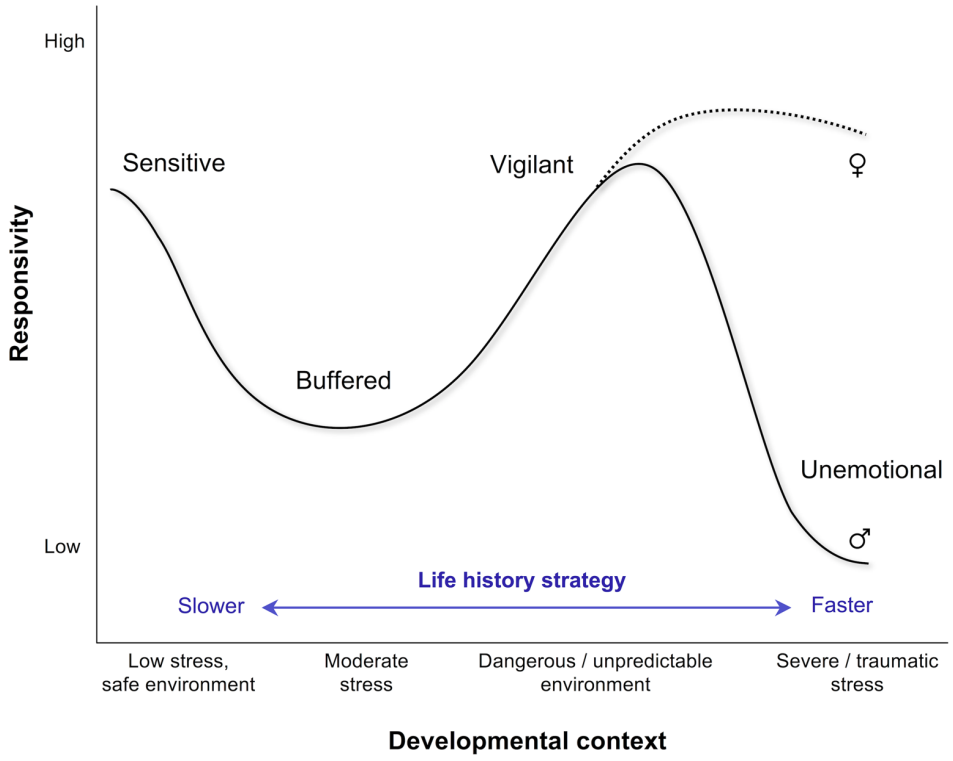

Figure 3. Predicted relation between environmental conditions and physiological responsivity in the adaptive calibration model.[8]

Moving toward faster life history strategies, *vigilant* patterns are predicted to develop in stressful contexts, where they enable people to cope with dangers and threats in the environment. High physiological responsivity mediates heightened attention to threats and high trait anxiety. In the ACM, vigilance is not associated with a single behavioral pattern, but rather with a distribution of patterns involving different mixtures of aggressive/externalizing and withdrawn/internalizing behaviors, also depending on an individual's sex. Finally, *unemotional* patterns are marked by a profile of low stress responsivity. Generalized unresponsivity inhibits social learning and sensitivity to social feedback; it can also increase risk-taking by blocking information about dangers and threats in the environments. The predicted correlates of this pattern are low empathy and cooperation, impulsivity, competitive risk-taking, and antisocial

behavior—particularly in males. Because of sex differences in optimal strategies, the distribution of responsivity patterns and their behavioral correlates is expected to become more sex-biased at increasing levels of environmental stress; accordingly, unemotional profiles should be more common in males, especially after puberty (Figure 3).

The ACM has significant implications for empirical research on early stress. Most notably, the predicted relation between environmental quality and physiological responsivity is strongly nonlinear (Figure 3). If this prediction is correct, researchers should not expect simple linear relations between SRS responsivity and behavioral traits such as aggression and impulsivity. In addition, a nonlinear relation between environmental conditions and responsivity patterns may explain why, in studies of prenatal stress, associations between maternal self-reported distress/anxiety and cortisol levels (typically tested with linear correlation/regression models) are often found to be weak and inconsistent.[34,35,37]

Another important feature of the ACM is that responsivity patterns are predicted to develop over time through a sequence of "switch points" marked by hormonal transitions.[8] Especially in long-lived species like humans, life history development is likely to involve multiple stages, with opportunities for revision and recalibration after initial "decisions".[74,78] Pre- and early postnatal development, the transition from early to middle childhood, and puberty are all potential switch points for the calibration of stress responsivity.[8] In the ACM, individual and sex differences in the functioning of the stress response system emerge according to the evolutionary function of each developmental stage; for example, some children (especially males) are predicted to switch from vigilant to unemotional responding as they move from early childhood to middle childhood and adolescence.

The broader implication is that superficially similar features of behavior and physiology (e.g., elevated SRS responsivity) may actually serve different life history strategies; conversely, the same overall strategy may be reflected in different types of behavior at different life stages. A life history framework promises to offers a more coherent picture of the relation between the immediate and delayed effects of early experience; for example, late-appearing traits (e.g., unemotional impulsivity and sexual promiscuity) and their developmental precursors (e.g., irritability and hyper-responsivity) may share deep functional connections even if they appear very different on the surface.[79] The same logic may explain why prenatal exposure to stress hormones seems to consistently increase SRS responsivity in infancy and early childhood (when survival and growth are the child's main biological tasks), while chronic stress in childhood may lead to both hyper- and hypo-responsive profiles of SRS activity in adolescence and adulthood.

Cooperation and Conflict in Prenatal Development

Adaptive models of early stress tend to view prenatal stress exposure as a cooperative transfer of information from mother to fetus. Hormones such as cortisol and catecholamines are released in the maternal bloodstream when stressful events challenge the mother's coping ability; sustained exposure to stress-related hormones—perhaps especially to recurrent hormonal peaks[34]—provides the fetus with useful information about the predictability of the environment, the presence of threats, and the availability of social support. Since the fetus does not have direct

access to the external environment, it benefits by letting maternal hormones shape its developmental trajectory. At the same time, the mother benefits by transmitting accurate information, thus maximizing phenotype- environment matching in her offspring and—indirectly—her own inclusive fitness.[49,58,80-82]

The unstated assumption in this account is that the interests of the mother and fetus are 100% aligned, so that fully cooperative interactions can evolve. The biological reality, however, is both more complex and more interesting. As first shown by Trivers,[83] the genetic interests of parents and offspring are only partially overlapping. Whenever a given trait or behavior results in a cost to the parent and a benefit to the offspring (or vice versa), parent and offspring can be expected to "disagree" about the optimal level of expression of that trait. Stated otherwise, the level of a trait that maximizes the parent's fitness will differ from the level that maximizes the offspring's fitness, resulting in a biological conflict of interest about the trait in question. The logic of *parent-offspring conflict* is easiest to illustrate in the case of parental investment (e.g., food provision). The mother has the same genetic relatedness with each of her offspring, and—all else being equal—will maximize her own fitness by allocating her investment in equal proportions. However, any individual offspring is more closely related to *itself* than to its siblings (both present and future); thus, natural selection favors those offspring who increase their share of maternal resources above the mother's optimum.[83] Both the intensity of conflict and its likely resolution (e.g., whether a compromise is reached or one of the actors gets to control the outcome) are affected by ecological factors such as resource abundance and by the details of a species' reproductive system.[84]

Parent-Offspring Conflict in Prenatal Stress

Because of the inevitable divergence between maternal and fetal interests, prenatal development is characterized by an intricate mixture of cooperation and conflict.[84-86] The fetus—or, more precisely, the fetoplacental unit—is an active player rather than a passive target of maternal decisions; as a result, its hormonal interactions with the mother involve both honest signaling and reciprocal manipulation. Manipulative tactics and the countermeasures they evoke may evolve into full-fledged "arms races", in which both actors pay significant physiological costs and expose themselves to the risk of occasional maladaptive outcomes when—for various reasons—conflict happens to escalate out of control.

The theory of parent-offspring conflict has been applied to various aspects of prenatal development,[84] most notably fetal nutrition (including blood glucose concentration and blood pressure)[85-88] and spontaneous abortion.[89] In both cases, stress-related hormones are involved in the physiology of conflict: placental corticotropin-releasing hormone (pCRH) is instrumental in raising maternal cortisol and blood glucose, while the abortogenic effects of cortisol at the beginning of pregnancy mediate the relation between maternal stress around conception and early pregnancy termination.[89,90] In both cases, prenatal conflict about the regulation of the mother's SRS parameters is going to indirectly affect the child's behavioral development, even if only as a side effect of passive hormonal exposure. However, there are reasons to believe that the behavioral effects of prenatal stress may become a matter of conflict in their own right.

In a recent paper,[34] I argued that parent-offspring conflict may arise because of the effects of prenatal stress on *postnatal plasticity*. As noted in a previous section, there is accumulating evidence that high SRS responsivity and emotional reactivity result in increased sensitivity to the effects of the postnatal environment, so that highly reactive infants and children are also more behaviorally plastic.[8,24,58,91] In species with prolonged maternal care and extended family interactions such as humans, the mother has ample opportunity to shape her offspring's behavior in (more or less subtly) self-interested ways. As a result, conflicts of interest arise in many areas of development, from feeding in infants to mate choice in young adults.[84] By definition, high postnatal plasticity means that the child will be more susceptible to the effects of maternal behavior, with beneficial long-term consequences for the mother. For this reason, selection should favor mothers who are able to *increase their children's plasticity* beyond the children's optimum; an obvious way to achieve this end is to increase fetal exposure to stress-related hormones by some (limited) amount. At the same time, fetuses should put up some resistance against maternal manipulation; however, they cannot simply ignore maternal signals, as the latter also provide useful information about the external environment.[92] Because of this strategic tension, the regulation of prenatal stress may evolve into a complex web of tactics and countermeasures revolving around the amount of stress-related hormones that reach the fetal brain.

While this hypothesis is still speculative, it has the potential to explain a number of puzzling features of prenatal stress physiology. For example, the placentally expressed enzyme 11β-hydroxysteroid dehydrogenase type 2 (11β-HSD2) inactivates cortisol to cortisone, and is commonly understood to provide an adaptive "filter" against maternal cortisol.[93] However, the filtering action of 11β-HSD2 is opposed by that of 11β-HSD1, an enzyme that converts cortisone to cortisol and is expressed by *maternal* tissues in close contact with the placenta. Such paradoxical findings make little sense under the standard assumptions, but can be easily explained in a conflict perspective.[34] In addition to making sense of this and other features of prenatal physiology, a conflict perspective can be employed to make new empirical predictions; for example, the idea that placental progesterone actively downregulates the responsivity of the mother's HPA axis suggests the hypothesis that the maternal brain may express biochemical countermeasure against the effects of progesterone metabolites on SRS activity.[34]

As shown in Figure 4, the logic of parent-offspring conflict adds a layer of complexity to adaptive models of early stress, and provides researchers with new insights as well as new challenges. To begin, the partial but pervasive conflict between the biological interest of parents and children raises the question of who is the real beneficiary of a given trait or outcome. Indeed, traits that are adaptive from the parent's perspective may not be adaptive when viewed from the child's perspective, and vice versa. Evidence that a given outcome is maladaptive for one of the actors (e.g., the mother) is no longer sufficient to infer dysregulation or mismatch, as the same outcome may be increasing the fitness of the other actor (e.g., the child).

Besides complicating the study of adaptation, parent-offspring conflict also increases the scope for genuine maladaptation (Figure 4). Because of the need to overshoot their target, physiological mechanisms involved in prenatal conflict are more likely to enter vicious cycles of escalation, with potentially catastrophic consequences and a range of maladaptive side effects.

This logic has been invoked to explain the etiology of gestational hypertension[85] and may contribute to explain the most severe pathological outcomes of early stress, such as autism and schizophrenia.[34] Finally, evolutionary conflict may arise not only between parent and child, but also between maternal and paternal chromosomes within the child's genome. *Imprinted genes* are genes whose expression level changes according to the parent of origin; since the genetic interests of mothers and fathers are typically divergent, imprinted genes of maternal and paternal origin often evolve so as to have opposite effects on development[94,95] While there is no room here for a detailed treatment of this topic, recent theoretical work suggests that imprinted genes may be involved in the regulation of early stress, the development of life history strategies, and the etiology of mental disorders.[34,84,96-99]

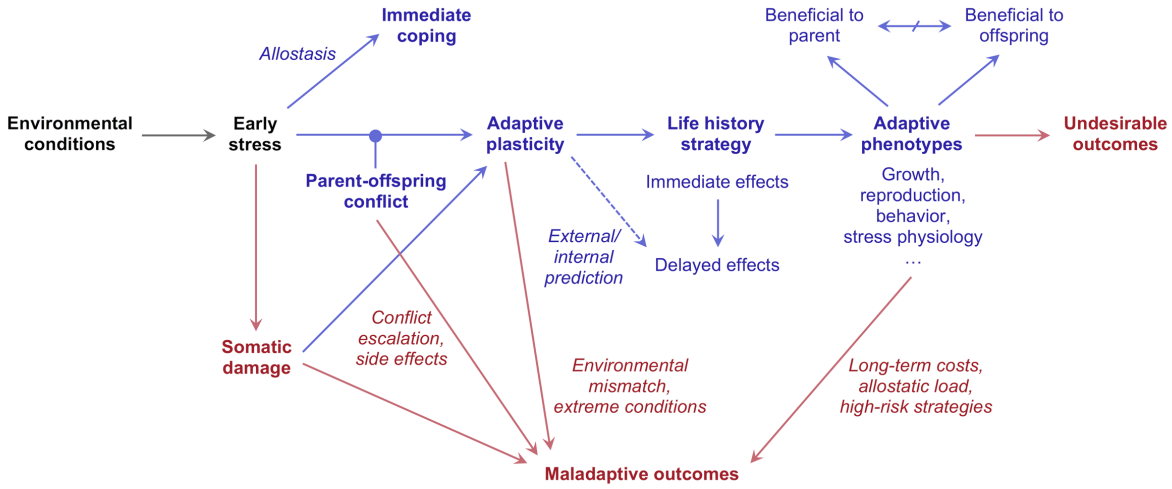

Figure 4. Implications of parent-offspring conflict for adaptive models of early stress. Adaptive processes and outcomes are shown in blue; maladaptive and/or undesirable processes and outcomes are shown in red.

Future Directions

In many ways, the models reviewed in this paper should be regarded as initial, tentative steps toward a satisfactory theory of early stress. The insights gained so far need to be refined with the aid of mathematical modeling, further integrated across domains and levels of analysis, and subjected to stringent empirical tests. Mathematical modeling will play a crucial role in assessing the validity of evolutionary hypotheses about the timing and function of life history transitions, the adaptiveness (or lack thereof) of early plasticity, the costs and benefits of different responsivity profiles, and so forth. While theoretical biology offers a wealth of general results, the details of a species' ecology and life history often matter a lot when it comes to finer-grained predictions. As more investigators incorporate the distinctive features of human ecology

into mathematical models of development,[74,75,99-101] theories of early stress will become increasingly powerful, detailed, and capable of generating robust quantitative predictions.

Another important avenue for future research concerns the interplay between the SRS and other neurobiological and endocrine systems involved in behavioral control. For example, the role of sex hormones in prenatal stress[49] is a crucial but under-investigated topic, especially in the human literature. Also, future extensions of life history models should give full consideration to SRS-immune interactions in the development of life history strategies, behavior, and psychopathology. There is extensive cross-talk between the SRS and the immune system, with inflammation emerging as a key functional link between psychosocial stress, immune functioning, and disease.[102-105] The immune response is an essential component of allostasis; like the SRS, the immune system collects life history-relevant information about mortality risk, and different life history strategies are likely to predict different patterns of immune functioning.[106] Indeed, the effects of early infections overlap considerably with those of psychosocial stress and prenatal exposure to stress-related hormones, including their association with later psychopathology.[102,107-109] Integrating immune functioning in life history models of early stress will be a major step toward a unified biological theory of human development.[9]

Conclusion

Understanding the role of early stress in human development is a major scientific challenge with myriad implications for prevention, treatment, and basic research in the medical and behavioral sciences. Here I showed how evolutionary thinking has contributed to enrich and transform the study of early stress, giving rise to new models that incorporate concepts from developmental plasticity, life history theory, and parent-offspring conflict. As models grow in scope and complexity, they become increasingly able to explain known phenomena and—even more importantly—generate novel, counterintuitive predictions. At the same time, they face researchers with new and sometimes formidable challenges in the design and interpretation of empirical studies. I hope the conceptual map sketched in this paper will serve as a useful starting point for explorations of this important, fascinating, and rapidly evolving field.

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