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Review

Evolutionary functions of early social modulation of hypothalamic-pituitary-adrenal axis development in humans

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ABSTRACT

The hypothalamic-pituitary-adrenal axis (HPAA) is highly responsive to social challenges. Because stress hormones can have negative developmental and health consequences, this presents an evolutionary paradox: Why would natural selection have favored mechanisms that elevate stress hormone levels in response to psychosocial stimuli? Here we review the hypothesis that large brains, an extended childhood and intensive family care in humans are adaptations resulting from selective forces exerted by the increasingly complex and dynamic social and cultural environment that co-evolved with these traits. Variations in the modulation of stress responses mediated by specific HPAA characteristics (e.g., baseline cortisol levels, and changes in cortisol levels in response to challenges) are viewed as phenotypically plastic, ontogenetic responses to specific environmental signals. From this perspective, we discuss relations between physiological stress responses and life history trajectories, particularly the development of social competencies. We present brief summaries of data on hormones, indicators of morbidity and social environments from our long-term, naturalistic studies in both Guatemala and Dominica. Results indicate that difficult family environments and traumatic social events are associated with temporal elevations of cortisol, suppressed reproductive functioning and elevated morbidity. The long-term effects of traumatic early experiences on cortisol profiles are complex and indicate domain-specific effects, with normal recovery from physical stressors, but some heightened response to negative-affect social challenges. We consider these results to be consistent with the hypothesis that developmental programming of the HPAA and other neuroendocrine systems associated with stress responses may facilitate cognitive targeting of salient social challenges in specific environments.

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1. Evolutionary paradox of psychosocial stress

Psychosocial challenges reliably stimulate the hypothalamic-pituitary-adrenal axis (HPAA) in humans and many other mammals (Hennessey et al., 2009; Yim et al., 2010). Given the apparent short- and long-term costs of HPAA activation to physical and mental health (Cohen, 2004; Kiecolt-Glaser et al., 2010; Shonkoff et al., 2009), this presents an evolutionary paradox: *Why do social interactions and relationships affect HPAA responses?* Currently no satisfactory explanations exist for why natural selection could have favored links between the HPAA and the neuropsychological mechanisms involved with assessment of the social environment. We do not fully understand why, in the sense of evolved function, these links are modifiable during ontogeny, such that early social experiences may permanently alter HPAA stress responses (Champagne, 2010; Glover et al., 2010). Furthermore, we have not evaluated thoroughly the unusual and perhaps unique characteristics of the evolved human social brain, including empathy and theory of mind (Adolphs, 2003a,b; Daly and Wilson, 1995; Geary, 2005) in regard to physiological stress responses to psychosocial challenges.

Our objectives for this paper are to provide a plausible theoretical model linking stress responses to the neural plasticity that enables adaptation to the dynamic social environment of the human child. We examine the apparent paradox of HPAA responses to psychosocial stimuli from the unifying paradigm of Niko Tinbergen (1963), who emphasized the importance of integrating proximate physiological explanations with ontogeny, phylogeny, and adaptive (evolutionary) function. We evaluate possible mechanisms and developmental trajectories that connect early life social events to physiological stress and androgen responses, psychological development, and health outcomes from conception through adolescence. We illustrate our ideas with brief overviews of our respective work in Guatemala and Dominica. This empirical portion of our review starts by analyzing stress as a modulator of women's reproductive function and the conflicts that can arise between mother and fetus. Next we focus on the specific effects of social challenges on postnatal ontogeny of HPAA responses, and subsequent health outcomes. We conclude by proposing a reconsideration of the concepts of adaptation and pathology in stress theory.

2. Physiological mechanisms, developmental plasticity and adaptive function

Most studies of social modulation of early HPAA development have been based on clinical, epidemiological and experimental (primarily nonhuman animal model) research paradigms. Tremendous advances have been made in understanding the physiological, neurobiological and genetic mechanisms that underpin stress responses (de Kloet et al., 2005b; Joëls and Baram, 2009; Lupien et al., 2009; McEwen, 2007; Sapolsky et al., 2000; Weaver et al., 2004). Explanations for early social modulation of HPAA development have centered on the concepts of allostasis (Romero et al., 2009; McEwen and Wingfield, 2003, 2010), developmental programming (Entringer et al., 2009; Kajantie and Räikkönen, 2010; Mirescu et al., 2004; Veenema, 2009) and mismatches to novel adverse environmental conditions (Gluckman et al., 2005, 2007; Loman and Gunnar, 2010; Sapolsky, 2005). The effects of early, extreme and chronic psychosocial stress are generally posited to be pathological (Anisman et al., 1998; Chrousos, 1998, 2009; Seckl

and Holmes, 2007; Seckl and Meaney, 2004). Moderate exposure to stressors, however, is thought to enable the development of coping responses that enhance resiliency (Gunnar et al., 2009a; Lyons et al., 2010; Macrì et al., 2009). We suggest that evolutionary developmental biology may provide important theoretical insights into this apparent contradiction.

2.1. Allostasis as a proxy for adaptation

Neuroendocrine systems such as the HPAA and the hypothalamic-pituitary-gonadal axis (HPGA) may be viewed as complex mechanisms produced by natural selection to communicate information within and between cells and tissues. Physiological stress responses regulate the allocation of energetic and other somatic resources to different bodily functions via a complex assortment of neuroendocrine mechanisms. Changing environments and conditions require adjustment of priorities. While being chased by a predator, organisms do not want to expend resources on digestion, growth, immunity and reproduction (Sapolsky, 2005). Neuroendocrine stress responses help release and direct glucose, fatty acids and other resources to tissues necessary for the task at hand. Chronic and traumatic stress can diminish health, evidently because resources are diverted away from important health maintenance functions such as immune regulation (Bartolomucci, 2007). Cortisol can inhibit inflammation (Elenkov et al., 1996; Elenkov and Chrousos, 1999), alter cytokine production (Derijk et al., 1997; Turnbull and Rivier, 1999), and increase monocyte apoptosis (Norbiato et al., 1997), which may translate into increased susceptibility to infections. The sum of these costs of HPAA activation is often referred to as "allostatic load," with "allostasis" being the general process of physiological/behavior change to maintain homeostasis (Korte et al., 2005; McEwen and Wingfield, 2003, 2010).

The diversion of resources may have particular significance during fetal and child development because of the additional demands of physical and mental growth with possible long-term ontogenetic consequences (Glover et al., 2010; Korosi et al., 2010; Nepomnaschy and Flinn, 2009). For example, environmental cues of high mortality risk may result in more rapid reproductive maturation (Chisholm et al., 2005; Stearns, 1992), whereas resource limitations may delay pubertal onset (Ellison, 2001) and modify metabolic processes (Gluckman et al., 2009; Kuzawa and Quinn, 2009; Sloboda et al., 2007).

The apparent negative consequences of HPAA responses and high allostatic loads for individual health are often viewed as pathological. Such an interpretation can produce confusion about evolved functions of the HPAA and its ontogeny. We suggest that this confusion is rooted partly in the different perspectives of clinical practice, general biological/physical sciences and evolutionary biology. The goal of clinical practice is to improve physical and mental health; the goal of general biological/physical sciences is to describe biochemical mechanisms that affect health; and the goal of evolutionary biology is to understand how mechanisms that affect health evolved by natural selection. Reconciling these perspectives can be difficult (Bateson et al., 2004; Nesse et al., 2006, 2009). For example, in pursuit of evolutionary (reproductive) fitness, natural selection can produce outcomes that do not maximize short-term physical and mental health (Buss, 2000; Muehlenbein, 2010). Traits are selected to increase replication of genetic materials through survivorship and reproduction. Simply put, natural selection does

not maximize one's happiness nor minimize stress. Otherwise we might never experience anxiety or low mood, which could be adaptive under certain circumstances (Nesse and Ellsworth, 2009). Caution is also warranted in assuming that the function of the HPAA is to maintain "homeostasis." The stress concepts of "allostasis," "allostatic load" and "homeostasis" are proxy measures that usually, but not always, track the evolved functions of a set of physiological mechanisms (Bonier et al., 2009; McEwen and Wingfield, 2010; Worthman and Panter-Brick, 2008). Identification of the evolved functions of the HPAA is further muddled by environmental effects on the ontogeny of the neuroendocrine mechanisms.

2.2. Ontogeny: life history trade-offs

Waddington (1956) referred to the lack of understanding of ontogeny, or the translation of genetic information into the phenotype during development, as the "great gap" in biology. All living organisms have significant portions of their genomes and epigenomes that perform developmental "regulatory" functions – in effect, switches that turn some genes off and others on during development (Qiu, 2006; West-Eberhard, 2003). Some of these regulatory switches are attuned to external environmental conditions in ways that can result in advantageous phenotypic modifications (Agrawal, 2001). The morphological, physiological, and behavioral mechanisms that organisms use to modify phenotype and respond to environmental challenges are posited to be evolved adaptations. Flexibility involves both immediate, transient responses and longer-term developmental changes. The ability to generate a variety of phenotypes from a single genotype in response to various environmental conditions is referred to as "phenotypic plasticity" (West-Eberhard, 2003).

The general objective of phenotypic plasticity is to modify the organism so as to meet better any present and future challenges. Natural selection favors organisms capable of generating efficiently a functionally plastic phenotype in response to environmental conditions that have occurred with some regularity in a species' evolutionary history. However, a key problem is lack of predictability of future conditions. How reliable are the present and past cues that are used to assess future contingencies? This difficulty of prediction increases with distances in time and space. Early preparation allows for improved specialization and economy of development; the sooner one can adjust development to suit future environments the better. In this way resources are not wasted maintaining abilities to respond to conditions that are unlikely to occur. The balance between predictability and specialization during development influences the ontogenetic trajectories of phenotypic plasticity. "Critical" or "sensitive" periods for environmental input involve this inherent temporal trade-off between the reliability of cues and the advantages of earlier specialization (Alexander, 1990; Mousseau et al., 2009; Shettleworth, 2010).

Physiological research on ontogenetic trajectories has targeted the homeostatic mechanisms of the HPAA system, which appear sensitive to exposure to high levels of corticotropin-releasing hormone (CRH), adrenocorticotropin hormone (ACTH), and cortisol during development. Glucocorticoid receptors (GRs) and neurons in the hippocampus and hypothalamus (which are part of the negative feedback loop regulating release of CRH and ACTH) can be affected by neurotoxic levels of cortisol, ACTH and CRH associated with traumatic events (Sapolsky, 1996, 2005). Hence early trauma is posited to result in permanent HPAA dysregulation and hypercortisolemia, with consequent deleterious effects on the hippocampus, thymus, and other key neural, metabolic, and immune system components (Mirescu et al., 2004; Zhang et al., 2002). In human and nonhuman primates, these effects are posited to have additional consequences for cognitive development because of the high density of GRs in the pre-frontal cortex (de Kloet et al., 1999; Patel et al., 2000; Sanchez

et al., 2000). If exposure to trauma had commonly occurred during a species' evolutionary history, and caused maladaptive (fitness reducing) effects, then it seems likely that natural selection would favor protective mechanisms. If the occurrence of trauma provided useful information regarding the future environment (e.g., probability of food shortages—Gluckman et al., 2007), then it seems likely that natural selection would favor mechanisms that would modify the phenotype to better suit the predicted conditions (Kaiser and Sachser, 2005).

Activation of various epigenetic mechanisms during critical periods could play important roles in producing this phenotypic plasticity (Oberlander et al., 2008; Szyf et al., 2007, 2008). For example, DNA methylation in the rat, set during a sensitive period in the first week after birth, is a mechanism connecting diminished maternal care (licking, grooming, and arched-back nursing) with long-term elevations of HPAA responses (Champagne, 2010). The methylation sites are specific to cells in different parts of the brain, consistent with the logic that it is adaptive to modify the expression of different genes contingent on cellular function. For example, DNA methylation affects hippocampal GR exon 17 promoter activity in response to maternal care altering the patterns of CRH release in rat offspring (Weaver et al., 2004, 2005). Histone modification is another epigenetic mechanism that can alter the activity of DNA and affect neurological functions (e.g., Tsankova et al., 2007). Glucocorticoids transferred during lactation may provide a complementary mechanism for trans-generational effects (Macrì and Wurbel, 2006).

Gestation and early childhood are especially critical periods for the development of the HPAA and its associated phenotypic traits (Champagne et al., 2008; Lupien et al., 2009; Maccari et al., 2003; Nepomnaschy and Flinn, 2009). While the relationship between early social trauma and variation in HPAA development in humans has not been documented as well as it has been in nonhuman animals, similar effects and intervening mechanisms likely exist. In humans, early childhood social experiences can have profound and permanent effects on later adolescent and adult HPAA regulation and stress responses (Champagne, 2010; cf. Flinn, 2009; Levine, 2005). For example, difficult social environments – such as maternal depression, family death, orphanage, neglect and abuse – are temporally linked with unusual HPAA responses (Essex et al., 2002; Heim et al., 2000, 2002; Lupien et al., 2005; McGowan et al., 2009; O'Connor et al., 2003; Slavich et al., 2010; Teicher et al., 2006). Although the evolutionary reasons for this are still equivocal (and may be species-specific, e.g., Wiedenmayer, 2004), early social modulation of HPAA responses may function to produce adaptive neural reorganization (Ademec et al., 2005; Flinn, 2006a; Huether, 1998; Kaiser and Sachser, 2005; Meaney, 2001; Rodriguez Manzanares et al., 2005). Alternatively, these may simply be the result of maladaptation to the novelty of chronic stress in social environments (McEwen, 1995; Sapolsky, 1996, 1999).

The former explanation is particularly appropriate for consideration in humans, since children face particularly challenging cognitive problems as a result of complex social interactions. An important role of stress responses here may be to assist in the management of mental processes to solve specific cognitive problems, like the threat of an approaching bully. The child needs to reallocate cognitive efforts to the task at hand: prepare for immediate contingencies by recalling salient information, enhancing relevant sensory input, and activating circuits for appropriate actions. Certain aspects of HPAA may have been selected to help enable not only the acute responses to such challenges, but also facilitate their modification during development, including learning. Human social and cultural environments may pose special problems for the ontogeny of the HPAA and its links to the limbic and other brain systems.

2.3. Childhood, family and the social brain

Intensive information processing and social communication are core human adaptations. The human brain that enables these abilities is an astonishing organ. Its cortex comprises about 30 billion neurons of 200 different types, each of which is interlinked, on average, by more than a thousand synapses, resulting in a million billion connections working at rates of up to ten billion interactions per second (Edelman, 2006; Koch, 1999; Williams and Herrup, 1988). Quantifying the transduction of these biophysical actions into specific cognitive activities (e.g., thoughts and emotions) is difficult, but it is likely that humans have more information processing capacity than any other species (Roth and Dicke, 2005).

The human brain evolved at a rapid pace: hominin cranial capacity nearly tripled (from an average of about 500 cm³ to 1350 cm³) in approximately two million years (Lee and Wolpoff, 2003)—an average increase of roughly 100,000 neurons and supportive cells per generation. Structural changes such as increased convolutions, thickly myelinated cortical neurons, lateral asymmetries, increased von Economo neurons, expansion of the neo-cortex, and enhanced integration of the cerebellum were all significant (Allman, 1999; Amodio and Frith, 2006; Schoenemann, 2006; Sherwood et al., 2006). In comparison with most other parts of the human genome, selection on genes involved with brain development was especially intense (Gilbert et al., 2005).

The human brain has high metabolic costs: approximately 50% of an infant's, and 20% of an adult's, energetic resources (primarily glucose) are used to support neurological activity (Aiello and Wheeler, 1995; Holliday, 1986). The increase in energetic resources allocated to the brain was accompanied by a corresponding decrease in digestive tissue. However, this does not explain what selective pressures for enhanced information processing were, nor why the resources conserved by reducing digestive tissues were not reallocated to reproductive functions. The obstetric difficulties associated with birthing a large-headed infant generate additional problems (Rosenberg and Trevathan, 2002). The selective advantages of increased intelligence must have been high to overcome these costs.

The human brain, in short, is a big evolutionary puzzle. It is developmentally and metabolically expensive, evolved rapidly, and enables unusual human cognitive abilities such as language, empathy, foresight, consciousness, mental time-travel, creativity, and theory of mind. Advantages of a larger brain may include enhanced information processing capacities to contend with ecological pressures that involve sexually dimorphic activities such as hunting and complex foraging (Kaplan and Robson, 2002). There is little evidence, however, of sufficient domain-specific enlargement of those parts of the brain associated with selective pressures from the physical environment (Adolphs, 2003a; Geary and Huffman, 2002). Indeed, human cognition has little to distinguish itself in the way of specialized ecological talents.

The human brain did not evolve as an isolated trait; concomitant changes in other traits may provide clues as to what selective pressures were important during hominin evolution (Flinn et al., 2007). Changes in life history patterns accompanied the evident increases in information processing and communication during the Pleistocene epoch (Dean et al., 2001). Length of gestation (pregnancy) was increased, but resultant offspring became even more altricial (Rosenberg, 2004). Human infants must be carried, fed, and protected for a longer period relative to our hominin ancestors and other primates such as chimpanzees. Human childhood and adolescence are also exceptionally lengthy (Bogin, 1999; Leigh, 2004; Smith, 1992). This extension of the juvenile period results in a delay of reproduction until at least fifteen years of age, resulting in prolonged exposure to extrinsic causes of mortality, as well as longer generation intervals. Parental and other kin investment continues for an unusually long time, often well into adulthood and perhaps even after the death of the parents. Like the big brain, human life history is an evolutionary puzzle (Geary and Flinn, 2001; Hill and Kaplan, 1999; Mace, 2000; Muehlenbein and Flinn, 2011).

Human childhood has traditionally been viewed as a period of edification: "immatures are enabled to live a protected existence while they learn skills necessary for adult life" (Bowlby, 1969, p. 63; see also Alexander, 1987). The primary question has been: What information is so important and difficult to acquire that so many years are needed for its mastery? Most juvenile primates spend considerable effort playing and practicing in their physical environment, developing predator avoidance and fighting skills (Pellegrini and Archer, 2005). But compared with other primates, our motor skills do not appear especially challenging; a terrestrial environment seems more easily mastered than an arboreal one. Children may need time to acquire knowledge for tool use and complex foraging including hunting (Darwin, 1871; Hill and Kaplan, 1999; see also Byrne, 2002a,b). An extraordinarily long developmental apprenticeship may be useful for acquiring solutions to ecological problems unique to a culture group's niche (Bock, 2005; cf. Bird and Bliege Bird, 2002; Blurton-Jones and Marlowe, 2002). Investment in "embodied capital" (i.e., information from learning retained in memories, procedural skills, etc.), via an extended childhood, has been suggested to have a fitness payoff from increased adult foraging ability (Kaplan et al., 2000).

A complementary approach to the problem of the evolution of human childhood involves consideration of the brain as a "social tool" (Alexander, 1989; Bjorklund and Rosenberg, 2005; Dunbar, 1998; Flinn et al., 2005a,b; Humphrey, 1983). This hypothesis suggests that many human cognitive and psychological adaptations function primarily to contend with social relationships, with ecological constraints (e.g., hunting or extractive foraging) being a more secondary or complementary force of recent evolutionary change (Joffe, 1997). It appears that some human cognitive competencies, such as theory of mind and language, are most readily understood in terms of social selection pressures (Bjorklund and Pellegrini, 2002; Flinn, 2004; Flinn, 2006b; Flinn and Alexander, 2007), although some cognitive competencies for interacting (e.g., navigating) with the physical world are evident as well (Geary and Huffman, 2002). Interactions with similarly intelligent conspecific competitors and cooperators appear to have been a major force shaping many of the distinctive changes in the human neocortex (Adolphs, 2003a,b; Allman et al., 2001; Flinn et al., 2005a,b; Gallagher and Frith, 2003). Predicting future behaviors of a social competitor/cooperator, and anticipating appropriate countermoves, makes the arms race of social success a difficult undertaking, particularly since this must be accomplished in multiple relationship networks with shifting coalitions and deception (Chagnon, 1988; Flinn and Coe, 2007; Gilbert, 2005).

Indeed, the potential variety of human social puzzles is apparently infinite; no two social situations are precisely identical, nor are any two individuals ever in the exact same social environment. Moreover, social relationships can change rapidly, requiring quick modification of strategy. Variability in these dynamics creates conditions that should favor the evolution of brain and cognitive systems above and beyond more traditional modular systems (Tooby and Cosmides, 2005). These systems include general intelligence, domain-general abilities, fluid intelligence (abstract reasoning) and executive functions that are capable of integrating and co-opting information processed by more restricted, domain-specific mechanisms (Adolphs, 2003a,b; Blakemore et al., 2004; Geary, 2005) and using mental simulations, or "scenario-building" (Alexander, 1989), to construct and rehearse potential responses to changing social conditions. These complex cognitive processes are more capable of contending with, and producing, novelties of cul-

tural change and individual-specific differences (Bjorklund, 2006; Flinn, 1997, 2006b; Tomasello, 1999).

The information processing capacity used in human social competition is considerable, and perhaps significantly greater than that involved with foraging skills (Rilling et al., 2002; Roth and Dicke, 2005; Schoenemann, 2006). Although knowledge of the basic neuroanatomical structures involved with human social aptitudes has increased dramatically (e.g., Allman, 1999; Damasio, 2003; Duvarci et al., 2005; Gallese, 2005; Gallese et al., 2004; Moll et al., 2005), the mechanisms that guide their ontogeny remain uncertain (Geary and Bjorklund, 2000). The neuroendocrine stress responses to social stimuli may provide important clues.

2.4. Phenotypic plasticity through programming of the limbic system and neocortex for human sociality

One function of neuroendocrine stress responses may be to guide adaptive neural reorganization, such as enhancing predator detection and avoidance mechanisms (Buwalda et al., 2005; Dal Zatto et al., 2003; LeDoux, 2000; Mateo, 2008; Meaney, 2001; Rodriguez Manzanares et al., 2005; Wiedenmayer, 2004). For example, exposure to cats can have long-term effects on the central amygdala (right side) in mice, resulting in increased fear sensitization (Ademec et al., 2005). The potential evolutionary advantages of this neural phenotypic plasticity are apparent (Rodriguez Manzanares et al., 2005). Prey benefit from adjusting alertness to match the level of risk from predators in their environments. Post traumatic stress disorder (PTSD) appears analogous to these fear conditioning models, and involves similar effects of noradrenergic (Pitman et al., 2002) and glucocorticoid systems (Brinks et al., 2009; de Quervain et al., 2009; Rohleder et al., 2010; Roozendaal et al., 2002, 2009; Schwabe et al., 2009) on associative long-term potentiation (LTP) of the amygdala and other neurological structures that underlie the emotional state of fear.

Social defeat also affects the amygdala and hippocampus, but in different locations (Amaral, 2003; Bartolomucci et al., 2005; Koolhaas et al., 1997), suggesting that neural remodeling and LTP is targeted and domain-specific (e.g., Rumpel et al., 2005). Glucocorticoids, perhaps in combination with peptide hormones and catecholamines, appear to facilitate the targeting of domain-specific remodeling and LTP in developmentally appropriate ways (e.g., Moriceau et al., 2006). The potentiating effects of cortisol on emotional memories and other socially salient information may be of special significance in human child development (Beylin and Shors, 2003; Fenker et al., 2005; Jackson et al., 2006; Lupien et al., 2002, 2009; Pitman, 1989; Roelofs et al., 2007). The neurological effects from stress responses may underlie adaptation to short-term contingencies and guide long-term ontogenetic adjustments of emotional regulation and associated behavioral strategies.

If physiological stress responses promote adaptive modification of neural circuits in the limbic and higher associative centers that function to solve psychosocial problems (Huether et al., 1999), then the apparent paradox of psychosocial stress would be partly resolved. Temporary elevations of cortisol in response to social challenges could have advantageous developmental effects involving long-term potentiation, synaptogenesis and neural reorganization (Buchanan and Lovallo, 2001; Huether, 1996, 1998). Such changes may be useful and necessary for coping with the demands of an unpredictable and dynamic social environment. An evolutionary advantage would result if elevating stress hormones in response to social challenges (a) enhances specific acute mental functions, (b) regulates energetic resources used by the brain, and (c) helps guide cortical remodeling (e.g., Shansky et al., 2009), including the neurological structures involved with emotional regulation.

Chronic destabilization of neuronal networks in the hippocampus or cerebral cortex, combined with enhanced fear circuits in the amygdala (e.g., Bauer et al., 2001; Phan et al., 2006), however, could result in apparently pathological conditions such as PTSD (Yehuda, 2002) and some types of depression (Preussner et al., 2005; Shansky and Morrison, 2009). Even normal (but perhaps novel) everyday stressors in modern societies, such as social discordance between what we desire and what we have (Dressler and Bindon, 2000), might generate some seemingly maladaptive HPAA responses. Individual differences in perception, emotional control, rumination, reappraisal, self-esteem and social support networks would be likely co-factors (Chisholm et al., 2005; Ellis et al., 2006; Geary and Flinn, 2002; Vigil et al., 2009, 2010).

2.5. Stress as a modulator of fecundability

The impact that the environment has on ontogeny cannot be over-emphasized. Environmental conditions will affect an organisms' future beginning even before the gametes fuse to form the conceptus. In all species with internal fertilization, the mother represents the first environment. Therefore the mother's overall condition may not only affect the chances of conceiving and maintaining a pregnancy but can also critically affect her offspring's chances of survival and overall adult phenotype. Consequently, a pregnancy conceived or maintained under stressful conditions may affect the mother's lifetime reproductive success and that of her offspring (Penn and Smith, 2007).

In humans, a healthy, well-nourished mother is necessary but not sufficient. Human offspring require comparatively very high levels of energetic resources, protection and training for a prolonged period of time in order to reach reproductive maturity and subsequent successful reproduce. These resources are provided not just by the mother but by a broad social network, one of the most extensive examples of alloparenting that exists in nature, composed of the mother's partner (often the biological father of the offspring), her relatives and friends (Hrdy, 2009; Walker et al., 2010). The human early environment is represented by a combination of available allocare in addition to maternal health and nutritional status. Importantly, there is a tight association between an individual's health and nutritional status and the size and quality of her social support network (Neumann, 2009). Variations in the quality of any of these factors can have a significant effect on her children's survival and future reproductive fitness.

Given the importance of maternal investment in offspring development, it has been hypothesized that when women's ability to invest (for various reasons including poor nutrition and small, poor social support networks) in new offspring deteriorates, reproductive *suppression* would be advantageous (Ellison, 2001; Nepomnaschy et al., 2004, 2006). Suppressing reproduction in the face of stress can help women survive the inauspicious times, helping already existing offspring to survive, while avoiding new pregnancies with reduced fitness prospects. How do women determine when the deterioration of conditions for reproduction make suppression the best temporary decision? And what are the neuropsychological and physiological mechanisms that cause reproductive suppression? The answers to these questions are linked.

A woman's conscious rationalizations about the convenience or not of conceiving or maintaining a pregnancy likely had little impact on actual fertility before the emergence of modern contraception and safe elective abortion. Unlike most other mammals that reproduce in specific seasons, women ovulate continuously throughout the year; this logically increases the chances of conception. Behavioral avoidance of intercourse could be used to limit fertility. Sex plays an important role, however, in creating and maintaining bonds in humans, and these bonds are likely to have

been linked to offspring survival at some points in human evolution (Alexander, 1989). In addition, sexual coercion could have easily trumped behavioral efforts to prevent untimely pregnancies. Behavioral avoidance of intercourse is unlikely to have been an efficient strategy to modulate the timing of reproductive ventures for most of human evolutionary history.

In contrast, physiological mechanisms underlying reproductive suppression would help women avoid untimely pregnancies independent of sexual activities. Nepomnaschy et al. (2004, 2006) have suggested that selective pressures could have favored the evolution of pathways that will foster the exchange of physiological information between the HPAA and the HPGA, leading to reproductive suppression when environmental (ecological and social) conditions deteriorate. Indeed, the presence of corticotrophin releasing factor receptors on the ovary (Ghizzoni et al., 1997) suggests a possible direct connection of HPAA activation with the downregulation of steroidogenesis exerted directly at the level of the ovaries (Chrousos et al., 1998; Tilbrook et al., 2002). While such a connection has been consistently supported by evidence derived from animal studies (e.g., Breen and Karsch, 2006; Brunton et al., 2008), the physiological data needed to test them in humans continues to be scarce.

2.5.1. Surviving mom: evolution of the defensive fetus and the postnatal consequences of surviving prenatal stress

While the mechanisms described above may reduce the likelihood of untimely conceptions or increase the chances of an early spontaneous abortion, no biological mechanism is infallible and challenges may appear after conception has taken place. In those cases the ability of a woman's body to prevent the development of a new pregnancy may clash with the interests and physiological defense mechanisms of the developing fetus. Mother and fetus may have different interests. Each fetus is a genetically unique entity, with only one opportunity to be born. Being alive is a prerequisite to achieving any other goals and, thus, being born should be a fetus's first priority. Here is where conflicts of interest with the mother may arise; there will be some conditions under which the mother would benefit from the interruption of gestation and the fetus would benefit from promoting its continuation (Trivers, 1974). These conflicts of interests might help explain why, within just hours after fertilization, embryos begin secreting a battery of metabolites that reduce the risk of miscarriage (Haig, 1993). In line with this argument Nepomnaschy et al. (2006) suggested that maternally-derived abortive mechanisms may lose efficiency as the fetus progressively gains physiological control of its own gestation. In other words, the more developed a fetus gets the more capable it should be of surviving periods of maternal stress. Whether the abortifacient effects of stress diminish as the fetus develops remains to be tested. A number of studies, however, suggest that pregnancies can continue despite acute stressors deriving from challenges experienced after placentation has taken place (Kaiser and Sachser, 2005; de Kloet et al., 2005b; Murphy et al., 2006). Surviving stressful maternal conditions, though, can have serious physiological and behavioral consequences for the fetus, and can lead to important variations in the resulting postnatal phenotype.

Experiments in non-human mammals, mainly rodents and non-human primates, suggest that prenatal stress can result in low birth weight and delayed postnatal physical growth, as well as affect motor and cognitive development. Significantly, one of the important consequences of prenatal stress appears to be a 'reprogramming' of HPAA basal function and regulation (de Kloet et al., 2005a). Animals experimentally exposed to prenatal stress show a shift in their circadian cortisol secretion profile (Koehl et al., 1999), and increased basal cortisol and ACTH levels (Buitelaar et al., 2003; Clarke et al., 1994; Schneider, 1992; Weinstock, 1997, 2008;

Weinstock et al., 1992; Welberg et al., 2000). When prenatally stressed rats are postnatally challenged, they present with a faster and stronger physiological response to the stressor compared to control animals (Fride et al., 1986; McEwen et al., 1995, 1995). Furthermore, prenatally stressed rats also take longer to recover and to habituate to a stressor (Takahashi et al., 1992). Prenatally stressed animals also tend to have higher plasma glucose levels than controls (Vallée et al., 1997) and have fewer hippocampal glucocorticoid and mineralocorticoid receptors (Szuran et al., 2000; Weinstock, 2005, 2009).

Neurophysiological changes observed in prenatally stressed animals have clear behavioral correlates. Animals experimentally subjected to stress during pregnancy display increased anxiety, shorter attention spans, and depressive-like symptoms such as learned helplessness and anhedonia (Cirulli et al., 2009; Frye and Wawrzycki, 2003; Morley-Fletcher et al., 2003). They also differ from controls in their behavioral strategies when facing novel situations such as the inclusion of new individuals in their social group, physical alterations of their environment, or when exposed to an open field (ibid).

Although human studies are more limited in scope and design, available reports are consistent with what has been observed in nonhuman animal experiments. Prenatal stress in humans has been linked with premature parturition, low birth weight for gestational age (Hedegaard et al., 1996; Wadhwa et al., 1998; Ruiz et al., 2002; Rondo et al., 2003), small head circumferences (Lou et al., 1994; Buitelaar et al., 2003), and variations in the rates of physical, mental, and motor development (Gluckman et al., 2007; Kajantie, 2006). Prenatal stress appears to also affect HPAA regulation in humans (Andrews and Matthews, 2004; Glover et al., 2004; Halligan et al., 2004; Meinlschmidt et al., 2010). For example, Gitau et al. (2001) report that piercing of the fetal trunk around the time of pituitary maturation (18th gestational week) leads to detectable increases of fetal β-endorphin levels, and that the same challenge two weeks later (after the adrenal glands mature) leads to increases in fetal cortisol.

The effects of prenatal stress on the HPAA can also be observed postnatally. Field et al. (2004) compared depressed and non-depressed pregnant women and their children. They report a strong association between the cortisol, catecholamines, and serotonin levels in their mother–children dyads. Similarly, Gutteling et al. (2004) report that maternal cortisol during gestation, as well as pregnancy-related fears, were positively associated with their children's cortisol levels before and after being vaccinated at ages 4–6 years, as well as during the first days of the school year (Gutteling et al., 2005). Prenatally stressed children also presented steeper circadian slopes.

Exposure to stressors in utero may affect the fetus's neurological development and its ability to habituate to challenges. Maternal stress levels during the third trimester have been associated with changes in fetal heart rate after vibroacoustic stimulation (Sandman et al., 1999). Children stressed prenatally have been reported to have increased tendency of depression, attention deficits (Buitelaar et al., 2003), difficult temperament (Van den Bergh, 1992), emotional problems, hyperactivity (Linnet et al., 2003; O'Connor et al., 2003) and difficulties in adapting to novel situations (Van den Bergh, 1992). Furthermore, prenatal stress has been linked to schizophrenia (Hultman et al., 1999; Imamura et al., 1999; Koenig et al., 2002; Van Os and Selten, 1998; Watson et al., 1999), criminal behavior, autism, and social withdrawal (Huttunen and Niskanen, 1978; McIntosh et al., 1995; Meijer, 1986; Schneider et al., 2004).

Still other studies have not identified statistical associations between prenatal stress and changes in HPAA functioning, motor and cognitive development, and postnatal behavior. For example, while individuals prenatally exposed to the Dutch famine

(1944–1945) show higher baseline salivary cortisol levels compared to unexposed controls, responses to psychological stress appear to not differ between the two (de Rooij et al., 2006). Other studies report positive effects of moderate gestational stress on development. DiPietro et al. (2006) concluded that mild maternal anxiety and depression in otherwise healthy women were associated with *enhanced* motor maturation in their two year-old children. These inconsistencies may be related to the broad range of differences in study designs as well as the multiple ethical and logistical limitations affecting human research on this subject. But these inconsistencies confirm that the relationships between prenatal stress and fetal programming are complex, and highlight how little we still know about this phenomenon.

The pathways through which prenatal stress may exert its effects are poorly understood (Huizink et al., 2004; de Weerth and Buitelaar, 2005). Glucocorticoids are logically suspected to be involved. Maternal cortisol levels are known to gradually increase during pregnancy, although the placental barrier keeps fetal cortisol levels 5–10 times lower than in the mother (Gitau et al., 1998; Predine et al., 1979). The placental enzyme 11β-hydroxysteroid dehydrogenase type 2 (11βHSD2) inactivates maternal cortisol by metabolizing it into cortisone before it crosses the placenta (Brown et al., 1993). Nonetheless, some maternal cortisol (about 10%) is believed to cross the placenta (Gitau et al., 1998). Given the difference in basal levels between mother and fetus, even small amounts of maternal cortisol can cause significant changes in fetal physiology (de Weerth and Buitelaar, 2005). These changes in cortisol levels have been reported to affect fetal growth (Banks et al., 1999), birth weight (Bloom et al., 2001), head circumference (French et al., 1999), HPAA functioning (Gitau et al., 1998), coronary function (Rotmensch et al., 1999; Subtil et al., 2003) and gastric function (Chin et al., 2003).

Stress metabolites may have additional effects on fetal development through alternative pathways. Placental production of CRH has been reported to increase with maternal stress (de Weerth and Buitelaar, 2005). CRH enters fetal circulation and can influence the development, distribution and abundance of glucocorticoid receptors in the fetus' central nervous system (Meaney et al., 1996; Majzoub and Karalis, 1999). Increases in glucocorticoids and catecholamines can reduce uterine blood flow, which, in turn, may restrict fetal growth and contribute to fetal hypoxia. This mechanism has been proposed as a potential explanation for the link between prenatal stress, low birth weight, prematurity, and poor neurologic outcomes (Schneider et al., 2004; Teixeira et al., 1999). Prematurity and low birth-weight have been linked with increased HPAA reactivity adults (Kajantie et al., 2002, 2003; Phillips et al., 2000, Reynolds et al., 2001).

Variation in placental 11βHSD2 may also contribute to variability in stress responses between mothers. Placental 11βHSD2 activity varies between women and within individuals according to gestational stage, protein content of diet, oxygen levels, and hormone levels (estradiol, progesterone, prostaglandins and catecholamines) (Bertram et al., 2001; Welberg et al., 2000). Variations in placental 11βHSD2 activity levels have been linked to changes in fetal HPAA development, fetal growth, survivorship, birth weight and adult coronary, renal and hepatic functions (Murphy et al., 2003). Nonhuman animal experiments suggest that alterations in placental function involving changes in the levels of prostaglandins, proopiomelanocortin (POMC), progesterone, and 11βHSD2 activity may mediate some of the effects that stress has on fetal development (Bloomfield et al., 2004).

Prenatal stress may exert its effects through a variety of other genetic, epigenetic and ontogenetic pathways. Fetal development depends on the synchronized occurrence of a large number of complex processes; stress related alterations of any of these processes or their tempos are likely to have an effect on the final outcome.
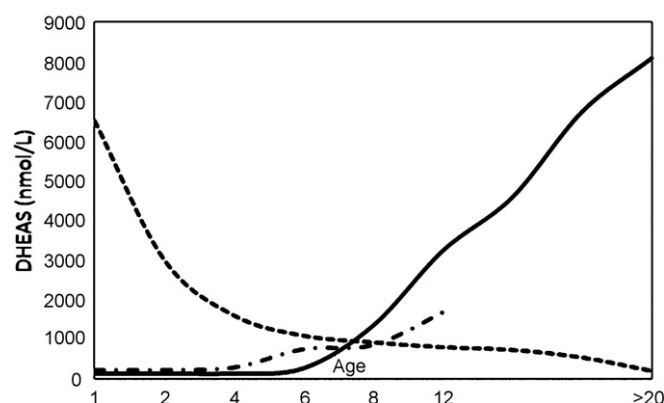

Fig. 1. Human (solid line) DHEAS levels from birth throughout juvenility compared to two other species of primates, rhesus macaques (dashed line) and chimpanzees (dash-dotted line). Data approximated using values from Copeland et al. (1985), Kemnitz et al. (2000) and Korth-Schutz et al. (1976).

At the neurological level, for example, disruption of cell differentiation, migration, positioning, and connection appear to be linked to outcomes such as dyslexia, schizophrenia, and mental retardation (Watson et al., 1999). Fetal factors also play important roles in any pathway mediating the relationship between gestational stress and fetal development (Meaney et al., 2007; Murphy et al., 2006; O'Donnell et al., 2009).

2.6. Social modulation of adrenal androgens

Other products of the HPAA worth mentioning here include the androgen dehydroepiandrosterone (DHEA) and its sulfated conjugate (DHEAS) (Maninger et al., 2009; Pérez-Neri et al., 2008). These hormones appear to be important biomarkers of longevity, immune functions, stress responses and psychological well-being (Buford and Willoughby, 2008; Chen and Parker, 2004; Enomoto et al., 2008; Maninger et al., 2009; Yen, 2001). They are synthesized in the cortex of the adrenal gland, where the region-dependent expression of several enzymes drives biosynthetic processes away from the production of cortisol towards the formation of the androgens (Hornsby, 1995; Nguyen and Conley, 2008; Pattison et al., 2009). As androgens, DHEA and DHEAS are relatively weak but they can be converted to sex steroids in target tissues (Labrie et al., 2005). They are the most prominent adrenocortical hormones produced in humans (Kime et al., 1980).

In humans, DHEA and DHEAS production begins with a sharp increase at adrenarche during mid-childhood followed by a steady increase that peaks in the mid-twenties, then steadily declining throughout senescence (Auchus and Rainey, 2004; Havelock et al., 2004) (Fig. 1). Adrenarche is particularly interesting because of the congruence of several psychobiological phenomena at this stage of child development (Campbell, 2006; Del Giudice, 2009), and because it appears to be shared only with a few Great Apes (Copeland et al., 1985; Cutler et al., 1978; Hornsby, 2004; Labrie, 2004; Nguyen et al., 2008; Smail et al., 1982) although measurable levels of DHEA and DHEAS are present in many non-human primates (Conley et al., 2004; Muehlenbein et al., 2003; Pattison et al., 2005).

Adrenal production of these androgens is virtually absent in other vertebrates (Conley et al., 2004; Labrie, 2004; Nguyen and Conley, 2008), with the exception of some rodents (hamster and red squirrel) and songbirds (Boonstra et al., 2008; Soma and Wingfield, 2001; Pieper and Lobocki, 2000). In these cases, the primary function of DHEA is likely the maintenance of aggressive behaviors outside the reproductive season (Soma et al., 2008). In songbirds,

aggressive interactions can result in elevated levels of DHEA (Soma et al., 2008; Wingfield et al., 2001), as well as its conversion to androstenedione within specific regions of the brain (Pradhan et al., 2010). DHEA could therefore act as a possible mediator of life history trade-offs between immune functions and reproduction (i.e., gonadal androgens; Wingfield and Sapolsky, 2003).

DHEA and DHEAS are synthesized de-novo in the brain where they perform neuroprotective and neuromodulatory functions (Baulieu and Robel, 1998; Corpechot et al., 1981; Do Rego et al., 2009; Majewska, 1995; Maninger et al., 2009; Pérez-Neri et al., 2008), likely as a direct result of their anti-glucocorticoid effects (Hazeldine et al., 2010; Maninger et al., 2009; McEwen, 2003). These functional relationships between glucocorticoids and adrenal androgens are complex. DHEA and DHEAS are synthesized and released in both the periphery and brain following exposure to acute and chronic stressors (Corpechot et al., 1981; Maninger et al., 2010). Empirical evidence points to a strong influence of CRH (Ibanez et al., 1999) and a permissive role of ACTH in regulating this DHEA and DHEAS release. For example, although DHEA does not show an awakening spike and is more stable throughout the day, its secretory patterns from the adrenals are similar to that of cortisol (Granger et al., 1999; Hucklebridge et al., 2005; Rosenfeld et al., 1971), and individuals with mutations in ACTH receptors have very low levels of DHEAS (Weber et al., 1997). On the other hand, patients with Cushing syndrome seem to maintain normal levels of DHEAS (Parker, 1989), thus ruling out a unique action of ACTH. Instead, glucocorticoids could regulate the production of DHEA through inhibition of 3-beta hydroxysteroid dehydrogenase (3βHSD) (Topor et al., 2010), although this scenario cannot explain the mismatch between DHEA and cortisol secretion throughout life.

The question still remains as to what selective pressures could have produced the evolution of adrenal secretion of DHEA and DHEAS. Increased social complexity of group-living animals that resulted in the evolution of larger brains (Byrne and Whiten, 1988; Dunbar and Schultz, 2007) would have been an important selective pressure for the production of neurochemicals that could buffer the negative effects of other chemicals (i.e., glucocorticoids) released during stress responses (Campbell, 2006). So why should these levels of neuroprotectants increase in mid-childhood?

Middle childhood is a life-history stage unique to humans. As discussed above, human children are very sensitive to perceived social relationships among kin and non-kin. Social hierarchies begin developing (Kohlberg et al., 1972; Strayer and Trudel, 1984), and their outcomes influence future social behavioral patterns (Weisfeld, 1999). Increased social complexity between these children and their peers as well as kin/non-kin adults can make it difficult to predict the outcomes of future social relationships, and these complex decision processes are stressful mental activities for children. The type of child-parent attachment could mediate how the child copes with their social environment and could be related to the development of personality and physiological attributes, both leading to individual differences in implicit and explicit reproductive strategies such as risk taking behaviors, onset of puberty and somatic growth (Belsky et al., 1991; Flinn et al., 1999).

Adrenarche, through an activation-reorganization of human attachment strategies before the onset of puberty (Del Giudice, 2009; Del Giudice et al., 2009) or through its neurosteroid action on neural plasticity, could act as a physiological event of hormonal production that shapes and primes behaviors that will allow children to better deal with the growing complexity of the social system made by peers and adults, preparing them for the intra-sexual competition during adolescence and adulthood. Early stressful experiences mediated by the family are expected to result in different life history strategies mediated by HPAA activity (Del Giudice, 2009; Del Giudice et al., 2009; Ellis and Essex, 2007; Flinn et al., 2009; Suomi, 2005). In line with this argument, DHEA and DHEAS do appear to

covary with child wellbeing. For example, prepubertal and pubertal children with major depression disorders exhibit low DHEA levels, and DHEA levels correlate with some comorbid aspects of the pathology (Goodyer et al., 1996). Premature adrenarche (i.e., high levels of DHEA and DHEAS for age) is associated with depressive symptoms (Dorn et al., 1999, 2008), and higher DHEA levels are present in pre- and peri-adolescent boys characterized with aggressive, antisocial behaviors (Van Goozen et al., 1998). DHEA levels are associated with higher resilience scores in abused children (Cicchetti and Rogosh, 2007). Low birth weight is also associated with higher levels of DHEAS during the catch-up growth phase in mid-childhood (Ong et al., 2004; Ibanez et al., 2006). 'Higher quality' parental care (including less marital conflict) also appears associated with adrenarche at a later age (Ellis and Essex, 2007).

Studies of human adults demonstrate that DHEAS levels are positively associated with physical and psychological performance in extremely stressful conditions (Morgan III et al., 2009; Taylor et al., 2007) and are negatively associated with negative mood after a stressful task (Izawa et al., 2008). High levels of DHEA, as well as a high DHEA to cortisol ratio, have been identified in individuals with post-traumatic stress disorders (Maninger et al., 2009) and have generally been associated with positive resilient outcomes (Haglund et al., 2007; Maninger et al., 2009).

Unfortunately, existing studies do not directly evaluate the effects of prenatal or early postnatal stress on adrenal androgens in humans. We need longitudinal studies in naturalistic settings targeting day-by-day variation of DHEA and DHEAS secretion in relation to pre- and post-natal stressful events. Furthermore, detailed analyses of DHEA and DHEAS levels following early life psychosocial stressors in nonhuman primates and certain rodents (e.g., hamster) are warranted. Because comparative data on adrenarche in naturalistic environments are scarce, it is difficult to hypothesize similarity of function.

3. Stress in the wild: HPAA responses in natural, everyday context

> "What is missing are long term prospective studies that track the nature and timing of early stress exposure and the linkages to children's later stress exposure, HPA functioning, and behaviors" (Essex et al., 2002, p. 777).

Investigating relations among HPAA responses, neural remodeling and cognitive adaptations to the social environment is not a simple or easy task (e.g., Pine et al., 2001). While cortisol can affect cognitive functioning and emotional states, cognitive processing and emotional regulation can also affect cortisol responses. Evaluating the causes and effects in ontogenetic sequence requires sequential data on physiological response profiles, environmental context and perception. Extensive research on hormonal stress responses has been conducted in clinical, experimental, school, and work settings (Dickerson and Kemeny, 2004; Hellhammer et al., 2009; Lupien et al., 2009; Panter-Brick and Pollard, 1999). We know relatively little about stress responses among children in normal everyday ("naturalistic") environments, particularly in non-industrial societies that are more similar to the environments of human evolutionary history.

Longitudinal monitoring of a child's daily activities, stress hormones, and psychological conditions provides a powerful research design for investigating naturally occurring stressors. Analyzing hormone levels from saliva (Ellison, 1988) can be a useful tool for examining the child's imperfect world and its developmental consequences, especially when accompanied by detailed ethnographic, medical and psychological information. Unfortunately, we do not yet have field techniques for assessment of corresponding ontogenetic changes in the relevant neurological mechanisms.

Assessment of early social modulation of HPAA responses during child development requires (a) longitudinal monitoring of social environment, emotional expressions, hormone levels, immune measures, and health, (b) control of extraneous effects from physical activity, circadian rhythms, and food consumption, (c) knowledge of individual differences in temperament, experience, and perception, and (d) awareness of specific social and cultural contexts. Multi-disciplinary research that integrates human biology, psychology and ethnography is necessary for meeting these demands. Physiological and medical assessment in tandem with ethnography including participant observation can provide intimate, prospective, longitudinal information that is not feasible in clinical studies.

In what follows, we briefly review results from our research on HPAA responses in rural communities in Guatemala and Dominica. Both studies are prospective, longitudinal, and naturalistic. The primary investigators have lived in the communities for long periods. Our objectives are to provide data useful for examining relations among hormonal measures of HPAA responses, events occurring in everyday life and developmental outcomes.

3.1. Conception and pregnancy

Investigation of relations between the maternal social environment and reproduction in humans has been limited by the paucity of large longitudinal studies that could help us better understand women's stress physiology and its interactions with reproductive function (Kajantie and Phillips, 2006). Women's stress research is often modeled on what has been learned from male stress models. This approach, however, is not appropriate. While in both sexes the HPAA and HPGA are intimately interconnected, in women, unlike men, the HPGA axis is continuously transitioning across reproductive stages making its interactions with the HPAA more dynamic and complex (Brummelte and Galea, 2010).

To further our understanding of the interactions between the HPAA and HPGA in women, Nepomnaschy and colleagues developed the "Society, Environment and Reproduction" (SER) Study. The SER study explores the effects that energetic, health and psychosocial challenges have on women's HPAA function and the impact that HPAA activation has on HPGA function. A total of 103 married Mayan women from a population in the highlands of southwest Guatemala provided biological specimens and answered questionnaires 3 times per week for up to a year. Longitudinal analyses of the interview data and hormonal profiles from a sub-set of 22 women were performed to assess the relationship between daily fluctuations in first morning urinary cortisol and reproductive hormones during the menstrual cycle and early pregnancy. These analyses revealed several interesting aspects of the role that daily challenges play in these women's lives and how they affect their reproductive physiology.

The more frequently self-reported concerns by the women participating in the SER study were health issues affecting them or their immediate family. We attribute the importance that women place on health concerns (i.e., infant diarrhea, respiratory problems, or obstetric complications) to the serious consequences that these problems can have in this rural population with little access to medical attention. The next most commonly reported concerns involved interpersonal problems, including marital quarrels. This is understandable in a patrilocal society where women are highly dependent on their husbands and their relatives for their subsistence and social support.

Economic problems were not a cause of frequent concern in this community, which is in stark contrast to those in most industrialized populations. In the SER study, social stratification of participants is minor, meaning that fluctuations in the availability of goods tend to affect all individuals equally. Furthermore, economic concerns appear to be minor for this community simply because their economic expectations are (based on previous experiences within this community) low, and so psychosocial stress related to such expectations is low. In contrast, loss of a member of a woman's support network due to illness or conflict can carry with it grave social and biological consequences, seriously impairing her ability to raise children.

Concerns reported by participants in the SER study were associated with elevated first morning urinary cortisol levels. In turn, within-woman increases in cortisol levels were linked with changes in profiles of reproductive hormones across the menstrual cycle. Specifically, raised cortisol levels were associated with untimely increases in gonadotrophins across the menstrual cycle, increases in follicular progesterone and decreases in mid-luteal progesterone (Fig. 2a) (Nepomnaschy et al., 2004). Increased progesterone, probably of adrenal origin, during the follicular phase has been previously reported to be associated with decreased fecundability (Baird et al., 1999). Low progesterone levels may lead to poor development and lack of vascularization of the endometrium (Clancy, 2009; Soules et al., 1989). An early drop in progesterone levels that lasts more than 24 h is likely to lead to an early termination of the luteal phase, all of which would negatively affect the chances of successful implantation (Clancy, 2009; King and Critchley, 2010). Energetic and psychosocial challenges had been previously reported to cause poor luteal progesterone levels in human and non-human primates (Ellison and Lager, 1986; Ferin, 1999; Xiao et al., 2002). Importantly, our results provide evidence for a potential pathway linking stress responses to luteal insufficiencies (Nepomnaschy et al., 2004), although the physiological evidence supporting this claim in humans is limited and sometimes contradictory (e.g. Ellison et al., 2007).

Work by Nepomnaschy and colleagues suggests a connection between daily challenges, stress axis activation, and reproductive suppression in women (Fig. 2a and b). For example, analyses of pregnancy fate and cortisol during the first 3 weeks of gestation (the period in which the placenta begins to develop and becomes functional) indicate that pregnancy loss was almost 3 times higher in women with increased cortisol levels (both means and number of peaks) during this period (Nepomnaschy et al., 2006).

In sum, there appears to be an intimate, hormonally-based connection between a woman expressing concerns, HPAA activation and reproductive suppression. In unfavorable circumstances, avoiding or interrupting reproduction could allow females to focus scarce resources on survival, improvement in overall condition, and investment in existing offspring (Nepomnaschy et al., 2004, 2006).

Understanding the multiple mechanisms through which prenatal stress affects fetal development and the resulting postnatal phenotype is a complex task that will require high-quality longitudinal research. Future studies will need to thoroughly assess the various factors that might be mediating the observed relationships. It would be important, for example, to (a) explore the genetic heritability of HPAA function from mothers to children, (b) separate the influence of the maternal HPAA functioning from stress related behaviors (such as alcohol or caffeine consumption), and (c) assess the differential effects of prenatal stress on HPAA functioning at the different stages of fetal development.

3.2. Infancy and childhood

Wayonne's dirt-clod missile struck the bright yellow dress hanging on the clothesline, making an impressive star-shaped smudge. His older cousin Jenny turned angrily from sweeping the house yard to chase him with her broom. Granny Deedee's yell halted their squabble. Jenny's face morphed from stifled argument to guilt, head bowed. She later confided to me that she felt upset because granny did not understand; her frustration was compounded by the
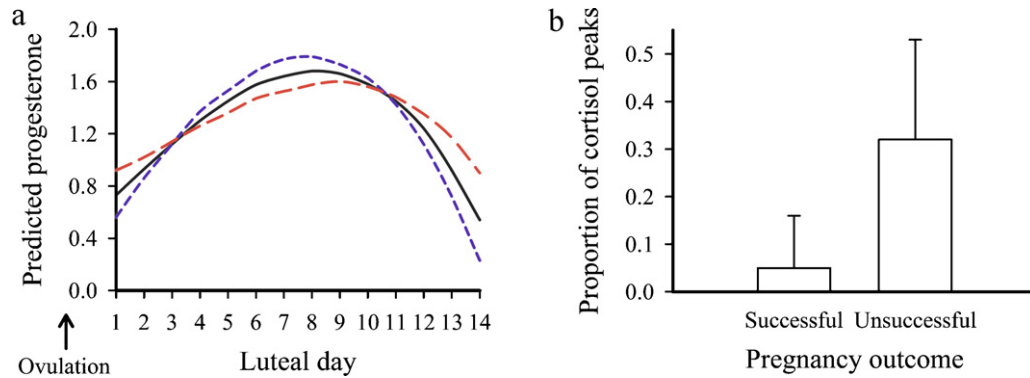
Fig. 2. (a) Progesterone levels as predicted by time and cortisol throughout the luteal phase according to the model developed by Nepomnaschy et al. (2004), based on data from 92 menstrual cycles provided by 24 healthy Mayan women. The blue dashed line represents the natural logarithm of progesterone levels as predicted by low cortisol (two standard deviations below each individuals' mean). The solid dark line represents progesterone levels as predicted by mean cortisol and the red dashed line represents progesterone levels as predicted by high cortisol levels (2 standard deviations above the mean). High cortisol levels predicted lower progesterone levels between days 4 and 10 after ovulation (day 0) (data from Nepomnaschy et al., 2004). Progesterone profiles were predicted using a random coefficients regression model (RCRM) (Brown and Prescott, 1999). The RCRM calculates a polynomial regression for the level of progesterone (the dependent variable) as predicted by time (day of the menstrual cycle) and each woman's cortisol levels and an overall polynomial for all the women. The degrees of freedom in the model are calculated based on the number of individuals included in the analyses adjusted to account for daily values missing from the record of each individual. We checked the adequacy of the model using residual diagnostic plots, influence statistics, and plots of predicted versus observed values. Associations between the progesterone, time, and cortisol were examined using mixed model analyses in Proc Mixed, SAS release 8.2 (Cary, NC) in all statistical analyses to take into account both fixed (e.g., day of the menstrual cycle) and random effects (individual participant). (b) Proportion of cortisol peaks (values > 90th percentile of the whole sample) and pregnancy outcome. Successful pregnancies had a significantly lower proportion of high cortisol peaks than did those pregnancies that resulted in spontaneous abortions ($P < 0.01$). Bar height indicates the average proportion of cortisol peaks observed for each pregnancy outcome. Error bars represent one standard deviation (data from Nepomnaschy et al., 2006). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

rule that she must accept granny's authority without debate (Flinn field notes, July 17, 1994). Jenny's cortisol level, measured from her saliva that was collected from all children in the community several times a day, rose from 1.4 to 4.2 μg/dl. The next day her secretory immunoglobulin-A levels dropped from 6.04 to 3.6 mg/dl. Four days later she had common cold symptoms: runny nose, headache, and low-grade fever (Fig. 3).

This exemplary case is illustrative of a common pattern. Children in this rural Dominican community are more than twice as likely to become ill during the week following a stressful event compared to when they had not recently experienced any significant stressors (Flinn, 2008; Flinn and England, 2003). This relation between social stress and illness is obviously not confined to Dominican children. Humans respond to challenges in their social environments by ele-

Fig. 3. Changes in cortisol and secretory immunoglobulin-A levels of a young girl in response to a conflict with her grandmother (figure based on data from Flinn, 2006a). Note the temporal pattern of the high cortisol spike associated with the stressful event, followed by low cortisol and secretory immunoglobulin-A, and then illness. Morbidity among children in this community is 2.7 times higher during a 2–5 day period following high stress events such as this (Flinn and England, 2003).

vating cortisol levels, often with negative consequences for their health (Cohen, 2004; Loman and Gunnar, 2010). Why should this be so? Why do social interactions, and a child's perceptions of them, affect stress physiology and morbidity? From the Tinbergen perspective, these "why?" questions ultimately involve understanding the evolutionary design of the ontogeny of the brain and HPAA of the human child.

Flinn has lived and conducted research in Jenny's village, located on the east coast of the island of Dominica, with the help of many colleagues including Ponzi and Muehlenbein, every year from 1988 to 2011. In this community, most of a child's mental efforts seem focused on negotiating social relationships with parents, siblings, grandparents, cousins and other kin, friends, teachers, bus drivers, neighbors, shop owners, and so forth. Foraging for mangos and guavas, hunting birds or even fishing in the sea from rock cliffs, are relatively simple cognitive enterprises, complicated by conflicts with property owners and decisions about which companions to garner and share calories with. The mind of the child seems more concerned with solving social puzzles than with utilitarian concerns of collecting food. Of course, some other populations have more difficult subsistence practices that require more extensive learning (e.g., Bock, 2005), but the social chess game nonetheless appears ubiquitous and cognitively demanding in all cultures (Hewlett and Lamb, 2005), as it likely was during human evolutionary history (Alexander, 1989).

3.2.1. Family environment

In their study of childhood stress and health in the community of Bwa Mawego, Flinn and colleagues use sequential longitudinal monitoring to assess children's physiological stress responses to everyday events, including social challenges such as the event described above. Their analyses indicate that social challenges are important stressors, with an emphasis on the family environment as both a primary source and mediator of stressful stimuli (Flinn and England, 1995, 1997).

In this community, high-stress events (cortisol increases from 100% to 2000% above average—similar to Nepomnaschy's assessment of cortisol "peaks" in the previous section) most commonly involve trauma from family conflict or change (Flinn et al.,
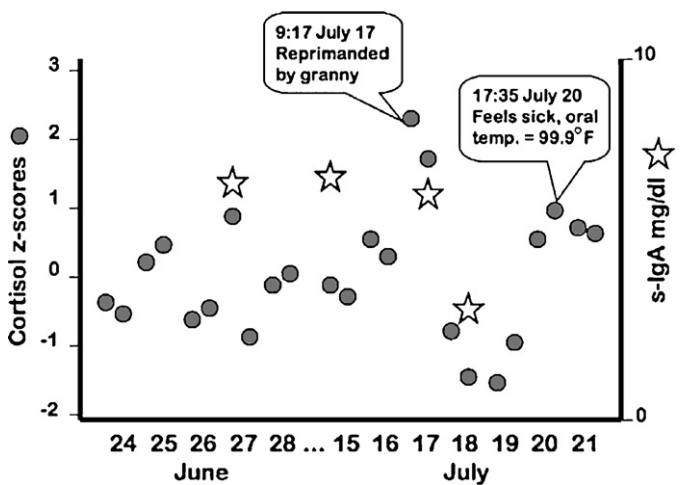
1996). Punishment, quarreling and residence change substantially increase cortisol levels, whereas calm, affectionate contact is associated with diminished (−10% to −50%) cortisol levels. High cortisol levels are temporally associated with traumatic family events (residence change of child or parent/caretaker, punishment, "shame," serious quarreling, and/or fighting) within a 24 hour period (Flinn and England, 2003).

There is considerable variability among children in cortisol responses to family disturbances. Not all individuals have detectable changes in cortisol levels associated with family trauma, and some children have significantly elevated cortisol levels during *some* episodes of family trauma but not during others. Elevated cortisol is sometimes followed by subnormal levels (e.g., note diminished cortisol levels on July 18–19 in figure three). Some children respond to stressful family environments by social withdrawal, which is often associated with a lack of cortisol response and generally flattened circadian profiles. Such results illustrate the fact that HPAA responses are not simple or uniform phenomena. Numerous factors, including preceding events, habituation, specific individual histories, context and temperament, can affect how children respond to particular situations (Kudielka et al., 2009; Luijk et al., 2010). Nonetheless, traumatic family events are associated with elevated cortisol levels for all ages of children more than any other factor that Flinn and colleagues have examined. These results suggest that family interactions are a critical psychosocial stressor in most children's lives, although the sample collection during periods of relatively intense family interaction (early morning and late afternoon) may exaggerate these associations.

Chronic elevation of cortisol levels is also most often associated with family difficulties. Children usually became habituated to stressful events, but absence of a parent often results in abnormal patterns of elevated and/or subnormal cortisol levels. Children living in families with high levels of marital conflict (observed and reported serious quarreling, fighting, residence absence) are more likely to have abnormal cortisol profiles than children living in more amiable families (Flinn and England, 2003). Long-term stress, however, may result in diminished cortisol response. In some cases, chronically stressed children had blunted response to physical activities that normally evoked cortisol elevation, surprisingly similar to cases of post-traumatic stress disorder (PTSD) (Pervanidou and Chrousos, 2010).

Comparison of cortisol levels during "non-stressful" periods (no reported or observed crying, punishment, anxiety, residence change, family conflict, or health problem during 24 hour period before saliva collection) indicates a striking reduction and, in many cases, reversal of the family environment-stress association (Flinn and England, 2003). Chronically stressed children sometimes have sub-normal cortisol levels when they are not in stressful situations. For example, cortisol levels immediately after school (saliva collected while walking home from school) and during noncompetitive play were lower among some chronically stressed children. Some chronically stressed children also appear socially "tough" or withdrawn, exhibiting little or no arousal to the novelty of the first few days of the saliva collection procedure and other minor social challenges. Again, these sub-normal profiles may be similar in some respects to those of individuals with PTSD (e.g., Yehuda et al., 2005). The relation between cortisol and level of arousal or interest is also apparent in the high reactivity of both shy (introverted) and surgent (extroverted) children to social gatherings.

Although elevated cortisol levels in children are usually associated with negative affect such as fear, anxiety, and anger, events that involve excitement and positive affect also stimulate stress responses (the following section provides an example from responses to Christmas). Cortisol response appears sensitive to social challenges with different affective states, and the cognitive effects of cortisol may vary with affective states, such as perceived

social support (Ahnert et al., 2004; Quas et al., 2004). There are additionally some age and sex differences in cortisol profiles, but it is difficult to assess the extent to which this is a consequence of neurological differences (e.g., Butler et al., 2005), physical maturation processes, or the different social environments experienced, for example, during adolescence as compared with early childhood (Flinn et al., 1996, 2009; Gunnar et al., 2009b; Romeo, 2010a,b).

The emerging picture of HPAA responses in the naturalistic context from our Dominica study is a combination of physical exertion and metabolic demands on the one hand, and sensitivity to social challenges on the other. The results are consistent with clinical and experimental studies (e.g., Dunn, 2004; Hetherington, 2003a,b) in suggesting that family environments and their developmental sequelae of affiliation, attachment and security are important.

Children in the Bwa Mawego study who were exposed to the stress of hurricanes and political upheavals during infancy or *in utero* do not have any apparent differences in cortisol profiles in comparison with children who were not exposed to such stressors (Flinn, 2006a). However, children exposed to the stressors of parental conflict and separation, death or abuse (hereafter "early family trauma") have significantly higher cortisol levels at age ten compared with other children (Flinn, 2006a). Based on analogy with the nonhuman animal research discussed previously, two key factors may be involved: (1) diminished hippocampal GR receptor functioning, resulting in less effective negative feedback regulation of cortisol levels; and (2) enhanced sensitivity to perceived social threats, mediated in part by emotional regulation. Cortisol increases in response to common activities such as eating meals, active play and hard work (e.g., carrying loads of wood to bay oil stills) among healthy children, but returns to normal levels within a few hours. If early family trauma has affected the negative feedback loop, then recovery to normal cortisol levels should be slower. Resumption of normal cortisol levels after physical stressors, however, is similar regardless of early experience of family trauma (Flinn, 2006a). In contrast, cortisol profiles following social stressors indicate that children who experienced early family trauma sustain elevated cortisol levels longer compared to other children (Flinn, 2006a, 2009). Hence the enhanced HPAA stress response of those children in this community that were exposed to early family trauma appears primarily focused on social challenges, suggesting that the ontogenetic effects of early trauma on stress response may be domain-specific and even context-specific. These results are consistent with studies of the effects of social defeat in nonhuman animal models (e.g., Kaiser and Sachser, 2005). The effects of early social trauma on HPAA, moreover, can be modulated by subsequent family environments (see also Coe and Lubach, 2005; Furlan et al., 2001; Lussier et al., 2002; Macrì et al., 2009). Children who experienced early trauma, but who received extensive alloparental care from grandparents and other kin, have cortisol levels that are not significantly different from children who did not experience early trauma (Flinn and Leone, 2006). Infants with cortisol profiles that were synchronous with their mothers (Fig. 4) also exhibited resilience to effects of early trauma, including lower subsequent morbidity levels over the next fifteen years. This synchrony effect may involve sleep regulation (e.g., Bernier et al., 2010) and oxytocin (Feldman et al., 2010; Heinrichs and Domes, 2008; Lee et al., 2009).

"Attachment" in humans appears to involve additional functions beyond security and protection; the flow of information from parents and other relatives, and recruitment into kin-based coalitions, emerge as critical challenges for the child. Predicting what one's social environment will be as an adult and modifying phenotypic trajectories of the hormonal, neurological, and psychological mechanisms that comprise "internal working models" seems extraordinarily complex, and unlikely to favor early canalization of neuroendocrine mechanisms. A more flexible system that allows inclusion of input throughout childhood and adolescence
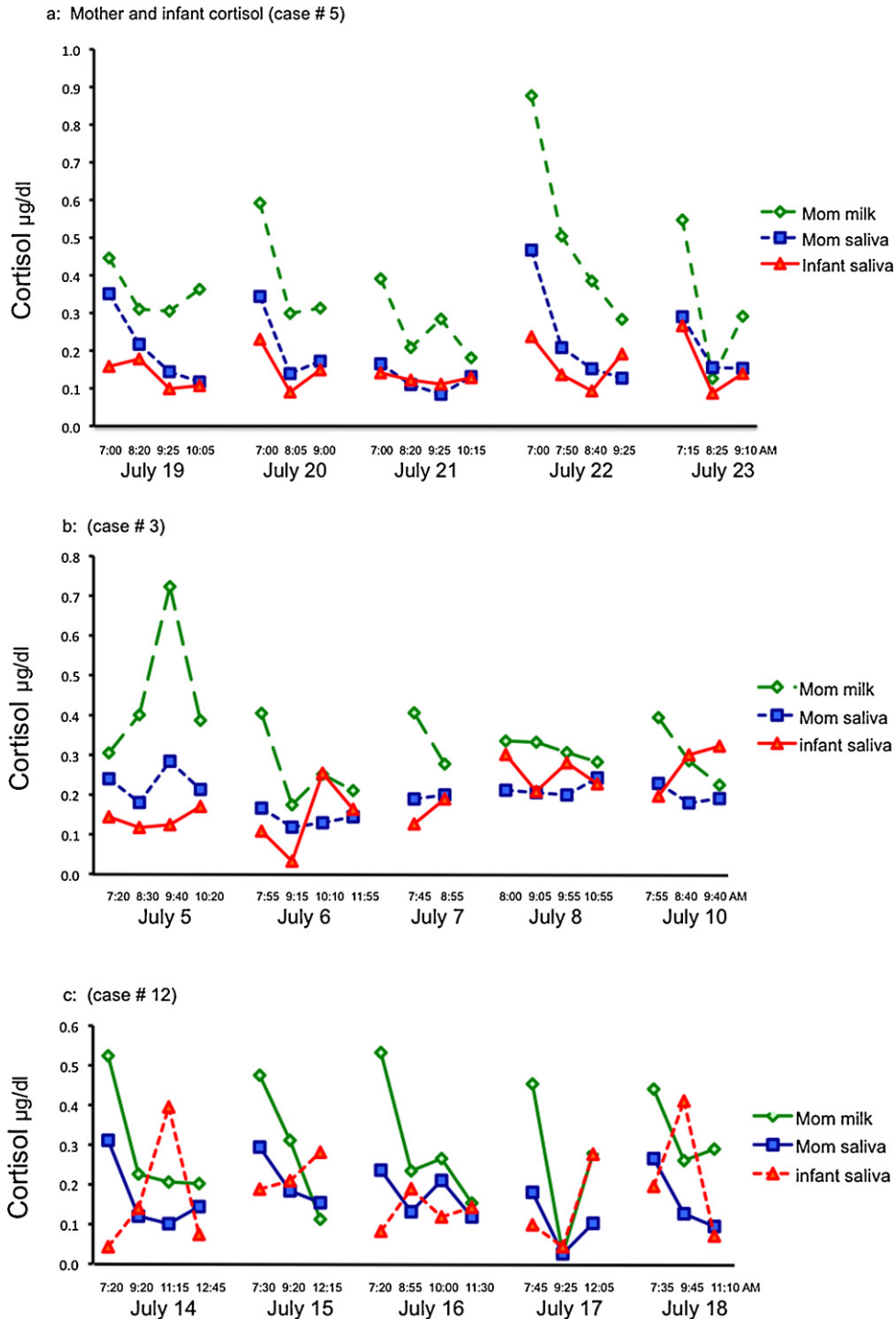
Fig. 4. Synchrony of mothers and their 8 month-old infants cortisol levels. Case #5 (a) exhibits moderate relation between a mother's salivary and breast milk cortisol levels and the salivary cortisol levels of her infant ($r = .743$ for saliva). Cases #3 (b) ($r = .123$ for saliva) and #12 (c) ($r = −.182$ for saliva) exhibit lower levels of relation. Biological samples collected by Mark Turner.

would have advantages over one primarily contingent on conditions during infancy.

Overall, the results of our research on early trauma and subsequent HPAA functioning have not found support for the hypothesis that early trauma has damaged the neuroendocrine regulatory mechanisms of the HPAA. Our findings suggest that in this population, relations between HPAA functioning and early trauma are mediated by higher order cognitive and emotional processes.

3.2.2. T'was the night before Christmas and all through the village most cortisol levels were high

Stress is often assumed to involve only negative events. As a final empirical example of viewing HPAA stress responses from an evolutionary perspective, we examine a vignette of children's cortisol levels in Bwa Mawego during Christmas holidays. This is a period of excitement and anticipation for many children in the study community. They are free from schoolwork, eat special food treats and enjoy various merrymaking activities. They often receive
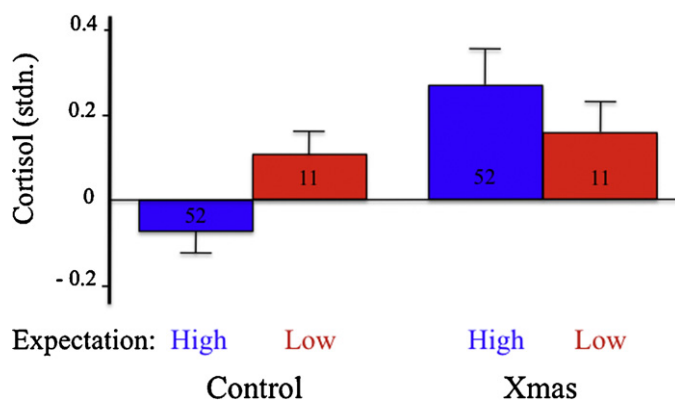
Fig. 5. Comparison of average cortisol levels of children with high expectations (reported anticipation of presents and/or other exciting activities) for Christmas day with children with low expectations (reported lack of expectation of gifts and special activities in family household). Control values represent samples collected during the summer. "Xmas" represents the day or two before Christmas (December 23rd and/or 24th, 1993 and 1998). Numbers of children are noted inside the bars. Samples collected during family conflict events were excluded (*N* = 7). Cortisol values are standardized by 5-minute intervals since wake-up time.

gifts from parents and other relatives. They are more likely to report feeling happy and to be having fun than on most other days of the year. If the key determinant of HPAA stress responses is the negative-positive valence of events and emotional states, we expect cortisol levels to be below average for children that are enjoying holiday festivities. Alternatively, if HPAA stress responses are more closely linked to arousal to social opportunities – both positive and negative – then we expect cortisol levels to be above average for children with high expectations. Overall cortisol levels on the two days before Christmas were above normal, with children from two-parent households and those reporting the most positive expectations having the highest cortisol levels (Fig. 5). It is unknown if cortisol elevations in response to positive emotional stimuli have different consequences on child health and cognitive development than elevations in response to negative stimuli.

In summary, results from our long-term naturalistic studies suggest the importance of interpreting various HPAA responses in light of functionally – and evolutionarily – relevant explanations of phenotypic plasticity in both behavioral and physiological outcomes, all of which must be done in specific reference to the complex social dynamics characteristic of our species.

4. Concluding remarks

Returning to the paradox of why natural selection favored sensitivity of stress response to social stimuli in the human child, several points emerge. Human childhood is a life history stage that appears necessary and useful for acquiring the information and practice to build and refine mental algorithms critical for negotiating the social coalitions that are key to success in our species. Mastering the social environment presents special challenges for the human child. Results from the Guatemala and Dominica studies indicate that family environment is a primary source and mediator of stressful events. The sensitivity of stress physiology to the social environment may facilitate adaptive responses to this most salient and dynamic puzzle.

Coping with social challenges, however, can have significant health consequences, ranging from dysregulation of emotional control and increased risk of psychopathology (Gilbert, 2001, 2005; Nesse et al., 2009) to broader health issues associated with social and economic disparities (Barker, 1998; Dressler et al., 2005; Marmot, 2004; Marmot and Wilkinson, 1999). The potential for

intergenerational cycles that perpetuate social relationships promoting stress and poor health are of particular concern (Belsky, 2005; Fleming et al., 1999; Gonzalez et al., 2009; Maestripieri et al., 2005).

We are still far from identifying the specific connections from family environment, to stress response, to the ontogenetic plasticity of components of the limbic system and pre-frontal cortex that are involved with the acquisition of social competencies. An evolutionary developmental perspective can be useful for understanding this critical aspect of a child's world by integrating knowledge of physiological causes with the logic of adaptive design by natural selection. It reminds us that our biology and psychology have been profoundly affected by our evolutionary history as fundamentally social creatures.[1]

References

Ademec, R.E., Blundell, J., Burton, P., 2005. Neural circuit changes mediating lasting brain and behavioral response to predator stress. Neurosci. Biobehav. Rev. 29, 1225–1241.

Adolphs, R., 2003a. Cognitive neuroscience of human social behavior. Nat. Rev. Neurosci. 4, 165–178.

Adolphs, R., 2003b. Is the human amygdala specialized for processing social information? Ann. N. Y. Acad. Sci. 985, 326–340.

Agrawal, A.A., 2001. Phenotypic plasticity in the interactions and evolution of species. Science 294, 321–326.

Ahnert, L., Gunnar, M.R., Lamb, M.E., Barthel, M., 2004. Transition to child care: associations with infant-mother attachment, negative emotion, and cortisol elevations. Child Dev. 75, 639–650.

Aiello, L.C., Wheeler, P., 1995. The expensive-tissue hypothesis: the brain and the digestive system in human and primate evolution. Curr. Anthropol. 36, 199–221.

Alexander, R.D., 1987. The Biology of Moral Systems. Aldine de Gruyter, Hawthorne, NY.

Alexander, R.D., 1989. Evolution of the human psyche. In: Mellars, P., Stringer, C. (Eds.), The Human Revolution: Behavioural and Biological Perspectives on the Origins of Modern Humans. Princeton University Press, Princeton, pp. 455–513.

Alexander, R.D., 1990. Epigenetic rules and Darwinian algorithms: the adaptive study of learning and development. Ethol. Sociobiol. 11, 1–63.

Allman, J., 1999. Evolving Brains. Scientific American Library, New York.

Allman, J.M., Hakeem, A., Erwin, J.M., Nimchinsky, E., Hof, P., 2001. The anterior cingulate cortex: the evolution of an interface between emotion and cognition. Ann. N. Y. Acad. Sci. 935, 107–117.

Amaral, D.G., 2003. The amygdala, social behavior, and danger detection. Ann. N. Y. Acad. Sci. 1000, 337–347.

Amodio, D.M., Frith, C.D., 2006. Meeting of minds: the medial frontal cortex and social cognition. Nat. Rev. Neurosci. 7, 268–277.

Andrews, M.H., Matthews, S.G., 2004. Programming of the hypothalamo-pituitary adrenal axis: serotonergic involvement. Stress 7, 15–27.

Auchus, R.J., Rainey, W.E., 2004. Adrenarche- physiology, biochemistry and human disease. Clin. Endocrinol. 60, 288–296.

Anisman, H., Zaharia, M.D., Meaney, M.J., Merali, Z., 1998. Do early-life events permanently alter behavioral and hormonal response to stressors? Int. J. Dev. Neurosci. 16, 149–164.

Baird, D.D., Weinberg, C.R., Zhou, H., Kamel, F., McConnaughey, D.R., Kesner, J.S., Wilcox, A.J., 1999. Preimplantation urinary hormone profiles and the probability of conception in healthy women. Fertil. Steril. 71, 40–49.

Banks, B.A., Cnaan, A., Morgan, M.A., Parer, J.T., Merrill, J.D., Ballard, P.L., Ballard, R.A., 1999. Multiple courses of antenatal corticosteroids and outcome of premature neonates. North American Thyrotropin-Releasing Hormone Study Group. Am. J. Obstet. Gynecol. 181, 709–717.

Barker, D.J., 1998. In utero programming of chronic disease. Clin. Sci. 95, 115–128.

Bartolomucci, A., 2007. Social stress, immune functions and disease in rodents. Front. Neuroendocrinol. 28, 28–49.

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[1] References and further reading may be available for this article. To view references and further reading you must purchase this article.

Bartolomucci, A., Palanza, P., Sacerdote, P., Panerai, A.E., Sgoifo, A., Dantzer, R., Parmigiani, S., 2005. Social factors and individual vulnerability to chronic stress exposure. Neurosci. Biobehav. Rev. 29, 67–81.

Bateson, P., Barker, D., Clutton-Brock, T., Deb, D., D'Udine, B., Foley, R.A., Gluckman, P., Godfrey, K., Kirkwood, T., Lahr, M.M., McNamara, J., Metcalfe, N.B., Monaghan, P., Spencer, H.G., Sultan, S.E., 2004. Developmental plasticity and human health. Nature 430, 419–421.

Baulieu, E.E., Robel, P., 1998. Dehydroepiandrosterone (DHEA) and dehydroepiandrosterone sulfate (DHEAS) as neuroactive neurosteroids. Proc. Natl. Acad. Sci. U.S.A. 95, 4089–4091.

Bauer, J.D., Ledoux, J.E., Nader, K., 2001. Fear conditioning and LTP in the lateral amygdala are sensitive to the same stimulus contingencies. Nat. Neurosci. 4, 687–688.

Belsky, J., 2005. Differential susceptibility to rearing influence: an evolutionary hypothesis and some evidence. In: Ellis, B.J., Bjorklund, D.F. (Eds.), Origins of the Social Mind: Evolutionary Psychology and Child Development. Guilford Press, New York, pp. 139–163.

Belsky, J., Steinberg, L.D., Draper, P., 1991. Childhood experience, interpersonal development, and reproductive strategy: an evolutionary theory of socialization. Child Dev. 62, 647–670.

Bernier, A., Carlson, S.M., Bordeleau, S., Carrier, J., 2010. Relations between physiological and cognitive regulatory systems: infant sleep regulation and subsequent executive functioning. Child Dev. 81, 1739–1752.

Bertram, C., Trowern, A.R., Copin, N., Jackson, A.A., Whorwood, C.B., 2001. The maternal diet during pregnancy programs altered expression of the glucocorticoid receptor and type 2 11β-hydroxysteroid dehydrogenase: potential molecular mechanisms underlying the programming of hypertension in utero. Endocrinology 142, 2841–2853.

Beylin, A.V., Shors, T.J., 2003. Glucocorticoids are necessary for enhancing the acquisition of associative memories after acute stressful experience. Horm. Behav. 43, 124–131.

Bird, D.W., Bliege Bird, R., 2002. Children on the reef: slow learning or strategic foraging? Hum. Nat. 13, 269–297.

Bjorklund, D.F., 2006. Mother knows best: epigenetic inheritance, maternal effects, and the evolution of human intelligence. Dev. Rev. 26, 213–242.

Bjorklund, D.F., Pellegrini, A.D., 2002. The Origins of Human Nature: Evolutionary Developmental Psychology. APA Press, Washington, DC.

Bjorklund, D.F., Rosenberg, J.S., 2005. The role of developmental plasticity in the evolution of human cognition. In: Ellis, B.J., Bjorklund, D.F. (Eds.), Origins of the Social Mind: Evolutionary Psychology and Child Development. Guilford Press, New York, NY, pp. 45–82.

Blakemore, S.-J., Winston, J., Frith, U., 2004. Social cognitive neuroscience: where are we heading? Trends Cogn. Neurosci. 8, 216–222.

Bloom, S.L., Sheffield, J.S., McIntire, D.D., Leveno, K.J., 2001. Antenatal dexamethasone and decreased birth weight. Obstet. Gynecol. 97, 485–490.

Bloomfield, F.H., Oliver, M.H., Hawkins, P., Holloway, A.C., Campbell, M., Gluckman, P.D., Harding, J.E., Challis, J.R., 2004. Periconceptional undernutrition in sheep accelerates maturation of the fetal hypothalamic-pituitary-adrenal axis in late gestation. Endocrinology 145, 4278–4285.

Blurton-Jones, N.G., Marlowe, F.W., 2002. Selection for delayed maturity: does it take 20 years to learn to hunt and gather? Hum. Nat. 13, 199–238.

Bock, J.A., 2005. Farming, foraging, and children's play in the Okavango Delta, Botswana. In: Pellegrini, A.D., Smith, P.K. (Eds.), The Nature of Play: Great Apes and Humans. Guilford Press, New York, NY, pp. 254–281.

Bogin, B., 1999. Patterns of Human Growth, 2nd edition. Cambridge University Press, Cambridge.

Boonstra, R., Lane, J.E., Boutin, S., Bradley, A., Desantis, L., Newman, A.E., Soma, K.K., 2008. Plasma DHEA levels in wild, territorial red squirrels: seasonal variation and effect of ACTH. Gen. Comp. Endocrinol. 158, 61–67.

Bowlby, J., 1969. Attachment. Basic Books, New York.

Bonier, F., Martin, P.R., Moore, I.T., Wingfield, J.C., 2009. Do baseline glucocorticoids predict fitness? Trends Ecol. Evol. 24, 634–642.

Breen, K.M., Karsch, F.J., 2006. New insights regarding glucocorticoids, stress and gonadotropin suppression. Front. Neuroendocrinol. 27, 233–245.

Brinks, V., Berger, S., Gass, P., de Kloet, E.R., Oitzl, M.S., 2009. Mineralocorticoid receptors in control of emotional arousal and fear memory. Horm. Behav. 56, 232–238.

Brown, H., Prescott, R. 1999. Applied Mixed Models in Medicine. John Wiley & Sons, New York.

Brown, R.W., Chapman, K.E., Edwards, C.R., Seckl, J.R., 1993. Human placental 11β-hydroxysteroid dehydrogenase: evidence for and partial purification of a distinct NAD-dependent isoform. Endocrinology 132, 2614–2621.

Brummelte, S., Galea, L.A., 2010. Depression during pregnancy and postpartum: contribution of stress and ovarian hormones. Prog. Neuropsychopharmacol. Biol. Psychol. 34, 766–776.

Brunton, P.J., Russell, J.A., Douglas, A.J., 2008. Adaptive responses of the maternal hypothalamic-pituitary-adrenal axis during pregnancy and lactation. J. Neuroendocrinol. 20, 764–776.

Buchanan, T.W., Lovallo, W.R., 2001. Enhanced memory for emotional material following stress-level cortisol treatment in humans. Psychoneuroendocrinology 26, 307–317.

Buford, T.W., Willoughby, D.S., 2008. Impact of DHEA(S) and cortisol on immune function in aging: a brief review. Appl. Physiol. Nutr. Metab. 33, 429–433.

Buitelaar, J.K., Huizink, A.C., Mulder, E.J., Robles De Medina, P.G., Visser, H.A., 2003. Prenatal stress and cognitive development and temperament in infants. Neurobiol. Aging 24, S53–S60.

Buss, D.M., 2000. The evolution of happiness. Am. Psychol. 55, 15–23.

Butler, T., Pan, H., Epstein, J., Protopopescu, X., Tuescher, O., Goldstein, M., Cloitre, M., Yang, Y., Phelps, E., Gorman, J., Ledoux, J., Stern, E., Silbersweig, D., 2005. Fear-related activity in subgenual anterior cingulate differs between men and women. Neuroreport 16, 1233–1236.

Byrne, R.W., Whiten, A., 1988. Machiavellian Intelligence. Oxford University Press, Oxford.

Buwalda, B., Kole, M.H.P., Veenema, A.H., Huininga, M., De Boer, S.F., Korte, S.M., Koolhaas, J.M., 2005. Long term effects of social stress on brain and behavior: a focus on hippocampal functioning. Neurosci. Biobehav. Rev. 29, 83–97.

Byrne, R.W., 2002a. In: Kaufman, J.C. (Ed.), The Evolution of Intelligence. Lawrence Erlbaum Associates, Mahwah, NJ, pp. 79–95.

Byrne, R.W., 2002b. Social and technical forms of primate intelligence. In: de Waal, F.B.M. (Ed.), Tree of Origin: What Primate Behavior Can Tell Us About Human Social Evolution. Harvard University Press, Cambridge, MA, pp. 145–172.

Campbell, B.C., 2006. Adrenarche and the evolution of human life history. Am. J. Hum. Biol. 18, 569–589.

Chagnon, N.A., 1988. Life histories, blood revenge, and warfare in a tribal population. Science 239, 985–992.

Champagne, D.L., 2010. Epigenetic influence of social experiences across the lifespan. Dev. Psychobiol. 52, 299–311.

Champagne, D.L., Bagot, R.C., van Hasselt, F., Ramakers, G., Meaney, M.J., de Kloet, E.R., Joels, M., Krugers, H., 2008. Maternal care and hippocampal plasticity: evidence for experience-dependent structural plasticity, altered synaptic functioning, and differential responsiveness to glucocorticoids and stress. J. Neurosci. 28, 6037–6045.

Chen, C.C.G., Parker Jr., C.R., 2004. Adrenal androgens and the immune system. Sem. Repro. Med. 22, 369–377.

Chin, S.O., Brodsky, N.L., Bhandari, V., 2003. Antenatal steroid use is associated with increased gastroesophageal reflux in neonates. Am. J. Perinatol. 20, 205–213.

Chisholm, J.S., Quinlivan, J.A., Petersen, R.W., Coall, D.A., 2005. Early stress predicts age at menarche and first birth, adult attachment, and expected lifespan. Hum. Nat. 16, 233–265.

Chrousos, G.P., 1998. Stressors, stress and neuroendocrine integration of the adaptive response: the 1997 Hans Selye Memorial Lecture. Ann. N. Y. Acad. Sci. 851, 311–335.

Chrousos, G.P., Torpy, D.J., Gold, P.W., 1998. Interactions between the hypothalamic-pituitary-adrenal axis and the female reproductive system: Clinical implications. Ann. Intern. Med. 129, 229–240.

Chrousos, G.P., 2009. Stress and disorders of the stress system. Nat. Rev. Endocrinol. 5, 374–381.

Cicchetti, D., Rogosh, F.A., 2007. Personality, adrenal steroid hormones, and resilience in maltreated children: a multilevel perspective. Dev. Psychopathol. 19, 787–809.

Cirulli, F., Francia, N., Berry, A., Aloe, L., Alleva, E., Suomi, S.J., 2009. Early life stress as a risk factor for mental health: role of neurotrophins from rodents to non-human primates. Neurosci. Biobehav. Rev. 33 (4), 573–585.

Clancy, B.H., 2009. Reproductive ecology and the endometrium: physiology, variation, and new directions. Year. Phys. Anthropol. 52, 137–154.

Clarke, A.S., Wittwer, D.J., Abbott, D.H., Schneider, M.L., 1994. Long-term effects of prenatal stress on HPA axis activity in juvenile rhesus monkeys. Dev. Psychobiol. 27, 257–269.

Coe, C.L., Lubach, G., 2005. Prenatal origins of individual variation in behavior and immunity. Neurosci. Biobehav. Rev. 29, 39–49.

Cohen, S., 2004. Social relationships and health. Am. Psych. 59, 676–684.

Conley, A.J., Pattison, J.C., Bird, I.M., 2004. Variations in adrenal androgen production among (nonhuman) primates. Sem. Repro. Med. 22, 311–326.

Copeland, K.C., Eichberg, J.W., Parker Jr., C.R., Bartke, A., 1985. Puberty in the chimpanzee: somatomedin-c and its relationship to somatic growth and steroid hormone concentrations. J. Clin. Endocrinol. Metab. 60, 1154–1160.

Corpechot, C., Robel, P., Axelson, M., Sjovall, J., Baulieu, E.E., 1981. Characterization and measurement of dehydroepiandrosterone sulfate in the rat brain. Proc. Natl. Acad. Sci. U.S.A. 78, 4704–4707.

Cutler, G.B., Glenn, M., Bush, M., Hodgen, G.D., Graham, C.E., Loriaux, D.L., 1978. Adrenarche: a survey of rodents, domestic animals, and primates. Endocrinology 103, 2112–2118.

Daly, M., Wilson, M., 1995. Discriminative parental solicitude and the relevance of evolutionary models to the analysis of motivational systems. In: Gazzaniga, M.S. (Ed.), The Cognitive Neurosciences. MIT Press, Cambridge, MA, pp. 1269–1286.

Dal Zatto, S., Marti, O., Armario, A., 2003. Glucocorticoids are involved in the long-term effects of a single immobilization stress on the hypothalamic-pituitary-adrenal axis. Psychoneuroendocrinology 28, 992–1009.

Damasio, A., 2003. Looking for Spinoza: Joy, Sorrow, and the Feeling Brain. Harcourt, New York.

Darwin, C.R., 1871. The Descent of Man and Selection in Relation to Sex. John Murray, London.

Dean, C., Leakey, M.G., Reid, D., Schrenk, F., Schwartz, G.T., Stringer, C., Walker, A., 2001. Growth processes in teeth distinguish modern humans from *Homo erectus* and earlier hominins. Nature 414, 628–631.

de Kloet, E.R., Oitzl, M.S., Joels, M., 1999. Stress and cognition: are corticosteroids good or bad guys? Trends Neurosci. 22, 422–426.

de Kloet, E.R., Joëls, M., Holsboer, F., 2005a. Stress and the brain: from adaptation to disease. Nat. Rev. Neurosci. 6, 463–475.

de Kloet, E.R., Sibug, R.M., Helmerhorst, F.M., Schmidt, M., 2005b. Stress, genes, and the mechanism for programming the brain for later life. Neurosci. Biobehav. Rev. 29, 271–281.

Del Giudice, M., 2009. Sex, attachment, and the development of reproductive strategies. Behav. Brain Sci. 32, 1–21.

Del Giudice, M., Angeleri, R., Manera, V., 2009. The juvenile transition: a developmental switch point in human life history. Dev. Rev. 29, 1–31.

de Quervain, D.J., Aerni, A., Schelling, G., Roozendaal, B., 2009. Glucocorticoids and the regulation of memory in health and disease. Front. Neuroendocrinol. 30, 358–370.

Derijk, R., Michelson, D., Karp, B., Petrides, J., Galliven, E., Deuster, P., Paciotti, G., Gold, P.W., Sternberg, E.M., 1997. Exercise and circadian rhythm-induced variations in plasma cortisol differentially regulate interleukin-1 (IL-1), IL-6, and Tumor Necrosis Factor-alpha (TNFα) production in humans: high sensitivity of TNF and resistance of IL-6. J. Clin. Endocrinol. Metab. 82, 2182–2191.

de Rooij, S.R., Painter, R.C., Phillips, D.I., Osmond, C., Michels, R.P., Bossuyt, P.M., Bleker, O.P., Roseboom, T.J., 2006. Hypothalamic-pituitary-adrenal axis activity in adults who were prenatally exposed to the Dutch famine. Eur. J. Endocrinol. 155, 153–160.

de Weerth, C., Buitelaar, J.K., 2005. Physiological stress reactivity in human pregnancy—a review. Neurosci. Biobehav. Rev. 29, 295–312.

Dickerson, S.S., Kemeny, M.E., 2004. Acute stressors and cortisol responses: a theoretical integration and synthesis of laboratory research. Psychol. Bull. 130, 355–391.

DiPietro, J.A., Novak, M.F., Costigan, K.A., Atella, L.D., Reusing, S.P., 2006. Maternal psychological distress during pregnancy in relation to child development at age two. Child Dev. 77, 573–587.

Do Rego, J.L., Seong, J.Y., Burel, D., Leprince, J., Lee-The, V., Tsutsui, K., Tonon, M.C., Pelletier, G., Vaudry, H., 2009. Neurosteroid biosynthesis: enzymatic pathways and neuroendocrine regulation by neurotransmitters and neuropeptides. Front. Neuroendocrinol. 30, 259–301.

Dorn, L.D., Hitt, S.F., Rotenstein, D., 1999. Biopsychological and cognitive differences in children with premature vs. on-time adrenarche. Arch. Pediatr. Adolesc. Med. 153, 137–146.

Dorn, L.D., Rose, S.R., Rotenstein, D., Susman, E.J., Huang, B., Loucks, T.L., Berga, S.L., 2008. Differences in endocrine parameters and psychopathology in girls with premature adrenarche versus on-time adrenarche. J. Pediatr. Endocrinol. Metab. 21, 439–448.

Dressler, W.W., Bindon, J.R., 2000. The health consequences of cultural dissonance: cultural dimensions of lifestyle, social support, and arterial blood pressure in an African American community. Am. Anthropol. 102, 244–260.

Dressler, W.W., Oths, K.S., Gravely, C.C., 2005. Race and ethnicity in public health research: models to explain health disparities. Annu. Rev. Anthropol. 34, 231–252.

Dunbar, R.I.M., 1998. The social brain hypothesis. Evol. Anthropol. 6, 178–190.

Dunbar, R.I.M., Schultz, S., 2007. Evolution in the social brain. Science 317, 1344–1347.

Dunn, J., 2004. Understanding children's family worlds: family transitions and children's outcome. Merrill-Palmer Quart. 50, 224–235.

Duvarci, S., Nader, K., LeDoux, J.E., 2005. Activation of extracellular signal-regulated kinase-mitogen-activated protein kinase cascade in the amygdala is required for memory reconsolidation of auditory fear conditioning. Euro. J. Neurosci. 21, 283–289.

Edelman, G.M., 2006. Second Nature: Brain Science and Human Knowledge. Yale University Press, New Haven.

Elenkov, I.J., Chrousos, G.P., 1999. Stress, cytokine patterns and susceptibility to disease. Baillieres Best Pract. Res. Clin. Endocrinol. Metab. 13, 583–595.

Elenkov, I.J., Papanicolaou, D.A., Wilder, R.L., Chrousos, G.P., 1996. Modulatory effects of glucocorticoids and catecholamines on human interleukin-12 and interleukin-10 production: clinical implications. Proc. Assoc. Am. Physicians 108, 374–381.

Ellis, B.J., Essex, M.J., 2007. Family environments, adrenarche, and sexual maturation: a longitudinal test of a life history model. Child Dev. 78, 1799–1817.

Ellis, B.J., Jackson, J.J., Boyce, W.T., 2006. The stress response systems: universality and adaptive individual differences. Dev. Rev. 26, 175–212.

Ellison, P., 1988. Human salivary steroids: methodological considerations and applications in physical anthropology. Year. Phys. Anthropol. 31, 115–142.

Ellison, P.T., 2001. On Fertile Ground, a Natural History of Human Reproduction. Harvard, Cambridge, MA.

Ellison, P.T., Lager, C., 1986. Moderate recreational running is associated with lowered salivary progesterone profiles in women. Am. J. Obstet. Gynecol. 154, 1000–1003.

Ellison, P.T., Lipson, S.F., Jasienska, G., Ellison, P.L., 2007. Moderate anxiety, whether acute or chronic, is not associated with ovarian suppression in healthy, well-nourished, Western women. Am. J. Phys. Anthropol. 134, 513–519.

Enomoto, M., Adachi, H., Fukami, A., Furuki, K., Satoh, A., Otsuka, M., Kumagae, S., Nanjo, Y., Shigetoh, Y., Imaizumi, T., 2008. Serum dehydroepiandrosterone sulfate levels predict longevity in men: 27-year follow-up study in a community-based cohort (Tanushimaru study). J. Am. Geriatr. Soc. 56, 994–998.

Entringer, S., Kumsta, R., Hellhammer, D.H., Wadhwa, P.D., Wüst, S., 2009. Prenatal exposure to maternal psychosocial stress and HPA axis regulation in young adults. Horm. Behav. 55, 292–298.

Essex, M.J., Klein, M.H., Cho, E., Kalin, N.H., 2002. Maternal stress beginning in infancy may sensitize children to later stress exposure: effects on cortisol and behavior. Biol. Psychiat. 52, 776–784.

Feldman, R., Gordon, I., Zagoory-Sharon, O., 2010. The cross-generation transmission of oxytocin in humans. Horm. Behav. 58, 669–676.

Fenker, D.T., Schott, B.J., Richardson-Klavehn, A., Heinze, H.-J., Düzel, E., 2005. Recapitulating emotional context: activity of amygdala, hippocampus and fusiform cortex during recollection and familiarity. Eur. J. Neurosci. 21, 1993–1999.

Ferin, M., 1999. Stress and the reproductive cycle. J. Clin. Endocr. Metab. 84, 1768–1774.

Field, T., Diego, M., Hernandez-Reif, M., Vera, Y., Gil, K., Schanberg, S., Kuhn, C., Gonzalez-Garcia, A., 2004. Prenatal maternal biochemistry predicts neonatal biochemistry. Int. J. Neurosci. 114, 933–945.

Fleming, A.S., O'Day, D.H., Kraemer, G.W., 1999. Neurobiology of mother-infant interactions: experience and central nervous system plasticity across development and generations. Neurosci. Biobehav. Rev. 23, 673–685.

Flinn, M.V., 1997. Culture and the evolution of social learning. Evol. Hum. Behav. 18, 23–67.

Flinn, M.V., 2004. Culture and developmental plasticity: evolution of the social brain. In: MacDonald, K.K., Burgess, R.L. (Eds.), Evolutionary Perspectives on Child Development. Sage, Thousand Oaks, CA, pp. 73–98.

Flinn, M.V., 2006a. Evolution and ontogeny of stress response to social challenge in the human child. Dev. Rev. 26, 138–174.

Flinn, M.V., 2006b. Cross-cultural universals and variations: the evolutionary paradox of informational novelty. Psychol. Inquiry 17, 118–123.

Flinn, M.V., 2008. Why words can hurt us: social relationships, stress, and health. In: Trevathan, W., Smith, E.O., McKenna, J. (Eds.), Evolutionary Medicine and Health. Oxford University Press, Oxford, pp. 247–258.

Flinn, M.V., 2009. Are cortisol profiles a stable trait during child development? Am. J. Hum. Biol. 21 (6), 769–771.

Flinn, M.V., Alexander, R.D., 2007. Runaway social selection. In: Gangestad, S.W., Simpson, J.A. (Eds.), The Evolution of Mind. Guilford Press, New York, pp. 249–255.

Flinn, M.V., Coe, K.C., 2007. The linked red queens of human cognition, coalitions, and culture. In: Gangestad, S.W., Simpson, J.A. (Eds.), The Evolution of Mind. Guilford Press, New York, pp. 339–347.

Flinn, M.V., England, B.G., 1995. Childhood stress and family environment. Curr. Anthropol. 36, 854–866.

Flinn, M.V., England, B.G., 1997. Social economics of childhood glucocorticoid stress response and health. Am. J. Phys. Anthropol. 102, 33–53.

Flinn, M.V., England, B.G., 2003. Childhood stress: endocrine and immune responses to psychosocial events. In: Wilce, J.M. (Ed.), Social & Cultural Lives of Immune Systems. Routledge Press, London, pp. 107–147.

Flinn, M.V., Geary, D.C., Ward, C.V., 2005a. Ecological dominance, social competition, and coalitionary arms races: Why humans evolved extraordinary intelligence. Evol. Hum. Behav. 26, 10–46.

Flinn, M.V., Leone, D.V., 2006. Early trauma and the ontogeny of glucocorticoid stress response: grandmother as a secure base. J. Dev. Process. 1, 31–68.

Flinn, M.V., Turner, M.T., Quinlan, R., Decker, S.D., England, B.G., 1996. Male–female differences in effects of parental absence on glucocorticoid stress response. Hum. Nat. 7, 125–162.

Flinn, M.V., Leone, D.V., Quinlan, R.J., 1999. Growth and fluctuating asymmetry of stepchildren. Evol. Hum. Behav. 20, 465–480.

Flinn, M.V., Muehlenbein, M.P., Ponzi, D., 2009. Evolution of neuroendocrine mechanisms linking attachment and life history: social endocrinology of the human child. Behav. Brain Sci. 32, 27–28.

Flinn, M.V., Quinlan, R.J., Ward, C.V., Coe, M.K., 2007. Evolution of the human family: cooperative males, long social childhoods, smart mothers, and extended kin networks. In: Salmon, C., Shackelford, T. (Eds.), Family Relationships. Oxford University Press, Oxford, pp. 16–38.

Flinn, M.V., Ward, C.V., Noone, R., 2005b. Hormones and the human family. In: Buss, D. (Ed.), Handbook of Evolutionary Psychology. Wiley, New York, pp. 552–580.

French, N.P., Hagan, R., Evans, S.F., Godfrey, M., Newnham, J.P., 1999. Repeated antenatal corticosteroids: size at birth and subsequent development. Am. J. Obstet. Gynecol. 180, 114–121.

Fride, E., Dan, Y., Feldon, J., Halevy, G., Weinstock, M., 1986. Effects of prenatal stress on vulnerability to stress in prepubertal and adult rats. Physiol. Behav. 37, 681–687.

Frye, C.A., Wawrzycki, J., 2003. Effect of prenatal stress and gonadal hormone condition on depressive behaviors of female and male rats. Horm. Behav. 44, 319–326.

Furlan, P.M., DeMartinis, N., Schweizer, E., Rickels, K., Lucki, I., 2001. Abnormal salivary cortisol levels in social phobic patients in response to acute psychological but not physical stress. Biol. Psychiat. 50, 254–259.

Gallagher, H.L., Frith, C.D., 2003. Functional imaging of 'theory of mind'. Trends Cogn. Sci. 7, 77–83.

Gallese, V., 2005. Embodied simulation: from neurons to phenomenal experience. Phenomenol. Cogn. Sci. 4, 23–48.

Gallese, V., Keysers, C., Rizzolatti, G., 2004. A unifying view of the basis of social cognition. Trends Cogn. Sci. 8, 396–403.

Geary, D.C., 2005. The Origin of Mind: Evolution of Brain, Cognition, and General Intelligence. American Psychological Association, Washington.

Geary, D.C., Bjorklund, D.F., 2000. Evolutionary developmental psychology. Child Dev. 71, 57–65.

Geary, D.C., Flinn, M.V., 2001. Evolution of human parental behavior and the human family. Parent. Sci. Pract. 1, 5–61.

Geary, D.C., Flinn, M.V., 2002. Sex differences in behavioral and hormonal response to social threat. Psychol. Rev. 109, 745–750.

Geary, D.C., Huffman, K.J., 2002. Brain and cognitive evolution: forms of modularity and functions of mind. Psychol. Bull. 128, 667–698.

Ghizzoni, L., Mastorakos, G., Street, M.E., 1997. Spontaneous thyrotropin and cortisol secretion interactions in patients with nonclassical 21-hydroxylase deficiency and control children. J. Clin. Endocrinol. Metab. 82, 3677–3683.

Gilbert, P., 2001. Evolutionary approaches to psychopathology: the role of natural defences. Aust. NZ. J. Psych. 35, 17–27.

Gilbert, P., 2005. Social mentalities: A biopsychosocial and evolutionary approach to social relationships. In: Baldwin, M.W. (Ed.), Interpersonal Cognition. Guilford Press, New York, pp. 299–333.

Gilbert, S.L., Dobyns, W.B., Lahn, B.T., 2005. Genetic links between brain development and brain evolution. Nat. Rev. Gen. 6, 581–590.

Gitau, R., Cameron, A., Fisk, N.M., Glover, V., 1998. Fetal exposure to maternal cortisol. Lancet 352, 707–708.

Gitau, R., Fisk, N.M., Teixeira, J.M.A., Cameron, A., Glover, V., 2001. Fetal hypothalamic–pituitary–adrenal stress responses to invasive procedures are independent of maternal responses. J. Clin. Endocrinol. Metab. 86, 104–109.

Glover, V., O'Connor, T.G., Heron, J., Golding, J., Avon Longitudinal Study of Parents Children (ALSPAC) Study Team, 2004. Antenatal maternal anxiety is linked with atypical handedness in the child. Early Hum. Dev. 79, 107–118.

Glover, V., O'Connor, T.G., O'Donnell, K., 2010. Prenatal stress and the programming of the HPA axis. Neurosci. Biobehav. Rev. 35, 17–22.

Gluckman, P.D., Hanson, M.A., Beedle, A.S., 2007. Early life events and their consequences for later disease: a life history and evolutionary perspective. Am. J. Hum. Biol. 19, 1–19.

Gluckman, P.D., Hanson, M.A., Buklijas, T., Low, F.M., Beedle, A.S., 2009. Epigenetic mechanisms that underpin metabolic and cardiovascular diseases. Nat. Rev. Endocrinol. 5, 401–408.

Gluckman, P.D., Hanson, M.A., Spencer, H.G., 2005. Predictive adaptive responses and human evolution. Trends Ecol. Evol. 20, 527–533.

Gonzalez, A., Jenkins, J.M., Steiner, M., Fleming, A.S., 2009. The relationship between early life adversity, cortisol awakening responses and diurnal salivary cortisol levels in postpartum women. Psychoneuroendocrinology 34, 79–86.

Goodyer, I.M., Herbert, J., Altham, P.M., Pearson, J., Secher, S.M., Shiers, H.M., 1996. Adrenal secretion during major depression in 8- to 16-year-olds, I. Altered diurnal rhythms in salivary cortisol and dehydroepiandrosterone (DHEA) at presentation. Psychol. Med. 26, 245–256.

Granger, D.A., Schwartz, E.B., Booth, A., Curran, M., Zakaria, D., 1999. Assessing dehydroepinadrosterone in saliva: a simple radioimmunoassay for use in studies of children, adolescents and adults. Psychoneuroendocrinol 24, 567–579.

Gunnar, M.R., Frenn, K., Wewerka, S.S., Van Ryzin, M.J., 2009a. Moderate versus severe early life stress: associations with stress reactivity and regulation in 10-12-year-old children. Psychoneuroendocrinology 34, 62–75.

Gunnar, M.R., Wewerka, S., Frenn, K., Long, J.D., Griggs, C., 2009b. Developmental changes in hypothalamus–pituitary–adrenal activity over the transition to adolescence: normative changes and associations with puberty. Dev. Psychopathol. 21, 69–85.

Gutteling, B.M., de Weerth, C., Buitelaar, J.K., 2004. Maternal prenatal stress and 4-6 year old children's salivary cortisol concentrations pre- and post-vaccination. Stress 7, 257–260.

Gutteling, B.M., de Weerth, C., Buitelaar, J.K., 2005. Pre-natal stress and children's cortisol reaction to the first day of school. Psychoneuroendocrinology 30, 541–549.

Haglund, M.E., Nestadt, P.S., Cooper, N.S., Southwick, S.M., Charney, D.S., 2007. Psychobiological mechanisms of resilience: relevance to prevention and treatment of stress-related psychopathology. Dev. Psychopathol. 19, 889–920.

Haig, D., 1993. Genetic conflicts in human pregnancy. Quart. Rev. Biol. 68, 495–532.

Halligan, S.L., Herbert, J., Goodyer, I.M., Murray, L., 2004. Exposure to postnatal depression predicts elevated cortisol in adolescent offspring. Biol. Psychiat. 55, 376–381.

Hennessey, M.B., Kaiser, S., Sachser, N., 2009. Social buffering of the stress response: Diversity, mechanisms, and function, Front. Neuroendocrin. 30, 470–482.

Hetherington, E.M., 2003a. Intimate pathways: changing patterns in close personal relationships across time. Fam. Relat. 52, 318–331.

Hetherington, E.M., 2003b. Social support and the adjustment of children in divorced and remarried families. Childhood 10, 217–236.

Havelock, J.C., Auchus, R.J., Raney, W.E., 2004. The rise in adrenal androgen biosynthesis: adrenarche. Sem. Repro. Med. 22, 337–347.

Hazeldine, J., Arlt, W., Lord, J.M., 2010. Dehydroepiandrosterone as a regulator of immune cell function. J. Steroid. Biochem. Mol. Biol. 120, 127–136.

Hedegaard, M., Henriksen, T.B., Secher, N.J., Hatch, M.C., Sabroe, S., 1996. Do stressful life events affect duration of gestation and risk of preterm delivery? Epidemiology 7, 3339–3345.

Heim, C., Newport, D.J., Heit, S., Graham, Y.P., Wilcox, M., Bonsall, R., Miller, A.H., Nemeroff, C.B., 2000. Pituitary–adrenal and autonomic responses to stress in women after sexual and physical abuse in childhood. J. Am. Med. Assoc. 284, 592–597.

Heim, C., Newport, D., Wagner, D., Wilcox, M., Miller, A., Nemeroff, C., 2002. The role of early adverse experience and adulthood stress in the prediction of neuroendocrine stress reactivity in women: a multiple regression analysis. Depress Anxiety 15, 117–125.

Heinrichs, M., Domes, G., 2008. Neuropeptides and social behaviour: effects of oxytocin and vasopressin in humans. Prog. Brain Res. 170, 337–350.

Hellhammer, D.H., Wust, S., Kudielka, B.M., 2009. Salivary cortisol as a biomarker in stress research. Psychoneuroendocrinology 34, 163–171.

Hewlett, B.S., Lamb, M.E. (Eds.), 2005. Hunter–Gatherer Childhoods. AldineTransaction, New Brunswick, NJ.

Hill, K., Kaplan, H., 1999. Life history traits in humans: theory and empirical studies. Ann. Rev. Anthropol. 28, 397–430.

Holliday, M.A., 1986. Body composition and energy needs during growth. In: Falkner, F., Tanner, J.M. (Eds.), Human Growth: A Comprehensive Treatise. Plenum Press, New York.

Hornsby, P.J., 2004. Aging of the human cortex. Sci. Aging Knowl. Environ. 35, re6.

Hornsby, P.J., 1995. Biosynthesis of DHEAS by the human adrenal cortex and its age-related decline. Ann. N. Y. Acad. Sci. 774, 29–46.

Hrdy, S.B., 2009. Mothers and Others: The Evolutionary Origins of Mutual Understanding. Harvard University Press, Cambridge, MA.

Hucklebridge, F., Hussain, T., Evans, P., Clow, A., 2005. The diurnal patterns of the adrenal steroids cortisol and dehydroepiandrosterone (DHEA) in relation to awakening. Psychoneuroendocrinology 30, 51–57.

Huether, G., 1996. The central adaptation syndrome: psychosocial stress as a trigger for adaptive modifications of brain structure and brain function. Prog. Neurobiol. 48, 568–612.

Huether, G., 1998. Stress and the adaptive self organization of neuronal connectivity during early childhood. Int. J. Dev. Neurosci. 16, 297–306.

Huether, G., Doering, S., Ruger, U., Ruther, E., Schussler, G., 1999. The stress-reaction process and the adaptive modification and reorganization of neuronal networks. Psychiatry Res. 87, 83–95.

Huizink, A.C., Mulder, E.J., Buitelaar, J.K., 2004. Prenatal stress and risk for psychopathology, specific effects or induction of general susceptibility? Psychol. Bull. 130, 115–142.

Hultman, C.M., Sparen, P., Takei, N., Murray, R.M., Cnattingius, S., 1999. Prenatal and perinatal risk factors for schizophrenia, affective psychosis, and reactive psychosis of early onset: case-control study. Br. Med. J. 318, 421–426.

Humphrey, N.K., 1983. Consciousness Regained. Oxford University Press, Oxford.

Huttunen, M.O., Niskanen, P., 1978. Prenatal loss of father and psychiatric disorders. Arch. Gen. Psychiatry 35, 429–431.

Ibanez, L., Jimenez, R., de Zegher, F., 2006. Early puberty-menarche after precocious pubarche: relation to prenatal growth. Pediatrics 117, 117–121.

Ibanez, L., Potau, N., Marco, M.V., de Zegher, F., 1999. Corticotropin-releasing hormone as adrenal androgen secretagogue. Pediatr. Res. 46 (3), 351–353.

Imamura, Y., Nakane, Y., Ohta, Y., Kondo, H., 1999. Lifetime prevalence of schizophrenia among individuals prenatally exposed to atomic bomb radiation in Nagasaki City. Acta Psychiatr. Scand. 100, 344–349.

Izawa, S., Sugaya, N., Shirotsuki, K., Yamada, K.C., Ogawa, N., Ouchi, Y., Nagano, Y., Suzuki, K., Nomura, S., 2008. Salivary dehydroepiandrosterone secretion in response to acute psychosocial stress and its correlations with biological and psychological changes. Biol. Psychol. 79, 294–298.

Jackson, E.D., Payne, J.D., Nadel, L., Jacobs, W.J., 2006. Stress differentially modulates fear conditioning in healthy men and women. Biol. Psychiat. 59, 516–522.

Joëls, M., Baram, T.Z., 2009. The neuro-symphony of stress. Nat. Rev. Neurosci. 10, 459–466.

Joffe, T.H., 1997. Social pressures have selected for an extended juvenile period in primates. J. Hum. Evol. 32, 593–605.

Kaplan, H., Hill, K., Lancaster, J., Hurtado, A.M., 2000. A theory of human life history evolution: diet, intelligence and longevity. Evol. Anthropol. 9, 156–183.

Kaplan, H.S., Robson, A.J., 2002. The emergence of humans: the coevolution of intelligence and longevity with intergenerational transfers. Proc. Natl. Acad. Sci. U.S.A. 99, 10221–10226.

Kaiser, S., Sachser, N., 2005. The effects of prenatal social stress on behaviour: mechanisms and function. Neurosci. Biobehav. Rev. 29, 283–294.

Kajantie, E., 2006. Fetal origins of stress-related adult disease. Ann. NY. Acad. Sci. 1083, 11–27.

Kajantie, E., Eriksson, J., Barker, D.J., Forsen, T., Osmond, C., Wood, P.J., Andersson, S., Dunkel, L., Phillips, D.I., 2003. Birth size, gestational age and adrenal function in adult life: studies of dexamethasone suppression and ACTH1-24 stimulation. Eur. J. Endocrinol. 149, 569–575.

Kajantie, E., Phillips, D.I., 2006. The effects of sex and hormonal status on the physiological response to acute psychosocial stress. Psychoneuroendocrinology 31 (2), 151–178.

Kajantie, E., Phillips, D.I., Andersson, S., Barker, D.J., Dunkel, L., Forsen, T., Osmond, C., Tuominen, J., Wood, P.J., Eriksson, J., 2002. Size at birth, gestational age and cortisol secretion in adult life: foetal programming of both hyper- and hypocortisolism? Clin. Endocrinol. 57, 635–641.

Kajantie, E., Räikkönen, K., 2010. Early life predictors of the physiological stress response later in life. Neurosci. Biobehav. Rev. 35, 23–32.

Kemnitz, J.W., Roecker, E.B., Haffa, A.L.M., Pinheiro, J., Kurzman, I., Ramsey, J.J., MacEwen, E.G., 2000. Serum dehydroepiandrosterone sulfate concentrations across the life span of laboratory-housed rhesus monkeys. J. Med. Primatol. 29, 330–337.

Kiecolt-Glaser, J.K., Gouin, J.-P., Hantsoo, L., 2010. Close relationships, inflammation, and health. Neurosci. Biobehav. Rev. 35, 33–38.

Kime, D.E., Vinson, G.P., Major, P.W., Kilpatrick, R., 1980. Adrenal-gonad relationships. In: Chester Jones, I., Henderson, I.W. (Eds.), General, Comparative and Clinical Endocrinology of the Adrenal Cortex. Academic Press, London, pp. 183–264.

King, A.E., Critchley, H.O.D., 2010. Oestrogen and progesterone regulation of inflammatory processes in the human endometrium. J. Steroid Biochem. Mol. Biol. 120, 116–126.

Koch, C., 1999. Biophysics of Computation. Information Processing in Single Neurons. Oxford University Press, New York.

Koehl, M., Darnaudéry, M., Dulluc, J., van Reeth, O., Le Moal, M., Maccari, S., 1999. Prenatal stress alters circadian activity of the hypothalamo–pituitary–adrenal

axis and hippocampal corticosteroid receptors in adult rats of both gender. J. Neurobiol. 40, 302–315.

Koenig, J.I., Kirkpatrick, B., Lee, P., 2002. Glucocorticoid hormones and early brain development in schizophrenia. Neuropsychopharmacology 27, 309–318.

Kohlberg, L., LaCrosse, J., Ricks, D., 1972. The predictability of adult mental health from childhood behavior. In: Wolman, B.B. (Ed.), Manual of Child Psychopathology. McGraw-Hill, New York.

Koolhaas, J.M., de Boer, S.F., de Ruiter, A.J.H., Meerlo, P., Sgoifo, A., 1997. Social stress in rats and mice. Acta Physiol. Scand. 161, 69–72.

Korosi, A., Shanabrough, M., McClelland, S., Liu, Z.-W., Borok, E., Xiao-Bing Gao, X.-B., Horvath, T.L., Baram, T.Z., 2010. Early-life experience reduces excitation to stress-responsive hypothalamic neurons and reprograms the expression of corticotropin-releasing hormone. J. Neurosci. 30, 703–713.

Korte, S.M., Koolhaas, J.M., Wingfield, J.C., McEwen, B.S., 2005. The Darwinian concept of stress: benefits of allostasis and costs of allostatic load and the trade-offs in health and disease. Neurosci. Biobehav. Rev. 29, 3–38.

Korth-Schutz, S., Levin, L.S., New, M.I., 1976. Dehydroepiandrosterone sulfate (DS) levels, a rapid test for abnormal adrenal androgen secretion. J. Clin. Endocrinol. Metab. 42, 1005–1013.

Kudielka, B.M., Hellhammer, D.H., Wüst, S., 2009. Why do we respond so differently? Reviewing determinants of human salivary cortisol responses to challenge. Psychoneuroendocrinology 34, 2–18.

Kuzawa, C.W., Quinn, E.A., 2009. Developmental origins of adult function and health: evolutionary hypotheses. Annu. Rev. Anthropol. 38, 131–147.

Labrie, F., 2004. Adrenal androgens and endocrinology. Semin. Reprod. Med. 22, 299–309.

Labrie, F., Luu-The, V., Bélanger, A., Lin, S.X., Simard, J., Pelletier, G., Labrie, C., 2005. Is dehydroepiandrosterone a hormone? J. Endocrinol. 187, 169–196.

LeDoux, J.E., 2000. Emotion circuits in the brain. Ann. Rev. Neurosci. 23, 155–184.

Lee, H.-J., Macbeth, A.H., Pagani, J.H., Young 3rd, W.S., 2009. Oxytocin: the great facilitator of life. Prog. Neurobiol. 88, 127–151.

Lee, S.H., Wolpoff, M.H., 2003. The pattern of evolution in Pleistocene human brain size. Paleobiology 29, 186–196.

Leigh, S.R., 2004. Brain growth, cognition, and life history in primate and human evolution. Am. J. Primatol. 62, 139–164.

Levine, S., 2005. Developmental determinants of sensitivity and resistance to stress. Psychoneuroendocrinology 30, 939–946.

Linnet, K.M., Dalsgaard, S., Obel, C., Wisborg, K., Henriksen, T.B., Rodriguez, A., Kotimaa, A., Moilanen, I., Thomsen, P.H., Olsen, J., Jarvelin, M.R., 2003. Maternal lifestyle factors in pregnancy risk of attention deficit hyperactivity disorder and associated behaviors: review of the current evidence. Am. J. Psychiatry 160, 1028–1040.

Loman, M.M., Gunnar, M.R., 2010. Early experience and the development of stress reactivity and regulation in children. Neurosci. Biobehav. Rev. 34, 867–876.

Lou, H.C., Hansen, D., Nordentoft, M., Pryds, O., Jensen, F., Nim, J., Hemmingsen, R., 1994. Prenatal stressors of human life affect fetal brain development. Dev. Med. Child Neurol. 36, 826–832.

Luijk, M.P.C.M., Nathalie Saridjan, N., Tharner, A., van IJzendoorn, M.H., Bakermans-Kranenburg, M.J., Jaddoe, V.W.V., Hofman, A., Verhulst, F.C., Tiemeier, H., 2010. Attachment, depression, and cortisol: deviant patterns in insecure-resistant and disorganized infants. Dev. Psychobiol. 52, 441–452.

Lupien, S., Fiocco, A., Wan, N., Maheu, F., Lord, C., Schramek, Thahn Tu, M., 2005. Stress hormones and human memory function across the lifespan. Psychoneuroendocrinology 30, 225–242.

Lupien, S.J., McEwen, B.S., Gunnar, M.R., Heim, C., 2009. Effects of stress throughout the lifespan on the brain, behaviour and cognition. Nat. Rev. Neurosci. 10, 434–445.

Lupien, S.J., Wilkinson, C.W., Briere, S., Menard, C., Kin, N.M.K.N.Y., Nair, N.P.V., 2002. The modulatory effects of corticosteroids on cognition: studies in young human populations. Psychoneuroendocrinology 27, 401–416.

Lussier, G., Deater-Deckard, K., Dunn, J., Davies, L., 2002. Support across two generations: children's closeness to grandparents following parental divorce and remarriage. J. Fam. Psychol. 16, 363–376.

Lyons, D.M., Parker, K.J., Schatzberg, A.F., 2010. Animal models of early life stress: implications for understanding resilience. Dev. Psychobiol. 52, 616–624.

Maccari, S., Darnaudery, M., Morley-Fletcher, S., Zuena, A.R., Cinque, C., Van Reeth, O., 2003. Prenatal stress and long-term consequences: implications of glucocorticoid hormones. Neurosci. Biobehav. Rev. 27, 119–227.

Mace, R., 2000. Evolutionary ecology of human life history. Anim. Behav. 59, 1–10.

Macrì, S., Granstrem, O., Shumilina, M., dos Santos, F.J.A.G., Berry, A., Saso, L., Laviola, G., 2009. Resilience and vulnerability are dose-dependently related to neonatal stressors in mice. Horm. Behav. 56, 391–398.

Macrì, S., Wurbel, H., 2006. Developmental plasticity of HPA and fear responses in rats: a critical review of the maternal mediation hypothesis. Horm. Behav. 50, 667–680.

Maestripieri, D., Lindell, S.G., Ayala, A., Gold, P.W., Higley, J.D., 2005. Neurobiological characteristics of rhesus macaque abusive mothers and their relation to social and maternal behavior. Neurosci. Biobehav. Rev. 29, 51–57.

Majewska, M.D., 1995. Neuronal actions of dehydroepiandrosterone. Possible roles in brain development, aging, memory, and affect. Ann. N. Y. Acad. Sci. 774, 111–120.

Majzoub, J.A., Karalis, K.P., 1999. Placental corticotropin-releasing hormone: function and regulation. Am. J. Obstet. Gynecol. 180, S242–S246.

Maninger, N., Wolkowitz, O.M., Reus, V.I., Epel, E.S., Mellon, S.H., 2009. Neurobiological and neuropsychiatric effects of dehydroepiandrosterone (DHEA) and DHEA sulfate (DHEAS). Front. Neuroendocrinol. 30, 65–91.

Maninger, N., Capitanio, J.P., Mason, W.A., Ruys, J.D., Mendoza, S.P., 2010. Acute and chronic stress increase DHEAS concentrations in rhesus monkeys. Psychoneuroendocrinology 35, 1055–1062.

Marmot, M.G., 2004. The Status Syndrome: How Social Standing Affects Our Health and Longevity. Times Books/Henry Holt, New York.

Marmot, M.G., Wilkinson, R.G. (Eds.), 1999. Social Determinants of Health. Oxford University Press, New York.

Mateo, J.M., 2008. Inverted-U shape relationship between cortisol and learning in ground squirrels. Neurobiol. Learn. Mem. 89, 582–590.

McEwen, B.S., 1995. Stressful experience, brain, and emotions: Developmental, genetic, and hormonal influences. In: Gazzaniga, M.S. (Ed.), The Cognitive Neurosciences. MIT Press, Cambridge, MA, pp. 1117–1135.

McEwen, B.S., 2003. Interacting mediators of allostasis and allostatic load: towards an understanding of resilience in aging. Metabolism 52 (10 Suppl 2), 10–16.

McEwen, B.S., 2007. Physiology and neurobiology of stress and adaptation: central role of the brain. Physiol. Rev. 87, 873–904.

McEwen, B.S., McCormick, M.C., Smythe, J.W., Sharma, S., Meaney, M.J., 1995. Stressful experience, glucocorticoid receptor density in adult rats. Dev. Brain Res. 84, 55–61.

McEwen, B.S., Wingfield, J.C., 2003. The concept of allostasis in biology and biomedicine. Horm. Behav. 43, 2–15.

McEwen, B.S., Wingfield, J.C., 2010. What is in a name? Integrating homeostasis, allostasis and stress. Horm. Behav. 57, 105–111.

McGowan, P.O., Sasaki, A., D'Alessio, A.C., Dymov, S., Labonté, B., Szyf, M., Turecki, G., Meaney, M.J., 2009. Epigenetic regulation of the glucocorticoid receptor in human brain associates with childhood abuse. Nat. Neurosci. 12, 342–348.

McIntosh, D.E., Mulkins, R.S., Dean, R.S., 1995. Utilization of maternal perinatal risk indicators in the differential diagnosis of ADHD and UADD children. Int. J. Neurosci. 81, 35–46.

Meaney, M.J., 2001. Maternal care, gene expression, and the transmission of individual differences in stress reactivity across generations. Ann. Rev. Neurosci. 24, 1161–1192.

Meaney, M.J., Diorio, J., Francis, D., Widdowson, J., LaPlante, P., Caldji, C., 1996. Early environmental regulation of forebrain glucocorticoid receptor gene expression: implications for adrenocortical responses to stress. Dev. Neurosci. 18, 49–72.

Meaney, M.J., Szyf, M., Seckl, J.R., 2007. Epigenetic mechanisms of perinatal programming of hypothalamic–pituitary–adrenal function and health. Trends Mol. Med. 13, 269–277.

Meijer, A., 1986. Child psychiatric sequelae of maternal war stress. Acta Psychiatr. Scand. 72, 505–511.

Meinlschmidt, G., Matin, C., Neumann, I.D., Heinrichs, M., 2010. Maternal cortisol in late pregnancy and hypothalamic–pituitary–adrenal reactivity to psychosocial stress postpartum in women. Stress 13, 163–171.

Mirescu, C., Peters, J.D., Gould, E., 2004. Early life experience alters response of adult neurogenesis to stress. Nat. Neurosci. 7, 841–846.

Moll, J., Zahn, R., de Oliveira-Souza, R., Krueger, F., Grafman, J., 2005. The neural basis of human moral cognition. Nat. Rev. Neurosci. 6, 799–809.

Morgan 3rd, C.A., Rasmusson, A., Pietrzak, R.H., Coric, V., Southwick, S.M., 2009. Relationships among plasma dehydroepiandrosterone and dehydroepiandrosterone sulfate, cortisol, symptoms of dissociation, and objective performance in humans exposed to underwater navigation stress. Biol. Psychiat. 66, 334–340.

Moriceau, S., Wilson, D.A., Levine, S., Sullivan, R.M., 2006. Dual circuitry for odor-shock conditioning during infancy: corticosterone switches between fear and attraction via amygdala. J. Neurosci. 26, 6737–6748.

Morley-Fletcher, S., Darnaudery, M., Koehl, M., Casolin, P., Van Reeth, O., Maccari, S., 2003. Prenatal stress in rats predicts immobility behavior in the forced swim test: effects of a chronic treatment with tianeptine. Brain Res. 989, 246–251.

Mousseau, T.A., Uller, T., Wapstra, E., Badyaev, A.V., 2009. Evolution of maternal effects: past and present. Philos. Trans. R. Soc. Lond. B. Biol. Sci. 364, 1035–1038.

Muehlenbein, M.P., 2010. Evolutionary medicine, immunity and infectious diseases. In: Muehlenbein, M.P. (Ed.), Human Evolutionary Biology. Cambridge University Press, Cambridge, pp. 127–142.

Muehlenbein, M.P., Richards, R.J., Campbell, B.C., Phillippi, K.M., Murchison, M.A., Myers, L., Svec, F., 2003. Dehydroepiandrosterone-sulfate as a biomarker of senescence in male non-human primates. Exp. Gerontol. 38, 1077–1085.

Muehlenbein, M.P., Flinn, M.V., 2011. Patterns and processes of human life history evolution. In: Flatt, T., Heyland, A., (Eds.), Mechanisms of Life History Evolution. Oxford University Press, New York, pp. 153–168.

Murphy, V.E., Smith, R., Giles, W.B., Clifton, V.L., 2006. Endocrine regulation of human fetal growth: the role of the mother, placenta, and fetus. Endocr. Rev. 27, 141–169.

Murphy, V.E., Gibson, P.G., Giles, W.B., Zakar, T., Smith, R., Bisits, A.M., Kessell, L.G., Clifton, V.L., 2003. Maternal asthma is associated with reduced female fetal growth. Am. J. Respir. Crit. Care Med. 168, 1317–1323.

Nepomnaschy, P., Flinn, M.V., 2009. Early life influences on the ontogeny of neuroendocrine stress response in the human child. In: Ellison, P., Gray, P. (Eds.), The Endocrinology of Social Relationships. Harvard University Press, Cambridge, MA, pp. 364–382.

Nepomnaschy, P.A., Welch, K., McConnell, D., Strassmann, B.I., England, B.G., 2004. Stress and female reproductive function: a study of daily variations in cortisol, gonadotrophins, and gonadal steroids in a rural Mayan population. Am. J. Hum. Biol. 16, 523–532.

Nepomnaschy, P.A., Welch, K.B., McConnell, D.S., Low, B.S., Strassmann, B.I., England, B.G., 2006. Cortisol levels and very early pregnancy loss in humans. Proc. Natl. Acad. Sci. U.S.A. 103, 3938–3942.

Nesse, R.M., Stearns, S.C., Omenn, G.S., 2006. Medicine needs evolution. Science 311, 1071.

Nesse, R.M., Ellsworth, P., 2009. Evolution, emotions, and emotional disorders. Amer. Psychol. 64, 129–139.

Nesse, R.M., Stearns, S.C., Omenn, G.S., 2009. Medicine needs evolution. Science 311, 1071.

Neumann, I.D., 2009. The advantage of social living: brain neuropeptides mediate the beneficial consequences of sex and motherhood. Front. Neuroendocrinol. 30, 483–496.

Nguyen, A.D., Conley, A.J., 2008. Adrenal androgens in humans and nonhuman primates: production, zonation and regulation. Endocr. Dev. 13, 33–54.

Nguyen, A.D., Mapes, S.M., Corbin, C.J., Conley, A.J., 2008. Morphological adrenarche in rhesus macaques: development of the zona reticularis is concurrent with fetal zone regression in the early neonatal period. J. Endocrinol. 199, 367–378.

Norbiato, G., Bevilacqua, M., Vago, T., Taddei, A., Clerici, M., 1997. Glucocorticoids and the immune function in the human immunodeficiency virus infection: a study in hypercortisolemic and cortisol-resistant patients. J. Clin. Endocrinol. Metab. 82, 3260–3263.

O'Connor, T.G., Heron, J., Golding, J., Glover, V., Avon Longitudinal Study of Parents Children Study Team, 2003. Maternal antenatal anxiety and behavioral/emotional problems in children: a test of a programming hypothesis. J. Child Psychol. Psychiat. 44, 1025–1036.

O'Donnell, K., O'Connor, T.G., Glover, V., 2009. Prenatal stress and neurodevelopment of the child: focus on the HPA axis and role of the placenta. Dev. Neurosci. 31, 285–292.

Oberlander, T.F., Weinberg, J., Papsdorf, M., Grunau, R., Misri, S., Devlin, A.M., 2008. Prenatal exposure to maternal depression, neonatal methylation of human glucocorticoid receptor gene (NR3C1) and infant cortisol stress responses. Epigenetics 3, 97–106.

Ong, K.K., Potau, N., Petry, C.J., Jones, R., Ness, A.R., the Avon Longitudinal Study of Parents Children Study Team, Honour, J.W., de Zegher, F., Lourdes Ibáñez, L., Dunger, D.B., 2004. Opposing influences of prenatal and postnatal weight gain on adrenarche in normal boys and girls. J. Clin. Endocrinol. Metabol. 89, 2647–2651.

Panter-Brick, C., Pollard, T.M., 1999. Work and hormonal variation in subsistence and industrial contexts. In: Panter-Brick, C., Worthman, C. (Eds.), Hormones, Health, and Behavior. Cambridge University Press, Cambridge, pp. 139–183.

Parker, L.N., 1989. Adrenal Androgens in Clinical Medicine. Academic Press, San Diego, CA.

Patel, P.D., Lopez, J.F., Lyons, D.M., Burke, S., Wallace, M., Shatzberg, A.F., 2000. Glucocorticoid and mineralocorticoid receptor mRNA expression in squirrel monkey brain. J. Psychiatr. Res. 34, 383–392.

Pattison, J.C., Abbott, D.H., Saltzman, W., Nguyen, A.D., Henderson, G., Jing, H., Pryce, C.R., Allen, A.J., Conley, A.J., Bird, I.M., 2005. Male marmoset monkeys express an adrenal fetal zone at birth, but not a zona reticularis in adulthood. Endocrinology 146, 365–374.

Pattison, J.C., Abbott, D.H., Saltzman, W., Conley, A.J., Bird, I.M., 2009. Plasticity of the zona reticularis in the adult marmoset adrenal cortex: voyages of discovery in the New World. J. Endocrinol. 203, 313–326.

Pellegrini, A.D., Archer, J., 2005. Sex differences in competitive and aggressive behavior: a view from sexual selection theory. In: Ellis, B.J., Bjorklund, D.F. (Eds.), Origins of the Social Mind: Evolutionary Psychology and Child Development. Guilford Press, New York, pp. 219–244.

Penn, D.J., Smith, K.R., 2007. Differential fitness costs of reproduction between the sexes. Proc. Nat. Acad. Sci. U.S.A. 104, 553–558.

Pérez-Neri, I., Montes, S., Ojeda-López, C., Ramírez-Bermúdez, J., Ríos, C., 2008. Modulation of neurotransmitter systems by dehydroepiandrosterone and dehydroepiandrosterone sulfate: mechanism of action and relevance to psychiatric disorders. Prog. Neuropsychopharmacol. Biol. Psychiat. 32, 1118–1130.

Pervanidou, P., Chrousos, G.P., 2010. Neuroendocrinology of post-traumatic stress disorder. Prog. Brain Res. 182, 149–160.

Phan, K.L., Fitzgerald, D.A., Nathan, P.J., Tancer, M.E., 2006. Association between amygdala hyperactivity to harsh faces and severity of social anxiety in generalized social phobia. Biol. Psychiat. 59, 424–429.

Phillips, D.I., Walker, B.R., Reynolds, R.M., Flanagan, D.E., Wood, P.J., Osmond, C., Barker, D.J., Whorwood, C.B., 2000. Low birth weight predicts elevated plasma cortisol concentrations in adults from 3 populations. Hypertension 35, 1301–1306.

Pieper, D.R., Lobocki, C.A., 2000. Characterization of serum dehydroepiandrosterone secretion in golden hamsters. Proc. Soc. Exp. Biol. Med. 224, 278–284.

Pine, D.S., Fyer, A., Grun, J., Phelps, E.A., Szeszko, P.R., Koda, V., Li, W., Ardekani, B., Maguire, E.A., Burgess, N., Bilder, R.M., 2001. Methods for developmental studies of fear conditioning circuitry. Biol. Psychiatry 50, 225–228.

Pitman, R.K., 1989. Post-traumatic stress disorder, hormones, and memory. Biol. Psychiat. 26, 221–223.

Pitman, R.K., Sanders, K.M., Zusman, R.M., Healy, A.R., Cheema, F., Lasko, N.B., Cahill, L., Orr, S.P., 2002. Pilot study of secondary prevention of posttraumatic stress disorder with propranolol. Biol. Psychiat. 51, 189–192.

Pradhan, D.S., Newman, A.E., Wacker, D.W., Wingfield, J.C., Schlinger, B.A., Soma, K.K., 2010. Aggressive interactions rapidly increase androgen synthesis in the brain during the non-breeding season. Horm. Behav. 57, 381–389.

Preussner, J.C., Baldwin, M.W., Dedovic, K., Renwick, R., Khalili Mahani, N., Lord, C., Meaney, M., Lupien, S., 2005. Self-esteem, locus of control, hippocampal volume, and cortisol regulation in young and old adulthood. NeuroImage 28, 815–826.

Predine, J., Merceron, L., Barrier, G., Sureau, C., Milgrom, E., 1979. Unbound cortisol in umbilical cord plasma and maternal plasma: a reinvestigation. Am. J. Obstet. Gynecol. 135, 1104–1108.

Qiu, J., 2006. Epigenetics: unfinished symphony. Nature 441, 143–145.

Quas, J.A., Bauer, A., Boyce, W.T., 2004. Physiological reactivity, social support, and memory in early childhood. Child Dev. 75, 797–814.

Reynolds, R.M., Walker, B.R., Syddall, H.E., Andrew, R., Wood, P.J., Whorwood, C.B., Phillips, D.I., 2001. Altered control of cortisol secretion in adult men with low birth weight and cardiovascular risk factors. J. Clin. Endocrinol. Metab. 86, 245–250.

Rilling, J., Gutman, D., Zeh, T., Pagnoni, G., Berns, G., Kilts, C., 2002. A neural basis for social cooperation. Neuron 35, 395–405.

Rodriguez Manzanares, P.A., Isoari, N.A., Carrer, H.F., Molina, V.A., 2005. Previous stress facilitates fear memory, attenuates GABAergic inhibition, and increases synaptic plasticity in the rat basolateral amygdala. J. Neurosci. 25, 8725–8734.

Roelofs, K., Bakvis, P., Hermans, E.J., van Pelt, J., van Honk, J., 2007. The effects of social stress and cortisol responses on the preconscious selective attention to social threat. Biol. Psychol. 75, 1–7.

Rohleder, N., Wolf, J.M., Wolf, O.T., 2010. Glucocorticoid sensitivity of cognitive and inflammatory processes in depression and posttraumatic stress disorder. Neurosci. Biobehav. Rev. 35, 104–114.

Romeo, R.D., 2010a. Pubertal maturation and programming of hypothalamic–pituitary–adrenal reactivity. Front. Neuroendocrinol. 31, 232–240.

Romeo, R.D., 2010b. Adolescence: a central event in shaping stress reactivity. Dev. Psychobiol. 52, 244–253.

Romero, L.M., Dickens, M.J., Cyr, N.E., 2009. The reactive scope model—a new model integrating homeostasis, allostasis, and stress. Horm. Behav. 55, 375–389.

Rondo, P.H., Ferreira, R.F., Nogueira, F., Ribeiro, M.C., Lobert, H., Artes, R., 2003. Maternal psychological stress and distress as predictors of low birth weight, prematurity and intrauterine growth retardation. Eur. J. Clin. Nutr. 57, 266–272.

Roozendaal, B., Quirarte, G.L., McGaugh, J.L., 2002. Glucocorticoids interact with the basolateral amygdala beta-adrenoceptor–cAMP/cAMP/PKA system in influencing memory consolidation. Euro. J. Neurosci. 15, 553–560.

Roozendaal, B., McEwen, B.S., Chattarji, S., 2009. Stress, memory and the amygdala. Nat. Rev. Neurosci. 10, 423–433.

Rosenberg, K., 2004. Living longer: Information revolution, population expansion, and modern human origins. Proc. Natl. Acad. Sci. U.S.A. 101, 10847–10848.

Rosenberg, K., Trevathan, W., 2002. Birth, obstetrics and human evolution. BJOG-Int. J. Obstet. Gy. 109, 1199–1206.

Rosenfeld, R., Hellman, L., Roffwang, H., Weitzman, E.D., Fukushima, D.K., Gallagher, T., 1971. Dehydroepiandrosterone is secreted episodically and synchronously with cortisol by normal man. J. Clin. Endocrinol. Metabol. 33, 87–92.

Roth, G., Dicke, U., 2005. Evolution of the brain and intelligence. Trends Cogn. Sci. 9, 250–257.

Rotmensch, S., Celentano, C., Liberati, M., Sadan, O., Glezerman, M., 1999. The effect of antenatal steroid administration on the fetal response to vibroacoustic stimulation. Acta Obstet. Gynecol. Scand. 78, 847–851.

Ruiz, R.J., Fullerton, J., Brown, C.E., Dudley, D.J., 2002. Predicting risk of preterm birth: the roles of stress, clinical risk factors, and corticotropin-releasing hormone. Biol. Res. Nurs. 4, 54–64.

Rumpel, S., LeDoux, J.E., Zador, A., Malinow, R., 2005. Postsynaptic receptor trafficking underlying a form of associative learning. Science 308, 83–88.

Sanchez, M.M., Young, L.J., Plotsky, P.M., Insel, T.R., 2000. Distribution of corticosteroid receptors in the rhesus brain: relative absence of glucocorticoid receptors in the hippocampal formation. J. Neurosci. 20, 4657–4668.

Sandman, C.A., Wadhwa, P., Glynn, L., Chicz-Demet, A., Porto, M., Garite, T.J., 1999. Corticotrophin-releasing hormone and fetal responses in human pregnancy. Ann. N. Y. Acad. Sci. 897, 66–75.

Sapolsky, R.M., 1996. Why stress is bad for your brain. Science 273, 749.

Sapolsky, R.M., 1999. Hormonal correlates of personality and social context: from non-human to human primates. In: Panter-Brick, C., Worthman, C. (Eds.), Hormones, Health, and Behavior: A Socio-ecological and Lifespan Perspective. Cambridge University Press, Cambridge, pp. 18–46.

Sapolsky, R.M., 2005. The influence of social hierarchy on primate health. Science 308, 648–652.

Sapolsky, R.M., Romero, L.M., Munck, A.U., 2000. How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. Endocrine Rev. 21, 55–89.

Schneider, M.L., 1992. Prenatal stress exposure alters postnatal behavioral expression under conditions of novelty challenge in rhesus monkey infants. Dev. Psychobiol. 25, 529–540.

Schneider, M.L., Moore, C.F., Kraemer, G.W., 2004. Moderate level alcohol during pregnancy, prenatal stress, or both and limbic-hypothalamic-pituitary-adrenocortical axis response to stress in rhesus monkeys. Child Dev. 75, 96–109.

Schoenemann, P.T., 2006. Evolution of the size and functional areas of the human brain. Ann. Rev. Anthropol. 35, 379–406.

Schwabe, L., Schächinger, H., de Kloet, E.R., Oitzl, M.S., 2009. Corticosteroids operate as switch between memory systems. J. Cogn. Neurosci. 22, 1362–1372.

Seckl, J.R., Holmes, M.C., 2007. Mechanisms of disease: glucocorticoids, their placental metabolism and fetal 'programming' of adult pathophysiology. Nat. Clin. Pract. Endocrinol. Metab. 3, 479–488.

Seckl, J.R., Meaney, M.J., 2004. Glucocorticoid programming. Ann. N. Y. Acad. Sci. 1032, 63–84.

Shansky, R.M., Hamo, C., Hof, P.R., McEwen, B.S., Morrison, J.J., 2009. Stress-Induced dendritic remodeling in the prefrontal cortex is circuit specific. Cereb. Cortex 19, 2479–2484.

Shansky, R.M., Morrison, J.J., 2009. Stress-induced dendritic remodeling in the medial prefrontal cortex: effects of circuit, hormones and rest. Brain Res. 1293, 108–113.

Sherwood, C.C., Stimpson, C.D., Raghanti, M.A., Wildman, D.E., Uddin, M., Grossman, L.I., Goodman, M., Redmond, J.C., Bonar, C.J., Erwin, J.M., Hof, P.R., 2006. Evolution of increased glia–neuron ratios in the human frontal cortex. Proc. Natl. Acad. Sci. U.S.A. 103, 13606–13611.

Shettleworth, S.J., 2010. Cognition, Evolution, and Behavior, 2nd ed. Oxford University Press, New York.

Shonkoff, J.P., Boyce, W.T., McEwen, B.S., 2009. Neuroscience, molecular biology, and the childhood roots of health disparities: building a new framework for health promotion and disease prevention. J. Am. Med. Assoc. 301, 2252–2259.

Slavich, G.M., O'Donovan, A., Epel, E.S., Kemeny, M.E., 2010. Black sheep get the blues: a psychobiological model of social rejection and depression. Neurosci. Biobehav. Rev. 35, 39–45.

Sloboda, D.M., Hart, R., Doherty, D.A., Pennell, C.E., Hickey, M., 2007. Age at menarche: influences of prenatal and postnatal growth. J. Clin. Endocrinol. Metab. 92, 46–50.

Smail, P.J., Faiman, C., Hobson, W.C., Fuller, G.B., Winter, J.S.D., 1982. Further studies on adrenarche in nonhuman primates. Endocrinology 111, 844–848.

Smith, B.H., 1992. Life history and the evolution of human maturation. Evol. Anthropol. 1, 134–142.

Soma, K.K., Wingfield, J.C., 2001. Dehydroepiandrosterone in songbird plasma: seasonal regulation and relationship to territorial aggression. Gen. Comp. Endocrinol. 123, 144–155.

Soma, K.K., Scotti, M.M., Newman, A.E., Charlier, T.D., Demas, G.E., 2008. Novel mechanisms for neuroendocrine regulation of aggression. Front. Neuroendocrinol. 29, 476–489.

Soules, M.R., Clifton, D.K., Cohen, N.L., Bremner, W.J., Steiner, R.A., 1989. Luteal phase deficiency: abnormal gonadotropin and progesterone secretion patterns. J. Clin. Endocrinol. Metab. 69, 813–820.

Stearns, S.C., 1992. The Evolution of Life Histories. Oxford University Press, New York.

Strayer, F.F., Trudel, M., 1984. Developmental changes in the nature and function of social dominance among young children. Ethol. Sociobiol. 5, 279–295.

Subtil, D., Tiberghien, P., Devos, P., Therby, D., Leclerc, G., Vaast, P., Puech, F., 2003. Immediate and delayed effects of antenatal corticosteroids on fetal heart rate: a randomized trial that compares betamethasone acetate and phosphate, betamethasone phosphate, and dexamethasone. Am. J. Obstet. Gynecol. 188, 524–531.

Suomi, S.J., 2005. Mother-infant attachment, peer relationships, and the development of social networks in rhesus monkeys. Hum. Dev. 48, 67–79.

Szuran, T.F., Pliska, V., Pokorny, J., Welzl, H., 2000. Prenatal stress in rats: effects on plasma corticosterone, hippocampal glucocorticoid receptors, and maze performance. Physiol. Behav. 71, 353–362.

Szyf, M., Weaver, I., Meaney, M., 2007. Maternal care, the epigenome and phenotypic differences in behavior. Reprod. Toxicol. 24, 9–19.

Szyf, M., McGowan, P., Meaney, M.J., 2008. The social environment and the epigenome. Environ. Mol. Mutagen. 49, 46–60.

Takahashi, L.K., Turner, J.G., Kalin, N.H., 1992. Prenatal stress alters brain catecholaminergic activity and potentiates stress-induced behavior in adult rats. Brain Res. 574, 131–137.

Taylor, M.K., Sausen, K.P., Potterat, E.G., Mujica-Parodi, L.R., Reis, J.P., Markham, A.E., Padilla, G.A., Taylor, D.L., 2007. Stressful military training: endocrine reactivity, performance, and psychological impact. Aviat. Space Environ. Med. 78, 1143–1149.

Teicher, M.H., Samson, J.A., Polcari, A., McGreenery, C.E., 2006. Sticks, stones, and hurtful words: relative effects of various forms of childhood maltreatment. Am. J. Psychiat. 163, 993–1000.

Teixeira, J.M., Fisk, N.M., Glover, V., 1999. Association between maternal anxiety in pregnancy and increased uterine artery resistance index: cohort based study. Br. Med. J. 318, 153–157.

Tilbrook, A.J., Turner, A.I., Clarke, I.J., 2002. Stress and reproduction: central mechanisms and sex differences in non-rodent species. Stress 5, 83–100.

Tinbergen, N., 1963. On aims and methods in ethology. Z. Tierpsychol. 20, 410–433.

Tomasello, M., 1999. The Cultural Origins of Human Cognition. Harvard University Press, Cambridge, MA.

Tooby, J., Cosmides, L., 2005. Evolutionary psychology: conceptual foundations. In: Buss, D.M. (Ed.), Handbook of Evolutionary Psychology. Wiley, New York.

Topor, L.S., Asai, M., Dunn, J., Majzoub, J.A., 2010. Cortisol stimulates secretion of dehydroepiandrosterone in human adrenocortical cells through inhibition of 3βHSD2. J. Clin. Endocrinol. Metab., doi:10.1210/jc.2010-0692.

Trivers, R.L., 1974. Parent-offspring conflict. Am. Zool. 14, 249–264.

Tsankova, N., Renthal, W., Kumar, A., Nestler, E.J., 2007. Epigenetic regulation in psychiatric disorders. Nat. Rev. Neurosci. 8, 355–376.

Turnbull, A.V., Rivier, C.L., 1999. Regulation of the hypothalamic-pituitary adrenal axis by cytokines: actions and mechanisms of action. Physiol. Rev. 79, 1–71.

Vallée, M., Mayo, W., Dellu, F., Le Moal, M., Simon, H., Maccari, S., 1997. Prenatal stress induces high anxiety and postnatal handling induces low anxiety in adult offspring: correlation with stress-induced corticosterone injection. J. Neurosci. 17, 2626–2636.

Van den Bergh, B.R.H., 1992. Maternal emotions during pregnancy and fetal and neonatal behavior. In: Nijhuis, J.G. (Ed.), Fetal Behaviour: Developmental and Perinatal Aspects. Oxford University Press, New York, pp. 157–178.

Van Goozen, S.H.M., Matthys, W., Cohen-Kettenis, P.T., Thijssen, J.H.H., van England, H., 1998. Adrenal androgens and aggression in conduct disorder prepubartal boys and normal controls. Biol. Psychiat. 43, 156–158.

Van Os, J., Selten, J.P., 1998. Prenatal exposure to maternal stress and subsequent schizophrenia: the May 1940 invasion of the Netherlands. Br. J. Psychiat. 172, 324–326.

Veenema, A.H., 2009. Early life stress, the development of aggression and neuroendocrine and neurobiological correlates: What can we learn from animal models?, Front. Neuroendocrinology 30, 497–518.

Vigil, J.M., Carle, A.C., Geary, D.C., Granger, D.A., Flinn, M.V., Pendleton, P., 2009. Maternal correlates of children's stress functioning following a major natural disaster. J. Child Adol. Trauma 2, 287–296.

Vigil, J.M., Geary, D.C., Granger, D.A., Flinn, M.V., 2010. Sex differences in salivary cortisol, alpha-amylase, and psychological functioning following hurricane Katrina. Child Dev. 81, 1227–1239.

Waddington, C.H., 1956. Principles of Embryology. Macmillan, New York.

Wadhwa, P.D., Porto, M., Garite, T.J., Chicz-DeMet, A., 1998. Maternal corticotropin-releasing hormone levels in the early third trimester predict length of gestation in human pregnancy. Am. J. Obstet. Gynecol. 179, 1079–1085.

Walker, R.S., Flinn, M.V., Hill, K.R., 2010. Evolutionary history of partible paternity in lowland South America. Proc. Natl. Acad. Sci. U.S.A. 107, 19195–19200.

Watson, J.B., Mednick, S.A., Huttunen, M., Wang, X., 1999. Prenatal teratogens and the development of adult mental illness. Dev. Psychopathol. 11, 457–466.

Weaver, I.C., Cervoni, N., Champagne, F.A., D'Alessio, A.C., Sharma, S., Seckl, J.R., Dymov, S., Szyf, M., Meaney, M.J., 2004. Epigenetic programming by maternal behavior. Nat. Neurosci. 7, 847–854.

Weaver, I.C.G., Champagne, F.A., Brown, S.E., Dymov, S., Sharma, S., Meaney, M.J., Szyf, M., 2005. Reversal of maternal programming of stress responses in adult offspring through methyl supplementation: altering epigenetic marking later in life. J. Neurosci. 25, 11045–11054.

Weinstock, M., 2005. The potential influence of maternal stress hormones on development and mental health of the offspring. Brain Behav. Immun. 19, 296–308.

Weinstock, M., 2008. The long-term behavioural consequences of prenatal stress. Neurosci. Biobehav. Rev. 32, 1073–1086.

Weinstock, M., Matlina, E., Maor, G.I., Rosen, H., McEwen, B.S., 1992. Prenatal stress selectively alters the reactivity of the hypothalamic–pituitary adrenal system in the female rat. Brain Res. 595, 195–200.

Weinstock, M., 1997. Does prenatal stress impair coping and regulation of the hypothalamic–pituitary–adrenal axis? Neurosci. Biobehav. Rev. 21, 1–10.

Weisfeld, G.E., 1999. Evolutionary Principles of Human Adolescence. Basic Books, New York.

Weber, A., Clark, A.J., Perry, L.A., Honour, J.W., Savage, M.O., 1997. Diminished adrenal androgen secretion implies a significant role for ACTH in the induction of adrenarche. Clin. Endocrinol. 46, 431–437.

Welberg, L.A., Seckl, J.R., Holmes, M.C., 2000. Inhibition of 11beta-hydroxysteroid dehydrogenase, the foeto-placental barrier to maternal glucocorticoids, permanently programs amygdala GR mRNA expression and anxiety-like behaviour in the offspring. Eur. J. Neurosci. 12, 1047–1054.

West-Eberhard, M.J., 2003. Developmental Plasticity and Evolution. Oxford University Press, Oxford.

Wiedenmayer, C.P., 2004. Adaptations or pathologies? Long term changes in brain and behavior after a single exposure to severe threat. Neurosci. Biobehav. Rev. 28, 1–12.

Williams, R.W., Herrup, K., 1988. The control of neuron number. Ann. Rev. Neurosci. 11, 423–453.

Wingfield, J.C., Sapolsky, R.M., 2003. Reproduction and resistance to stress: when and how. J. Neuroendocrinol. 15, 711–724.

Wingfield, J.C., Lynn, S., Soma, K.K., 2001. Avoiding the 'costs' of testosterone: ecological bases of hormone-behavior interactions. Brain Behav. Evol. 57, 239–251.

Worthman, C.M., Panter-Brick, C., 2008. Homeless street children in Nepal: use of allostatic load to assess the burden of childhood adversity. Dev. Psychopathol. 20, 233–255.

Xiao, E., Xia-Zhang, L., Ferin, M., 2002. Inadequate luteal function is the initial clinical cyclic defect in a 12-day stress model that includes a psychogenic component in the Rhesus monkey. J. Clin. Endocrinol. Metab. 87, 2232–2237.

Yehuda, R., 2002. Current concepts—post-traumatic stress-disorder. New Engl. J. Med. 346, 108–114.

Yehuda, R., Engel, S.M., Brand, S.R., Seckl, J., Marcus, S.M., Berkowitz, G.S., 2005. Transgenerational effects of posttraumatic stress disorder in babies of mothers exposed to the World Trade Center attacks during pregnancy. J. Clin. Endocrinol. Metab. 90, 4115–4118.

Yen, S.S., 2001. Dehydroepiandrosterone sulfate and longevity: new clues for an old friend. Proc. Natl. Acad. Sci. U.S.A. 98, 8167–8169.

Yim, I.S., Quas, J.A., Cahill, L., Haykawa, C.M., 2010. Children's and adults' salivary cortisol responses to an identical psychosocial laboratory stressor. Psychoneuroendocrinology 35, 241–248.

Zhang, L.X., Levine, S., Dent, G., Zhan, Y., Xing, G., Okimoto, D., Gordon, M.K., Post, R.M., Smith, M.A., 2002. Maternal deprivation increases cell death in the infant rat brain. Dev. Brain Res. 133, 1–11.