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Habits of the Heart: Life History and the Developmental Neuroendocrinology of Emotion

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Abstract

Humans exhibit striking, pervasive, and partly heritable personality differences that draw attention to their possible adaptive value. Psychiatric disorders have been linked to genetic roots associated with personality features also found in non-affected individuals (Fanous and Kendler 2004; Krug et al. 2008). These circumstances, combined with the burdens imposed by mental illness, have fostered speculation that carriers for alleles associated with mental disorder must experience advantages that maintain allelic variation (Akiskal and Akiskal 2005). But an adaptationist analysis necessarily goes deeper than this by asking why personality and temperament, or acquired and biologically based emotional-behavioral styles of experiencing and relating to the world, exist at all and why they vary. The larger questions of design prompt an analysis of adaptive demands on human cognition and the possible role of emotion and emotion regulation in meeting those demands. This report evaluates evidence that affective processing meets critical adaptive demands of sociality by facilitating and coordinating allocation of scarce cognitive and physiologic resources. Evidence of adaptive value heightens the need to trace sources of individual difference in personality and temperament, social cognition, and behavior.

Recent reports detailing the roles of genes, environment, and gene-environment interactions in the development of differences in styles of social cognition and behavior have begun to illuminate the grounds for psychobehavioral differences and differential mental health (Canli and Lesch 2007; Tsankova et al. 2007). But this exciting work has not yet begun to investigate the role of culture and ambient social conditions in constituting environments of rearing and function, and thus determining the formation and consequences of psychobehavioral differences. Nor has it been much concerned with physical health. Research has addressed stress, trauma, and adversity, but is

confined to western post-industrial populations that represent a privileged extreme in the spectrum of human conditions. To enrich the ecological validity and cross-cultural robustness of emerging models in this field, data are urgently needed from non-Western settings where the preponderance of humanity lives and the exposure to adversity is most severe and pervasive.

Reciprocally, human biologists and bioanthropologists investigate determinants of human function, health, and adaptation within a comparative, worldwide frame. But other than attending to the physical health consequences of psychosocial stress and its implications for revealing sociocultural bases of health inequity (Goodman and Leatherman 1999; Panter-Brick and Worthman 1999b), these fields scarcely have been concerned with emotion, cognition, or revelations from the neurosciences about their action, formation, and dysfunction. Yet mental illness has become a dominant health concern with its position as a leading global cause of human suffering and death. Currently, depression is the second largest source for the global burden of disease at ages 15–44 years, and will become so for humans of all ages by 2020 (Murray and Lopez 1996). An alliance between these two domains of research would appear timely and strategic.

This integrative analysis aims to promote a combined agenda by bridging concerns of each field with cognition, psychobehavioral development, and mental health on the one side, and with adaptation, variation, and cultural-ecological comparison on the other. It commences by considering the adaptive demands for social intelligence in humans, the role of emotion in resolving those demands, and the implication for resource allocation and life history construction. Neuro-endocrine mechanisms for responding to challenge are briefly discussed, and the role of and differences in appraisal are evaluated with a focus on stress. Then, recent literature on epigenetic pathways in development of emotion processing and regulation, and their links to variation in social cognition and behavior, are reviewed. For simplicity, discussion focuses on serotonergic pathways as an example. Sources of genetic and environmental difference within and between populations are considered, and in closing, implications for life history and health are assessed.

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ADAPTIVE DEMANDS ON COGNITION

The coevolution of unusually large brains, food sharing, and language use in humans long has been attributed to demands of intense sociality (Corballis and Lea 1999; Deacon 1997). But the design demands on cognition and its constituents has been less fully considered. Accordingly, demands for social intelligence in humans and the role of emotion in meeting those demands are discussed below.

Demands of social intelligence in humans

Several factors compound the adaptive pressures for social intelligence in humans, particularly competition from conspecifics, demands of reciprocity, and niche partitioning. As members of the same species with common needs and capacities, people are their own greatest mutual source of competition for limited material (food, shelter, territory) and social (information, relationships, prestige) resources. Conversely, establishing effective relationships with others represents the major avenue for reliably obtaining those limited social and material goods. But this solution further escalates the

computational burden. Establishing, maintaining, and negotiating social relationships demand attention, well-directed action, and durable memory for relevant detail. Indeed, these pressures alone have been proposed as prime movers for evolution of expanded cranial capacity (Perez-Barberia et al. 2007), and as determinants of social network configurations and sustainable group sizes in humans (Dunbar 2008). Besides being populous and complex, social landscapes also are highly unstable. Group membership fluctuates through migration, birth, and mortality, and processes of life course development, learning, and aging ensure continuous changes in each group member's capacities and needs. Thus, navigation of the social landscape necessitates capacities for rapid, contingent shifts in ends, modes, and means for social behavior and its informing cognitions. The complexities are nicely captured in Chagnon's classic study documenting shifts in usage of kinship terminology by Yanomamö contigent upon gender and marriagability of both interlocutor and addressee (Chagnon 1988).

The habitual obligatory reciprocity practiced by humans also involves substantial and distinctive cognitive demands. The value of social relationships for buffering competition and increasing reliable access to limited and valuable resources was noted above. Humans are remarkable for the extent and forms of sharing and exchange, involving not only material goods such as food but also immaterial ones such as information (Kaplan et al. 2000; Worthman 2003). Furthermore, reciprocity is displaced across space, time, and currency. Thus, the grandson of a deceased healer who cured the daughter of a clan member twenty years previously, may be offered marriage with a member of that clan from another village. The logics hold for both reward and revenge: the grandson of a deceased warrior who violated the daughter of a clan member twenty years previously, may be killed by a member of that clan from another village. The cognitive capacities required for such translations across currencies (life for marriage partner; virginity for life), time (generations), and space (villages) involve not only recall of an exchange or debt incurred, but also ability to defer reward and tolerate the attendant uncertainties, connect social action with its context (kin/clan, morality), transmit knowledge about the debt, and maintain motivation to reciprocate. Note also that accounts for each person must be located and tracked within the social matrix. These cognitive capacities have established neural bases (Bechara and Damasio 2005; Weber and Huettel 2008) that are both specific and rare (Tomasello 1999).

Niche partitioning offers an excellent means to reduce local competition and saturate usable environments (Bolnick et al. 2003; Pachepsky et al. 2007). Indeed, individual niche variation increases and consequently species niche widens where interspecific competition is low (Costa et al. 2008), as is the case among humans. Divisions of labor, social distinctions (by kin, caste, class), and role specialization are characteristic of human societies. Thus, societies afford opportunities for claiming or carving out a social niche. The often considerable effort and creativity deployed in niche construction and maintenance rely heavily on cognitive and behavioral capacities. To succeed in the chosen or allotted niche requires the ability to identify or create possible niches, cultivate attributes of the chosen niche, and acquire or adapt skills, expertise, or faculties. Personality–in terms of a set of emotional-behavioral dispositions regarding experience processing and relations with the world–can facilitate the process of niche partitioning. For instance, Sulloway (Sulloway 2001) has used sibling competition and birth order to predict personality characteristics such as novelty seeking, extraversion, or amiability among samples from western populations. Additionally, personality amplifies individual distinctiveness and may thereby reinforce social recall about that

individual, including the record of material and social contributions and exchanges (Worthman and Brown 2005).

Emotion and cognition

The role of emotion in cognition recently has been thoroughly reconceptualized. Western thought long viewed emotions as disruptive "noise" that disturbed the orderly processes of rational thought, deliberation, and responsible behavior (Damasio 1994). Extensive empirical evidence now demonstrates that, on the contrary, emotion processing is an intrinsic and necessary component of the processes comprising effective thought and action, particularly in the area of social cognition and behavior (Adolphs 2003). Brain structures involved in emotion processing mediate internal representations of stimuli, link the representations to emotional responses, ongoing cognitive processes, and behavioral motivation, and furthermore contribute to an internal model of the social milieu and one's relations to it. In other words, emotions ground social intelligence.

Returning to an adaptationist perspective on design draws attention to several cognitive features required for effective processing, evaluation, and response to experience. First is the problem of speed. In the flow of daily behavior and interactions in social settings, large amounts of multidimensional information (expressions, movements, speech; multiple actors; partial/degraded stimuli) must be absorbed and processed instantaneously to apprehend what is happening and to act appropriately. Speed, therefore, is of the essence. Second is the problem of selection. Any setting, much less a dynamic social one, offers myriad orders of information to which one might attend. But much of this information is irrelevant to pragmatic concerns of social or material need. Under these conditions, knowing what to ignore is critical, followed by knowing what to notice and at what level of detail (Baars 2002). To maximize speed and minimize necessary input, the brain fills information gaps with heuristics based on experience (tables are rectangular, objects persist). Habituation, attentional focusing, and filling in permit actors selectively to track ambient conditions; such mechanisms underlie failures to see unexpected phenomena when attention is focused elsewhere (inattentional blindness, change blindness)(Simons 2000). A famous video example elicits failure to detect a passing gorilla by telling the viewer to track ball-passing by one of two teams (Most et al. 2005). Selection therefore is crucial but contingent, conditioned by experience and expectation (Raz and Buhle 2006).

Emotion processing helps meet the need for speed and selectivity, especially in social cognition. It does so by recursive appraisal of information at various levels of preconscious processing to drive what comes to consciousness, with what intensity and valence, and how long. Throughout information processing, emotion recruits memory formation and recall (LaBar and Cabeza 2006). Emotion mechanisms and their somatic correlates signal possible meanings of ongoing events and project possible consequences of situations and actions that inform the alerting, orienting, and executive networks in attention (Bechara and Damasio 2005). Thus, emotion processing dramatically accelerates situation appraisal and concurrently organizes preparedness for appropriate action. Damage to areas involved in these systems produces deficits in emotion expression and impaired decision-making, dramatically slowing judgment formation and yielding disadvantageous choices.

Of interest here is that subjective states inform not only cognition and behavior, but also physiologic states: feelings are visceral as well as cerebral. The physiologic effects of

emotions have deep evolutionary roots in their function to promote survival by mobilizing, directing, and coordinating cognitive and physical resources to meet current demands (Porges 1995). Sensory feedback from the somatic effects of emotions also affects cognitive processing, creating a mind-body loop. The "somatic marker" hypothesis (Damasio 1994) suggests that dynamically interacting central and somatic states of emotion and sensory processing generate representations of internal and external conditions that permit distinctions of self-not self. Distinctions of self-not self representations permit projection of possible actions and interactions that support rapid assessment, strategic decisions, and appropriate self-sustaining action. Mounting evidence supports this model (Bechara and Damasio 2005).

Emotion and resource allocation

Negotiation of individual needs and goals with external demands and opportunities represents an adaptive challenge at many levels (physiologic, developmental, psychobehavioral, social) throughout the life course. The nervous system, with the brain at its core, plays a central adaptive role in negotiating the inside-outside interface. This role is generally conceived in cognitive-behavioral terms–internalizing information about the world and driving actions in it. Emotion plays a significant part in allocation of limited and valuable cognitive resources, by continuously guiding attentional systems to effect selective, relevant, and timely allocation of limited capacity in consciousness on a momentary basis. Emotions also inform motivation and prompt stances of action readiness, or "being poised, oriented, ready, or inclined toward a course of action" (Cole et al. 2004)(p. 321). These mechanisms have extraordinary power to shape experience by determining what we notice, how we experience it, and what we do with it. Therefore, factors that influence those mechanisms will play determinative roles in lives as they are experienced and enacted. Anthropology long has regarded culture as chief among such influences, and asked how deep and far culture's influence on cognition, experience, and behavior may reach to explain human diversity (Stocking 1989–1999).

As suggested in the previous section, emotion does more than influence cognition and behavior, it links central processing to physiologic function. These links are forged by extensive neuro-endocrine mechanisms to be reviewed below; via these mechanisms, the brain speaks to the body, and the body talks back. The effects of autonomic and neuroendocrine outflow from emotion states on organic systems direct allocation of resources for situation preparedness from among competing systemic demands such as for metabolism, immune function, cardiovascular function, repair, or development (Sapolsky 1998). Reciprocally, interoception, or the central representation of conditions in the physical body, is integral to emotion states and sense of self (Craig 2002). Here the brain's centrality for managing the inside-outside interface extends to physical survival and the life history projects of development and reproduction. Thus, it monitors bodily states for prioritizing competing demands and orchestrating resources for virtually any aspect of acute and long-term function. Via their place in brain function, emotion processes thereby direct key life history parameters, in terms of growth, maintenance, and reproduction over the life course. Hence, emotion works to allocate not only limited cognitive resources, but valuable material bodily resources and their disposition in constructing life history.

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NEURO-ENDOCRINE MEDIATION OF RESPONSES TO CHALLENGE

Distinctions between the nervous and endocrine systems have dissolved in the face of evidence that they function as a neuro-endocrine continuum (Panter-Brick and Worthman 1999a); therefore, here the term "neuro-endocrine" will refer to that continuum. Life history construction is mediated through a suite of neuro-endocrine mechanisms that regulate resource partitioning among competing acute and life course goals and demands. Stress responses illustrate this point. Perceived threat or challenge triggers dual signals from brain to body transmitted via endocrine and neural pathways (Boyce and Ellis 2005). One route involves the hypothalamo-pituitary-adrenocortical (HPA) pathway that triggers cortisol release, while the other involves autonomic nervous system activation that triggers both "fight or flight" organ responses and direct sympathetic neural release of catecholamines in the adrenal medulla (SAM). Each component of the suite of coordinated central and peripheral responses has deep evolutionary roots grounded in common survival demands (Porges 1995) that shift priorities to immediate survival (accelerated heart rate, attentional focusing, elevated glucose) and away from deferrable activity (immunity and repair, digestion, growth, reproduction). The acute value of stress responses therefore comes at a cost that accumulates as responses repeatedly are triggered: the cumulative cost of trade-offs and the accompanying physical burden of meeting life's ordinary and extraordinary demands compounds as allostatic load (McEwen and Wingfield 2003). Variation in the extent of aggregated physical effects from meeting life's demands that are represented in allostatic load form the basis of differential risk to physical and mental health so pervasively associated with material and psychosocial hardship (Joëls 2008; Krieger and Davey Smith 2004).

Triggers and buffers of stress

Not all stressors elicit stress responses with the same reliability and intensity: Table 2 lists characteristic situations reliably associated with physiologic stress or fight/flight responses in the preclinical and human literatures, as well as their stress-alleviating counterparts. Conditions that provoke stress and anxiety share at least one of the following features: 1. unfamiliarity or unpredictability or/and uncertainty or ambiguity; 2. real or perceived lack of control (either suffices), as well as perceived control refuted by events; 3. low or negative relative status, or loss of status; and 4. social isolation and social threat or loss (reviewed in Sapolsky 1998; meta-analysis in Dickerson and Kemeny 2004). Responses to experience consistently associated with production or exacerbation of stress are internalization, frustration, and social defeat. The corresponding situations that prevent or palliate stress are as follows: 1. predictability or familiarity and/or feeling that things make sense; 2. feeling in control, whether the control is real or sustainably partial-to-illusory, or experiencing increased control; 3. social status good or favorable relative to others, or status improves; 4. social integration or presence of social support. Effective behavioral responses that avert or relieve stress frequently recruit one of these buffering conditions, but also commonly include aggression or redirected aggression; denial is another prevalent though less effective response.

TABLE 2

Triggers and buffers of stress response*

Triggers	**Buffers**
Unpredicability, unfamiliarity	Predictability, familiarity
∞ uncertainty, ambiguity	∞ certainty, coherence
Lack of control	Control
∞ perceived lack of control	∞ perceived control
∞ non-control with perceived control	∞ illusion of control
Relative status negative	Relative status positive
∞ perceived loss	∞ perceived gain, improvement
Isolation, social threat/loss	Social support, social integration
Internalization	Aggression
∞ frustration	∞ redirected aggression

*Reviewed in Sapolsky 1998, also Dickerson and Kemeny 2004.

Sources and effects of differences in appraisal

The translation from stressor to psychosocial stress is mediated largely by emotional processes of appraisal that are shaped through developmental, experiential, and genetic factors. Relatedly, emotion regulation, as the ability to manage emotion processing and its impact on other cognitive processes, is subject to similar influences (Cole et al. 2004; Compas et al. 2004). Clearly, emotion processing and its regulation strongly influence the impact of and responses to experience and as such, are important bases of social competence and psychosocial well-being (Davidson 2000). Insofar as social relations and perceived stress also affect physical well-being, affective style furthermore affects physical health. For these reasons, the sources of individual and population variation in affective styles have been intensively investigated. Capacities for emotion regulation, expression, and detection develop during infancy and childhood (Erickson and Schulkin 2003; Posner and Rothbart 2000) subject to external and internal conditions (Fox and Calkins 2003; Pollak 2005) including brain development (Lewis and Stieben 2004). But the relative contributions of biological and contextual factors in individual affective styles have been unclear. The widely studied concept of temperament refers to early emotional biases seen in infants and presumed to be constitutional, or fixed and biologically based. Thus, samples of behaviorally inhibited (fearful, novelty avoidant) American infants and children have been identified with distinctive neurological and psychophysiological characteristics (Fox et al. 2000) as well as long-term psychosocial and mental health risk (Kagan et al. 2007). Yet rearing environment, particularly early on, strongly influences the development of emotion processing systems as reflected in behavioral self regulation and in psychobiological markers such as the reactivity of the HPA stress response (threshold, speed, and intensity) to novelty or threat (Gunnar 2000). For example, Flinn observed acute and enduring effects of early trauma on HPA responses to psychosocial challenge in Dominican children (Flinn 2006).

Against this background of conceptual ambiguity about innate-biological versus experiential-contextual determinants of affective styles and emotion regulation, empirical reports from primate and human studies increasingly have documented person x environment interactions of context dependency in the relationship of a specific genotype or phenotype to psychobehavioral or health outcomes. Such observations indicate that the effects of a given genotype or phenotype on function or health are not fixed, but contingent on circumstance. What is problematic in one context may be neutral or advantageous in another. An early non-human primate report identified high behavioral reactivity in rhesus infants with low adult social status if given poor maternal care, and high adult social status if given good care (Suomi 1991). Quality of maternal care made little difference for adult social status among infants with low reactivity. In a human example, cardiovascular reactivity in children was associated with more frequent respiratory illness under suboptimal daycare conditions, but much lower frequencies under good conditions (Boyce et al. 1995). Children with low cardiovascular reactivity showed less sensitivity to context, but actually experienced higher rates of illness under good than poor daycare conditions. Thus, the lowest rates of illness were observed in high reactivity children under good conditions, just as highest adult social status was observed in reactive rhesus that received excellent mothering. Note that respiratory illness is a major source of mortality in human children, and that social status predicts fitness in rhesus. Therefore, implications of geno/phenotype-environment interactions for life history are significant.

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GENE-ENVIRONMENT INTERACTIONS IN EMOTION REGULATION, SOCIAL COGNITION, AND BEHAVIOR

The mapping of the human genome at the outset of the millennium immediately triggered a demand to understand the epigenetic mechanisms that bring the code to life. Thus the life science focus shifted to micro- to macro-contexts and, in less than a decade, much has been learned about the mechanisms that use contextual information for biological action (Robinson 2004; Slotkin and Martienssen 2007; van de Vijver et al. 2002). Our understanding of complex traits such as behavior has benefited with this move along with the explosion of neuroimaging techniques for observing the living brain operating under increasingly naturalized experimental conditions. These advances have clarified uncertainties highlighted above, and illuminated dynamics of genes and context that underlie variation in emotion regulation, cognition, and behavior patterns. The time is ripe for translation of these insights into comparative population-based studies by human biologists and biocultural anthropologists who excel at studies of both context and biology spanning the breadth of conditions that humans create and occupy. Existing paradigms open vast new opportunities to explore biocultural dynamics underlying human behavior variation. Reciprocally, such comparative work across a wide range of cultural and material ecologies would test and then enrich existing models in the light of real world conditions. The following brief review addresses key models and findings to stimulate such comparative research.

Epigenetic programming by maternal behavior

Before turning to gene-environment interactions in psychobehavioral variation, the operation of solely epigenetic mechanisms that induce similar effects should be noted. The most powerful evidence concerns non-genomic mechanisms for inter-generational transmission of stress reactivity and maternal behavior. It comes from a line of experimental research that probes why rat maternal behavior toward young during the first postnatal week is associated with enduring differences in offspring behavior, including their own maternal behavior, that were faithfully reproduced in their offspring (Meaney 2001). Specifically, Meaney and colleagues have discovered that variation in amount of maternal licking-grooming and arched-back nursing behavior (MLG-ABN), key elements of normal maternal care, alter development of pup neuro-endocrine regulation and consequent behavior. Offspring of high MLG-ABN mothers are behaviorally less irritable, fearful and responsive to stressful conditions, and exhibit less HPA stress responsivity, than offspring of low MLG-ABN mothers. The effects can be reversed: pups of low MLG-ABN mothers cross-fostered within the first week of life to care by MLG-ABN mothers resemble pups born to high MLG-ABN mothers, and vice versa.

Apparently, intergenerational transmission of a distinct suite of neuro-endocrine and behavioral features occurs through programming by an expectable environment of rearing, namely maternal care. Ongoing work by this group has traced specific epigenetic effects on HPA feedback sensitivity that are mediated by stable marking (methylation) of offspring DNA that alters HPA regulation: high MLG-ABN antagonizes DNA methylation at the glucocorticoid receptor promoter region in the hippocampus, thus increasing sensitivity to glucocorticoid negative feeback (Weaver 2007). One review noted that adult “offspring of mothers with low levels of nurturing behaviour were at a molecular disadvantage” for handling stressors because of their

reduced ability to moderate HPA activity (Tsankova et al. 2007), p. 362). But that may be true only under sheltered laboratory conditions.

Genetic variability in neuroregulation

Such recent evidence suggests that environmental induction of specific epigenetic changes in the genome may represent an important basis for variation in complex phenotypes such as behavior. But the genetic bases of temperament and psychobehavioral risk have received much more extensive scrutiny. Due in large part to its links with depression and the success of pharmacologic treatments such as selective serotonin reuptake inhibitors (SSRIs), the serotonergic system has been studied closely and will be the focus here.

Serotonin, or 5-hydroxytryptamine (5-HT), is widely distributed throughout the body and is involved in an unusually large array of functions, including regulation of appetite, sensory processing, motor activity (muscle contraction), cardiovascular function, learning and memory, mood and emotion, and in concert with gonadal steroids, sexual behavior. The bioavailability and thus the action of serotonin are regulated by multiple factors, chief among which are synaptic reuptake and breakdown by the serotonin transporter (5-HTT) and monoamine oxidase (MAO), respectively. The serotonin transporter mediates active removal of 5-HT from the synaptic cleft into the presynaptic cell, and therefore decisively determines the length and strength of serotonin interaction with post- and pre-synaptic targets. Two major functional alleles influencing 5-HTT expression–one short, one long–comprise a gene-linked polymorphic region (5-HTTLPR) upstream from the promoter of the 5-HTT gene. The short allele (5-HTTLPR-short for convenience) contains 14 copies of a 20–23 base pair irregular repeat unit, while the long (5-HTTLPR-long) contains 16 copies: the fewer repeats in the short variant reduces transcription of the 5-HTT gene. Relative loss of 5-HTT activity has been associated with greater vulnerability to environmental stressors in mice and human and non-human primates (Canli and Lesch 2007). The two alleles exhibit balanced equilibrium with average 60% population prevalence of the long allele, although populations vary substantially in allele frequencies (Gelernter et al. 1997).

MAO inactivates serotonin and thereby regulates its bioavailability. Of the two key MAO isoenzymes MAO-A and –B, MAOA has variants in the gene promoter region that differ in number of repeats in a 30-bp sequence 1–1.2 kb upstream from the mapped transcription site. Apparently, there is an optimal number of repeats, because the 3.5- and 4-repeat alleles yield 2-to 10-fold greater transcription efficiency than the 3- of 5-fold repeats. Again, large population differences in population frequencies have been observed (Sabol et al. 1998). But average population frequency of the 3-repeat allele is nearly 36%: those with this allele will process 5-HT less efficiently, leaving more available intracellular serotonin. Population frequency of the 4-repeat allele averages 62%.

Gene x environment interactions in psychobehavioral vulnerability to life stressors

Characterization of genetic variation in serotonergic neurotransmission has provided valuable tools to probe the bases of differences in emotion regulation, behavior and behavior problems. The results document systematic interactions of genes and environment. Commencing with the proximal environment of internal milieu, even

normative differences in endocrine function may alter the effect of genotype on behavior. For example, normal variation in testosterone (T) levels in CSF among adult men interacts with MAOA genotype to predict levels of antisocial behavior (Sjoberg et al. 2008): antisocial behavior increases sharply with T in men having 3- or 5-repeat MAOA alleles, and is significantly lower at low levels of T and higher at high T than in men with 3.5- or 4-repeat alleles, in whom T is unrelated to antisocial behavior. T, as well as glucocorticoids, interact with the MAOA promoter to influence gene transcription and is associated with reduced serotonin production, although its effects are not as powerful as glucocorticoids (Glatz et al. 2003). At the reduced levels of transcription with 3- or 5-repeat alleles, the T effect produces a strong correlation between T and MAOA activity, while it makes no difference at the higher transcription rates of 3.5- and 4-repeat alleles. Note that cortisol exerts similar yet stronger effects.

As expected from observational studies, variation in the impact of differing early environments on later psychobehavioral outcomes relates to genotype and is mediated by effects on neuro-endocrine development. Such phenomena were found to explain the aforementioned effects of rearing conditions on social competence in rhesus observed by Suomi and colleagues: rearing conditions interact with infant 5-HTT genotype to determine reactivity to stressors and vulnerability to substance use and abuse as adults. Peer-reared 5-HTTLPR-short heterozygotes showed exaggerated HPA responses to stressors relative to their homozygous 5-HTTLPR-long peers. But mother-reared heterozygotes were the only group who displayed complete buffering of HPA under stress exposure (Barr et al. 2004). Rearing condition had little effect on HPA stress response in 5-HTTLPR-long homozygotes.

The variable effects of genotype—advantageous in one condition, disadvantageous in another—have been found repeatedly in humans. For example, a family study showed a strong impact of exposure to adverse early family conditions with greatly increased depressive symptoms among 5-HTTLPR-short homozygotes relative to 5-HTTLPR-long hetero- and homozygotes (Taylor et al. 2006). Notably, the 5-HTTLPR-short homozygotes who did not experience poor family conditions had much the lowest risk for depressive symptoms. The same effects were found for interactions of current levels of stress with genotype in relation to depressive symptoms. Another example of cross-over effects were reported for men in a large longitudinal cohort study in New Zealand, where those having genotypes with low MAOA activity exhibited greatly elevated rates of antisocial behavior if they had experienced severe childhood maltreatment. But again, men with the low MAOA activity genotype who did not experience such hardship had lower rates of antisocial behavior than did those with high activity genotype (Caspi et al. 2002). These findings excited such intense interest that multiple replications have been attempted; a recent meta-analysis found that the gene-environment interaction is robust (Kim-Cohen et al. 2006). Those with low MAOA activity genotype show enhanced environmental sensitivity to trauma for mental health outcomes, which are better than in persons with high MAOA activity under no exposure but much worse with exposure to early abuse. Such dynamics establish the bases for production of alternative life history strategies that shift cognitive-behavioral modes contigent on the conditions encountered early and later in life. The shifts also create advantage under some conditions but carry costs in others, and thus carry situation-dependent adaptive trade-offs.

Emotion processing and social cognition

Effects of genetic variation in neuro-endocrine regulation operate through emotion processing and social cognition. They contribute to differences in how people "see" the world such that they can be in the same physical place but inhabit different cognitive-behavioral spaces. Biases in social cognition have been linked to functional polymorphisms in studies using functional imaging. For example, 5-HTTLPR-short carriers show increased amygdala activation (fear/threat processing) to negative pictures, increased implicit (preconscious) processing of negative words, and visuospatial matching of fearful with angry faces (Canli and Lesch 2007).Moreover, the impact of facial stimuli on activity of two key limbic structures in emotion processing and memory, the amygdala and hippocampus, manifested interactive effects between genotype and amount of life stress (Canli et al. 2006). Specifically, presence of the short allele was associated with a negative correlation between life stress and limbic activation by facial stimuli: face processing declined as life stress increased. Conversely, long allele homozygotes showed a positive association wherein activation to facial stimuli correlated positively with life stress. These studies also identified a significant interaction effect of 5-HTT genotype and life stress on resting level activation in the amygdala and hippocampus. Activity in both structures increased with life stress among carriers of the short allele, but decreased with stress among homozygotes for the long allele.

The differential effects of life stress, as a function of serotonin transporter genotype, on face processing and resting limbic activity along with other known interactions, may represent neural bases for situation-dependent differences in emotional tone, in social processing, in styles of coping with stressors, and in vulnerability to mood disorders such as depression. The importance of sociality and adaptive demands on social cognition for humans, discussed at the outset, suggest that variation in face processing is significant. Faces are vital means for social identification and communication, including the projection and reading of emotions; therefore, reading facial expressions is integral to social cognition and competence. Consequently, situation-dependent variation in activation to faces, interacting with genotype, suggests one of likely many bases for diversity in social experience that establish parameters for different experiential worlds and social niches.

Population variation

Recent comparative macaque data have probed social correlates of variability in population genetic structure for functional polymorphisms in serotonin regulation (Wendland et al. 2006). Macaques are the most geographically widespread primate genus aside from humans, occupy a wide range of habitats, exhibit well-studied temperamental differences, and vary markedly in degree of aggression-based social structure. Number of functional alleles in promoter regions for MAOA and 5-HTT present was counted (range 1–3) in samples of six macaque species (Macaca tonkeana, sylvanus, thibetana, arctoides, fascicularis, nemestrina, mulatta). Social organization of each species was scaled for degree of social in/tolerance, hierarchy, and nepotism. The species with less hierarchical, more tolerant social organization showed no or minimal genetic diversity in either the MAOA or 5-HTT promoter region, while the most rigidly hierarchical species, *M. mulatta*, showed the greatest number of variants at both loci. The pattern suggests possible relationships between species variation in social structure and genetic variation in regulators of neuroendocrine activity.

Humans most resemble rhesus macaques in having polymorphisms at each locus (2 for 5-HTTLPR, 4 for MAOA). Moreover, human populations differ in allele frequencies for both loci: HTTLPR-short ranges from 0.25 to 0.8, MAOA 3-repeat ranges .29 – .61 (Gelernter et al. 1999; Gelernter et al. 1997; Sabol et al. 1998). Linkage disequilibrium was apparent in a few populations, but balanced polymorphism was more common. Sample sizes are rather small, representativeness uncertain, and ecological correlates unknown. Nonetheless, the relatively high average frequency of the non-dominant functional polymorphisms, the evidence for variability among populations, and the possible presence of selective pressures for specific haplotypes in some samples suggest that population genetics of neuroregulatory loci merits investigation.

Such genetic studies would need to collect substantial information on socioecological conditions and psychobehavioral outcomes. Mere variation in population genetic structure likely will be uninteresting unless considered in relation to material and social ecology that structures the conditions under which individuals live, the kinds of experiences or insults to which they are exposed, and how those circumstances are viewed. Additionally, given the evidence for gene-environment interactions and developmental effects discussed above, combinations of history and circumstance will condition the phenotypes generated from the genetic structure, and thus influence the impact of that structure on corresponding experience, welfare, behavior, and the balance of selective pressures upon genetic diversity. Such gene-environment interactions and their consequences for function and welfare deserve investigation across a wide range of human cultures and conditions. Such study bears exciting possibility for unlocking dynamics among culture, social conditions, the nature and distribution of social niches, and selection pressures operating on allelic variants.

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CONCLUSION

The recent empirical findings raise several noteworthy points. First, genetic variability in neuroregulatory mechanisms is substantial and differs among populations. Second, gene-environment interactions are widespread, and operate both developmentally and in adulthood. Such interactions produce conditional sensitivity to context, where impact of experience varies by genotype. Third, evidence for situation-dependent adaptive value of neuroregulatory genes is strong. Contrary to an outmoded eugenic view of "good" and "bad" genes, alleles associated with "risky" outcomes under risky conditions may yield the most favorable outcomes under low risk. Other alleles may reduce environmental sensitivity with little difference in outcome regardless of circumstance, but at a cost to relative performance under optimal conditions. Fourth, gene-environment interactions establish a basis for contigent life history strategies, whereby affective-behavioral stances are altered by the conditions experienced early in life, and further influence processing of experience and modes of behavior into adulthood. These dynamics offer plausible mechanisms for temperament, niche partitioning, and condition-dependent construction of life history that were posed as solutions to adaptive pressures on social cognition at the outset of this discussion. Identification of the salient environmental features at play in gene-environmental interactions would have high scientific and practical value.

Fifth, the importance of social relationships and social context in gene-environment interactions merits emphasis. Early rearing environments repeatedly emerge as decisive for shaping the psychobehavioral outcomes discussed here (temperament, affective-

behavioral styles, mental health risk), and caregivers are key determinants of early conditions and experience (van IJzendoorn and Sagi 1999). This is especially true of species with altricial young such as humans, and laboratory rats for that matter. Chisholm provides both theory and evidence for the significance of early family environments and signals of future environmental quality in life history strategies of the young that involve biological (rates of physical maturation) and psychobehavioral (attachment, risk-taking, instrumentality) components (Chisholm 1999). Thus, early signals of risk and uncertainty have been linked to adjusted reproductive strategies with accelerated maturation, earlier childbearing, reduced social attachment, and lower expected life span (Chisholm et al. 2005). Indeed, the disruptions of maternal behavior reflected in low lick-groom and arched-back nursing that organize offspring aggressiveness and irritability in the rat model (Weaver 2007) may transduce early signals of environmental stress into alternate sociobehavioral strategies.

Sixth, neuro-endocrine mechanisms tie cognitive and particularly emotion processes with physiologic functions responsible for resource allocation (Williams 2008). For instance, perceived stress induces physiologic shifts toward immediate demands and away from longer-term goals such as growth or repair. Reciprocally, hormones influence neuroactivity (Caldu and Dreher 2007). For example, 5-HTT gene expression is modulated by both T and glucocorticoids. Indeed, relationships of animal personality to differences in metabolism and energy expenditure have been advanced to explain weak or absent associations between energy expenditure and fitness (Careau et al. 2008) Thus, cognition and affective-behavioral styles shape life history not only directly through perception and behavior, but also through hormonal mediation of resource partitioning among growth, reproduction, and maintenance (Worthman 1999; Worthman 2003).

Implications for health and human welfare

The models and evidence considered here also bear widely on health. First, they delineate epigenetic mechanisms behind differential health and thereby open well-marked avenues for research into variable effects of life's vicissitudes. For instance, although adversity contributes to onset of depression, not everyone who experiences trauma becomes depressed: in girls, vulnerability to hardship is exacerbated epigenetically through fetal conditions (Costello et al. 2007). Current research engages a narrow range of cultural and geopolitical diversity, but the insights and methods used can be adapted rigorously for cross-cultural work across a more representative range of populations. This move will permit more comprehensive delineation of key gene-environment interactions and reveal historical and circumstantial determinants of their importance for health. Second, the findings refocus attention on context and particularly the formation of context through human relationships, social ecology, and culture (social organization, practices, meanings). Demonstration of the differential impact of life stress depending on, for example, previous maternal experience, experience of early life stress, exposure to postnatal adversity, and/or current endocrine status (e.g., T levels), sheds light on pathways by which structural factors (poverty, class, resource uncertainty, family/community fragility) and traumas (warfare, natural disaster, personal loss) may place differential burdens on persons, subgroups, and populations. Current struggles to explain health disparities and track how culture gets under the skin may be advanced using the models discussed here (Krieger and Davey Smith 2004).

Third and relatedly, epigenetics clearly form an avenue for intergenerational transmission of behavioral characteristics through shared conditions, shared biology, or both. Thus, the laboratory rat transmits styles of behavior via maternal behavior effects on offspring neuroregulation that subsequently organize their own maternal behavior. Differences in both exposure and response to stressors contribute substantially to health disparities within and between populations. Embodied imprints of prior conditions that are communicated across generations represents a potent potential source for compounding vulnerability that may characterize social and material hardship or inequalities by gender, caste/class, or region. Nevertheless, the literature on health effects of birthweight notes complications in this line of thought (Kuzawa 2005).

Finally, the work discussed here primarily concerns stress and mental health, which are ascendant global issues. Indeed, this discussion has emphasized the importance of social cognition, emotional processing, and behavioral competence in human function and well-being. However, research on mental health often runs independently from that on physical health. Yet the two are integral and co-constitutive aspects of human welfare. Thus, alliances of fields concerned with mental and with physical health are needed. The overarching purpose of this review has been to suggest that integration of models and methods from developmental cognitive-behavioral sciences and mental health research with those from human biology and bioanthropology offers enormous potential for building a more comprehensive, powerful, and widely generalizable approach to human health.

TABLE 1

Glossary

arousal	"a dimension of emotion that varies from calm to excitement" or low to high intensity	LeBar & Cabeza 2006, p. 54
attention	a. operations that volutionarily select conscious events from a stream of competing sensory information	Feinstein *et al.* 2004
	b. "preparedness for and selection of certain aspects of our physical environment…or some ideas in our mind that are stored in memory"	Raz and Buhle 2006, p. 367

consciousness	"fleeting memory capacity in which only one consistent content can be dominant at any given moment"	Baars 2002, p. 47
conscious perception	"awareness of a sensory stimulus"	Feinstein *et al.*2004, p. 324
emotion	a. "a collection of changes in body and brain states triggered by a dedicated brain system that responds to specific contents of one's perceptions, actual or recalled, relative to a particular object or event"	Bechara & Damasio, p. 339
	b. "appraisal-action readiness stances, a fluid and complex progression of orienting toward the ongoing stream of experience…usually unseen (and unfelt)"	Cole et al. 2004, p. 320
emotion regulation	changes in valence, intensity, or time course of an activated emotion due to one's own or another's activity	Cole et al. 2004, p. 321
emotional intelligence	"abilities at the intersection of emotion and behavior—specifically limited to the set of abilities involved in reasoning about emotions and using emotions to enhance reasoning"	Mayer 2008, p. 514
interoception	"the sense of the physiological condition of the body"	Craig 2002, p. 655

preconscious, preattentive	"processing that occurs before attention is engaged and is therefore capable of affecting performance without awareness"	Robertson 2005, p. 99
self regulation	"the ability to manipulate one's own emotions, thoughts or actions on direction from the self or another person"	Raz and Buhle 2006, p. 368
valence	"a dimension of emotion that varies from unpleasant (negative) to pleasant (positive), with neutral often considered an intermediate value"	LeBar & Cabeza 2006, p. 54
temperament	"biologically based biases toward the experience and expression of certain emotions"	Cole et al. 2004, p. 321

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LITERATURE CITED

1. Adolphs R. Cognitive neuroscience of human social behaviour. Nature Reviews Neuroscience. 2003;4:165–178. [PubMed]
2. Akiskal KK, Akiskal HS. The theoretical underpinnings of affective temperaments: Implications for evolutionary foundations of bipolar disorder and human nature. J Affect Disord. 2005;85:231–239.[PubMed]

3. Baars BJ. The conscious access hypothesis: Origins and recent evidence. Trends in Cognitive Sciences. 2002;6:47–52. [PubMed]
4. Barr CS, Newman TK, Shannon C, Parker C, Dvoskin RL, Becker ML, Schwandt M, Champoux M, Lesch KP, Goldman D, et al. Rearing condition and rh5-HTTLPR interact to influence limbic-hypothalamic-pituitary-adrenal axis response to stress in infant macaques. Biol Psychiatry. 2004;55:733–738. [PubMed]
5. Bechara A, Damasio AR. The somatic marker hypothesis: A neural theory of economic decision. Games and Economic Behavior. 2005;52:336–372.
6. Bolnick DI, Svanback R, Fordyce JA, Yang LH, Davis JM, Hulsey CD, Forister ML. The ecology of individuals: Incidence and implications of individual specialization. American Naturalist. 2003;161:1–28. [PubMed]
7. Boyce WT, Chesney M, Alkon A, Tschann JM, Adams S, Chesterman B, Cohen F, Kaiser P, Folkman S, Wara D. Psychobiologic reactivity to stress and childhood respiratory illnesses: Results of two prospective studies. Psychosom Med. 1995;57:411–422. [PubMed]
8. Boyce WT, Ellis BJ. Biological sensitivity to context. I. An evolutionary-developmental theory of the origins and functions of stress reactivity. Dev Psychopathol. 2005;17:271–301. [PubMed]
9. Caldu X, Dreher J-C. Hormonal and genetic influences on processing reward and social information. Ann N Y Acad Sci. 2007;1118:43–73. [PubMed]
10. Canli T, Lesch K-P. Long story short: The serotonin transporter in emotion regulation and social cognition. Nat Neurosci. 2007;10:1103–1109. [PubMed]
11. Canli T, Qiu M, Omura K, Congdon E, Haas BW, Amin Z, Herrmann MJ, Constable RT, Lesch KP. Neural correlates of epigenesis. Proc Natl Acad Sci U S A. 2006;103:16033–16038.[PMC free article] [PubMed]
12. Careau V, Thomas D, Humphries MM, Reale D. Energy metabolism and animal personality. Oikos. 2008;117:641–653.
13. Caspi A, McClay J, Moffitt TE, Mill J, Martin J, Craig IW, Taylor A, Poulton R. Role of genotype in the cycle of violence in maltreated children. Science. 2002;297:851–854. [PubMed]
14. Chagnon NA. Yanomamö manipulations of kinship classifications of female kin for reproductive advantage. In: Betzig L, Bogrgerhoff Mulder M, Turke P, editors. Human reproductive behaviour: A Darwinian perspective. Cambridge: Cambridge University Press; 1988.
15. Chisholm JS. Death, hope and sex: Steps to an evolutionary ecology of mind and morality. New York, NY, US: Cambridge University Press; 1999.
16. Chisholm JS, Quinlivan JA, Petersen RW, Coall DA. Early stress predicts age at menarche and first birth, adult attachment, and expected lifespan. Human Nature-an Interdisciplinary Biosocial Perspective. 2005;16:233–265. [PubMed]
17. Cole PM, Martin SE, Dennis TA. Emotion regulation as a scientific construct: Methodological challenges and directions for child development research. Child Dev. 2004;75:317–333. [PubMed]
18. Compas JJ, Frankel CB, Camras L. On the nature of emotion regulation. Child Dev. 2004;75:377–394. [PubMed]
19. Corballis MC, Lea SEG. The descent of mind: Psychological perspectives on hominid evolution.Oxford: Oxford University Press; 1999.
20. Costa GC, Mesquita DO, Colli GR, Vitt LJ. Niche expansion and the niche variation hypothesis: Does the degree of individual variation increase in depauperate assemblages? American Naturalist. 2008;172:868–877. [PubMed]

21. Costello EJ, Worthman CM, Erkanli A, Angold A. Prediction from low birth weight to female adolescent depression - a test of competing hypotheses. Arch Gen Psychiatry. 2007;64:338–344.[PubMed]
22. Craig AD. How do you feel? Interoception: The sense of the physiological condition of the body. Nature Reviews Neuroscience. 2002;3:655–666. [PubMed]
23. Damasio A. Descartes' error: Emotion, reason, and the human brain. New York: Grosset/Putnam; 1994.
24. Davidson RJ. Affective style, psychopathology, and resilience: Brain mechanisms and plasticity. Am Psychol. 2000;55:1196–1214. [PubMed]
25. Deacon TW. The symbolic species: The co-evolution of language and the brain. New York: W.W. Norton; 1997.
26. Dickerson SS, Kemeny ME. Acute stressors and cortisol responses: A theoretical integration and synthesis of laboratory research. Psychological Bulletin. 2004;130:355–391. [PubMed]
27. Dunbar RIM. Cognitive constraints on the structure and dynamics of social networks. Group Dynamics-Theory Research and Practice. 2008;12:7–16.
28. Erickson K, Schulkin J. Facial expressions of emotion: A cognitive neuroscience perspective. Brain Cogn. 2003;52:52–60. [PubMed]
29. Fanous AH, Kendler KS. The genetic relationship of personality to major depression and schizophrenia. Neurotoxicity Research. 2004;6:43–50. [PubMed]
30. Flinn MV. Evolution and ontogeny of stress response to social challenges in the human child. Dev Rev. 2006;26:138–174.
31. Fox MA, Calkins SD. The development of self-control of emotion: Intrinsic and extrinsic influences. Motivation and Emotion. 2003;27:7–26.
32. Fox NA, Schmidt LA, Henderson HA. Developmental psychophysiology: Conceptual and methodological perspectives. In: Cacioppo JT, Tassinary LG, editors. Handbook of psychophysiology. 2. New York: Cambridge University Press; 2000. pp. 665–686.
33. Gelernter J, Cubells JF, Kidd JR, Pakstis AJ, Kidd KK. Population studies of polymorphisms of the serotonin transporter protein gene. Am J Med Genet. 1999;88:61–66. [PubMed]
34. Gelernter J, Kranzler H, Cubells JF. Serotonin transporter protein (SLC6A4) allele and haplotype frequencies and linkage disequilibria in African- and European-American and Japanese populations and in alcohol-dependent subjects. Hum Genet. 1997;101:243–246. [PubMed]
35. Glatz K, Mossner R, Heils A, Lesch KP. Glucocorticoid-regulated human serotonin transporter (5-htt) expression is modulated by the 5-HTT gene-promotor-linked polymorphic region. J Neurochem. 2003;86:1072–1078. [PubMed]
36. Goodman AH, Leatherman TL. Building a new biocultural synthesis: Political-economic perspectives on human biology. Ann Arbor: University of Michigan Press; 1999.
37. Gunnar MR. Early adversity and the development of stress reactivity and regulation. In: Nelson CE, editor. The effects of early adversity on neurobehavioral development. Mahwah, NJ: Lawrence Erlbaum; 2000. pp. 163–200.
38. Joëls M, editor. Stress hormone actions in brain, in health and disease - possibilities for new pharmacotherapies. Eur J Pharmacol. 2008;583:173–378. [PubMed]

39. Kagan J, Kahn V, Snidman N, Towsley S. The preservation of two infant temperaments in to adolescence 2007 [PubMed]
40. Kaplan H, Hill KR, Lancaster J, Hurtado AM. A theory of human life history evolution: Diet, intelligence, and longevity. Evolutionary Anthropol. 2000;9:156–185.
41. Kim-Cohen J, Caspi A, Taylor A, Williams B, Newcombe R, Craig IW, Moffitt TE. MAOA, maltreatment, and gene-environment interaction predicting children's mental health: New evidence and a meta-analysis. Mol Psychiatry. 2006;11:903–913. [PubMed]
42. Krieger N, Davey Smith G. "Bodies count," and body counts: Social epidemiology and embodying inequality. Epidemiol Rev. 2004;26:92–103. [PubMed]
43. Krug A, Markov V, Leube D, Zerres K, Eggermann T, Nothen MM, Skowronek MH, Rietschel M, Kircher T. Genetic variation in the schizophrenia-risk gene neuregulin1 correlates with personality traits in healthy individuals. European Psychiatry. 2008;23:344–349. [PubMed]
44. Kuzawa CW. Fetal origins of developmental plasticity: Are fetal cues reliable predictors of future nutritional environments? Am J Hum Biol. 2005;17:5–21. [PubMed]
45. LaBar KS, Cabeza R. Cognitive neuroscience of emotional memory. Nature Reviews Neuroscience. 2006;7:54–64. [PubMed]
46. Lewis MD, Stieben J. Emotion regulation in the brain: Conceptual issues and directions for developmental research. Child Dev. 2004;75:371–376. [PubMed]
47. McEwen BS, Wingfield JC. The concept of allostasis in biology and biomedicine. Horm Behav. 2003;43:2–15. [PubMed]
48. Meaney MJ. Maternal care, gene expression, and the transmission of individual differences in stress reactivity across generations. Annu Rev Neurosci. 2001;24:1161–1192. [PubMed]
49. Most SB, Scholl BJ, Clifford ER, Simons DJ. What you see is what you set: Sustained inattentional blindness and the capture of awareness. Psychol Rev. 2005;112:217–242. [PubMed]
50. Pachepsky E, Bown JL, Eberst A, Bausenwein U, Millard P, Squire GR, Crawford JW. Consequences of intraspecific variation for the structure and function of ecological communities part 2: Linking diversity and function. Ecol Model. 2007;207:277–285.
51. Panter-Brick C, Worthman CM. Contributions of biological anthropology to the study of hormones, health and behavior. In: Panter-Brick C, Worthman CM, editors. Hormones, health, and behavior: A socio-ecological and lifespan perspective. New York: Cambridge University Press; 1999a. pp. 1–17.
52. Panter-Brick C, Worthman CM, editors. Hormones, health, and behavior: A socio-ecological and lifespan perspective. New York, NY: Cambridge University Press; 1999b.
53. Perez-Barberia FJ, Shultz S, Dunbar RIM. Evidence for coevolution of sociality and relative brain size in three orders of mammals. Evolution. 2007;61:2811–2821. [PubMed]
54. Pollak SD. Early adversity and mechanisms of plasticity: Integrating affective neuroscience with developmental approaches to psychopathology. Dev Psychopathol. 2005;17:735–752. [PubMed]

55. Porges SW. Orienting in a defensive world: Mammalian modifications of our evolutionary heritage. A polyvagal theory. Psychophysiology. 1995;32:301–318. [PubMed]
56. Posner MI, Rothbart MK. Developing mechanisms of self-regulation. Dev Psychopathol. 2000;12:427–441. [PubMed]
57. Raz A, Buhle J. Typologies of attentional networks. Nature Reviews Neuroscience. 2006;7:367–379.[PubMed]
58. Robinson GE. Genomics. Beyond nature and nurture. Science. 2004;304:397–399. [PubMed]
59. Sabol SZ, Hu S, Hamer D. A functional polymorphism in the monoamine oxidase a gene promoter. Hum Genet. 1998;103:273–279. [PubMed]
60. Sapolsky RM. Why zebras don't get ulcers: An updated guide to stress, stress-related diseases, and coping. New York: W.F. Freeman; 1998.
61. Simons DJ. Change blindness and visual memory. Visual Cognition. 2000;7:1–412.
62. Sjoberg RL, Ducci F, Barr CS, Newman TK, Dell'osso L, Virkkunen M, Goldman D. A non-additive interaction of a functional MAO-A VNTR and testosterone predicts antisocial behavior. Neuropsychopharmacology. 2008;33:425–430. [PMC free article] [PubMed]
63. Slotkin RK, Martienssen R. Transposable elements and the epigenetic regulation of the genome. Nature Reviews Genetics. 2007;8:272–285. [PubMed]
64. Stocking GW, editor. History of anthropology series. Madison, WI: University of Wisconsin Press; 1989–1999.
65. Sulloway FJ. Birth order, sibling competition, and human behavior. In: Holcomb HR, editor. Conceptual challenges in evolutionary psychology: Innovative research strategies. Boston: Kluwer Academic; 2001. pp. 39–83.
66. Suomi S. Early stress and adult emotional reactivity in rhesus monkeys. In: Bock G, Whelan J, editors. The childhood environment and adult disease. Chichester, NY: Wiley; 1991. pp. 171–188.
67. Taylor SE, Way BM, Welch WT, Hilmert CJ, Lehman BJ, Eisenberger NI. Early family environment, current adversity, the serotonin transporter promoter polymorphism, and depressive symptomatology. Biol Psychiatry. 2006;60:671–676. [PubMed]
68. Tomasello M. The human adaptation for culture. Annu Rev Anthropol. 1999;28:509–529.
69. Tsankova N, Renthal W, Kumar A, Nestler EJ. Epigenetic regulation in psychiatric disorders. Nature Reviews Neuroscience. 2007;8:355–367. [PubMed]
70. van de Vijver G, Speybroeck L, de Waele D. Epigenetics: A challenge for genetics, evolution, and development? Ann NY Acad Sci. 2002;981:1–6. [PubMed]
71. van IJzendoorn MH, Sagi A. Cross-cultural patterns of attachment: Universal and contextual dimensions. In: Cassidy J, Shaver PR, editors. Handbook of attachment: Theory, research, and clinical applications. London: Guilford Press; 1999. pp. 713–734.
72. Weaver ICG. Epigenetic programming by maternal behavior and pharmacological intervention. Nature versus nurture: Let's call the whole thing off. Epigenetics. 2007;2:22–28. [PubMed]

73. Weber BJ, Huettel SA. The neural substrates of probabilistic and intertemporal decision making. Brain Res. 2008;1234:104–115. [PMC free article] [PubMed]
74. Wendland JR, Lesch K-P, Newman TK, Timme A, Gachot-Neveu H, Thierry B, Suomi SJ. Differential functional variability of serotonin transporter and monoamine oxidase A genes in macaque species displaying contrasting levels of aggression-related behavior. Behav Genet. 2006;36:163–172. [PubMed]
75. Williams TD. Individual variation in endocrine systems: Moving beyond the 'tyranny of the golden mean' Philos Trans R Soc B-Biol Sci. 2008;363:1687–1698. [PMC free article] [PubMed]
76. Worthman CM. The epidemiology of human development. In: Panter-Brick C, Worthman CM, editors. Hormones, health, and behavior: A socio-ecological and lifespan perspective. Cambridge: Cambridge University Press; 1999. pp. 47–104.
77. Worthman CM. Energetics, sociality, and human reproduction: Life history theory in real life. In: Wachter KW, Bulatao RA, editors. Offspring: Human fertility behavior in biodemographic perspective. Washington, DC: National Academies Press; 2003. pp. 289–321.
78. Worthman CM, Brown RA. A biocultural life history approach to the developmental psychobiology of male aggression. In: Stoff DM, Susman EJ, editors. Developmental psychobiology of aggression.New York: Cambridge University Press; 2005. pp. 187–222.