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Pathways Linking Early Life Stress to Adult Health

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A Lifespan Model of Responses to Threat

Both animal and human investigations reveal that adult mental and physical health is rooted in early experiences with threat. Early life experience helps to shape psychological and biological reactions to stress that persist across the lifespan (e.g., Liu et al., 1997; Repetti, Taylor, & Seeman, 2002) and affects the likelihood of developing stress-related health disorders (e.g., McEwen, 1998). How these early life experiences are instantiated in enduring form has consequently been an important area for research, because it is not immediately obvious why experiences in the first few years of life would affect the likelihood of early-onset chronic illness often decades later.

To address this issue, some investigators have focused heavily on the vulnerability of developing biological stress regulatory systems to extreme, recurring, or prolonged stress (e.g., Cacioppo & Patrick, 2008; McEwen, 1998; Seeman, Singer, Horwitz, & McEwen, 1997). Others have focused more heavily on the development of psychosocial factors that regulate socioemotional responses to stress (e.g., Cacioppo & Patrick, 2008; Folkman & Moskowitz, 2004; Taylor & Stanton, 2007). Genetic contributions to mental and physical health across the lifespan have been increasingly explored (e.g., Caspi et al., 2002; Caspi et al., 2003). The potential importance of critical periods in development is becoming understood as well (Meaney, 2001).

In this article, we present a developmental model of responses to early life stress that integrates sociodemographic, genetic, psychosocial, neural, physiological, and health-related evidence concerning the pathways that may explain the often surprisingly strong relations between stress in early life and adult health. The schematic model that guides our analysis is

shown in Figure 1. We hasten to add that many other health psychologists and social neuroscientists adopt a similar model, but may emphasize somewhat different variables in the pathways to adult health. For example, Cacioppo and colleagues especially emphasize social support and loneliness (Cacioppo & Patrick, 2008), Matthews and colleagues emphasize the development of chronic emotional states and their adverse effects on health outcomes (Gallo & Matthews, 2003), and biological stress researchers focus on the accumulating damage to physiological systems (e.g., Seeman, McEwen, Rowe, & Singer, 2001).

In our approach (Figure 1), genetic predispositions and aspects of the early environment are represented as joint predictors of the ability to develop psychosocial resources. Early life stress is known to compromise: emotion regulation; coping skills; the ability to make effective use of social support; individual differences in psychological resources; and chronic negative emotional states. These psychosocial factors, in turn, influence and are influenced by neural responses to threat in the brain that regulate autonomic, neuroendocrine, and immune responses to threatening circumstances. The cumulative impact of these inputs ultimately influences health risks. In addition, there are direct paths from genes and the early environment to compromised physiological functioning that do not route through psychosocial resources.

As such, Figure 1 characterizes 1) a developmental model of stress-related health outcomes across the lifespan, 2) the metatheoretical perspective that has guided our work, and 3) the methodological procedures that have guided specific research investigations. Whether these are the primary variables and pathways linking early life experience to adult health outcomes remains to be determined by future research; at present, they represent our best efforts to identify pivotal variables. In the subsequent sections, we focus especially on our own research program, because it directly addresses the model in Figure 1.

Developmental Origins

Research indicates that health across the lifespan has origins in both early environmental and genetic factors. Low childhood socioeconomic status has been tied to a broad array of adult disorders, including depression, anxiety, coronary heart disease, cardiovascular disease, and immune-related disorders (e.g., Adler, Marmot, McEwen, & Stewart, 1999; Cohen, Doyle, Turner, Alper, & Skoner, 2004; Galobardes, Lynch, & Davey Smith, 2004; Galobardes, Smith, & Lynch, 2006; Hemingway et al., 2003; Hertzman, 1999) and all-cause mortality (Kittleson et al., 2006; Kuh, Hardy, Langenberg, Richards, & Wadsworth, 2002). Similar patterns are found when an early family environment is assessed directly. A harsh family upbringing has been related to depression (Repetti et al., 2002); to acute disorders, such as susceptibility to respiratory infections (Cohen et al., 2004); to risk factors for chronic disease, including compromised metabolic functioning (e.g., Lehman, Taylor, Kiefe, & Seeman, 2005), immunologic functioning (e.g., Taylor, Lehman, Kiefe, & Seeman, 2006), and elevated blood pressure (e.g., Lehman, Taylor, Kiefe, & Seeman, 2009); and to major mental and physical health disorders (e.g., Felitti et al., 1998).

As noted, a viable hypothesis as to why these relationships exist is that early stress compromises the functioning of biological stress regulatory systems. At the physiological level, stress-related changes in autonomic and neuroendocrine functioning include: 1) activation of the sympathetic nervous system, which leads to increases in heart rate and blood pressure, among other changes and 2) activation of the hypothalamic-pituitary-adrenal axis (HPA axis), which leads to the production of corticosteroids, including cortisol, which are necessary for energy mobilization (Sapolsky, 1993). 3) Stress inductions have also been associated with changes in

proinflammatory cytokine activity (e.g., Dickerson, Kemeny, Aziz, Kim, & Fahey, 2004), effects that may be driven, in part, by autonomic and HPA axis activity.

The theory of allostatic load (McEwen, 1998) maintains that stress, in conjunction with genetic risks, leads to a cascade of adverse biological changes that over time may erode the resiliency of stress systems, laying the groundwork for illness. Increasingly, researchers are identifying indicators of allostatic load that cumulatively enhance risk for disease (Seeman, McEwen, Rowe, & Singer, 2001; Seeman, Singer, Ryff, Dienberg Love, & Levy-Storms, 2002).

Genetic Antecedents

Genetic factors are implicated in stress reactivity both in their own right and in interaction with a stressful early environment. For example, genes involved in the development of stress systems, such as the glucocorticoid receptor gene, in conjunction with the early environment, play a lifelong role in stress responses (Meaney & Szyf, 2005; Miller & Chen, 2007). Genes in the opioid system, such as the μ opioid receptor gene, and genes in the oxytocin and vasopressin systems likely play roles in both stress regulation and the deployment of psychosocial resources (Way & Taylor, in press, for a review). Genetic factors that increase vulnerability to specific health disorders, such as diabetes, heart disease, or cancer, likely interact with stress processes to increase risk, precipitate acute events, or accelerate the course of existing health problems.

A harsh early environment contributes to lifespan risk for health disorders not only directly, but also via gene-environment interactions. For example, in rhesus monkeys, genetic variation in the promoter region of the serotonin transporter gene interacts with rearing environment to affect hypothalamic-pituitary-adrenal (HPA) axis responses to social stress (Barr et al., 2004). Specifically, reduced maternal interaction potentiatiates the stress response among

monkeys with a short allele and also increases aggressive behavior. Related effects have now been found in humans (Miller & Chen, 2007).

Risk for depression in humans is also affected by allelic variation in the promoter region of the serotonin transporter (5-HTTLPR) gene. Recent investigations have found that people carrying at least one copy of the short (s) allele of this gene are more at risk for depression, especially if they have grown up in an environment marked by maltreatment (see Caspi et al., 2003). In a recent investigation, we examined whether a supportive early environment might reverse this risk (Taylor, Way et al., 2006). Participants completed assessments of early family environment, recent stressful events, and depressive symptomatology. A gene-by-environment interaction was observed between the 5-HTTLPR and early family environment, such that people homozygous for the short allele (s/s) had greater depressive symptomatology if they had experienced early adversity but significantly less depressive symptomatology if they reported a supportive early environment, compared to people with s/l or the l/l genotypes. This study, then, provides exciting evidence that the beneficence of the early environment can actually reverse the effects of a genetic risk.

Genetic and early environmental factors contribute to aggressive as well as depressive responses to stress. The MAO-A genetic polymorphism has been linked to hostile, aggressive behavior toward others. People with low expression of MAO-A (MAOA-L) have been found to be more aggressive than those with high expression (MAOA-H), particularly when they come from an adverse early environment (e.g., Caspi et al., 2002). Exactly why has not been known. One possibility is that MAOA-L individuals are less socially sensitive and thus commit violent acts because they do not care about harming others or the repercussions of so doing. Alternatively, MAOA-L individuals may be more sensitive to negative social experiences and

respond to such episodes with defensively aggressive behavior (Blair, Peschardt, Budhani, Mitchell, & Pine, 2006).

To evaluate these alternative accounts, we examined how allelic variation in the promoter region of the MAOA gene related to (self-reported) aggression (e.g., "having the urge to harm someone"), interpersonal hypersensitivity (e.g., "feeling very self-conscious with others"), and neural responses to an episode of social exclusion in the scanner. During this fMRI task, the participant plays catch with two other (virtual) participants, but over time, is excluded from the play; this task has previously been found to produce psychological distress and corresponding activation in the dorsal anterior cingulate cortex (dACC) (Eisenberger, Lieberman, & Williams, 2003). MAOA-L individuals reported higher levels of trait aggression than MAOA-H individuals, consistent with prior research. MAOA-L individuals also reported greater trait interpersonal hypersensitivity and showed greater dACC activity to social rejection than MAOA-H individuals. These results suggest that the MAOA-L-aggression link is the result of heightened sensitivity to negative social experiences and not insensitivity.

Psychosocial Resources

Psychosocial resources are critical for regulating responses to threat and have been demonstrated to beneficially affect both mental and physical health. Four such resources that have been consistently tied to these benefits are optimism, mastery, self esteem, and social support.

Optimism refers to outcome expectancies that good things rather than bad things will happen to the self (Scheier, Weintraub, & Carver, 1986). It predicts greater psychological well-being (e.g., Scheier & Carver, 1992), lower vulnerability to infection (Cohen, Doyle, Turner, Alper, & Skoner, 2003; Segerstrom, Taylor, Kemeny, & Fahey, 1998), faster recovery from

illness (Scheier et al., 1989), and a slower course of advancing disease (Antoni & Goodkin, 1988) (see Carver & Scheier, 2002, for a review).

Personal control or mastery refers to whether a person feels able to control or influence his/her outcomes (Thompson, 1981). Studies have shown relationships between a sense of control and better psychological health (Rodin, Timko, & Harris, 1985; Taylor, Helgeson, Reed & Skokan, 1991) and better physical health outcomes, including lower incidence of coronary heart disease (CHD) (Karasek, Theorell, Schwartz, Pieper, & Alfredsson, 1982), better self-rated health, better functional status, and lower mortality (Seeman & Lewis, 1995).

A positive sense of self or high self-esteem is also protective against adverse mental and adverse health outcomes. For example, research consistently ties a positive sense of self to lower autonomic and cortisol responses to stress (e.g., Seeman & Lewis, 1995; Creswell, Welch, Taylor, Sherman, Gruenewald, & Mann, 2005). Ties to health outcomes are modest but consistently positive (Adler, Marmot, McEwen, & Stewart, 1999; Taylor & Seeman, 1999).

Social support is defined as the perception or experience that one is loved and cared for by others, esteemed and valued, and part of a social network of mutual assistance and obligations (Wills, 1991). Research consistently demonstrates that social support reduces negative affect during times of stress and promotes psychological adjustment to a broad array of chronically stressful conditions (see Cacioppo & Patrick, 2008; Taylor, 2009, for reviews). Social support also contributes to physical health and survival, and the impact of social ties on health is as powerful a predictor of health and longevity as well-established risk factors for chronic disease and mortality, including smoking, lipids, obesity, and physical activity (e.g., Berkman & Syme, 1979; House, Landis, & Umberson, 1988). Thus, each of these four constructs has robust and well-documented mental and physical health effects.

Psychosocial resources may represent a vital link from genes and early environment to health outcomes across the lifespan. It has long been suspected that psychosocial resources have genetic origins. For example, twin studies indicate that approximately 25% of the variance in optimism appears to be genetically-based (Plomin et al., 1992). Similarly, Kessler, Kendler, Heath, Neale, and Eaves (1992) reported a genetic basis for social support, which may reflect either the ability to perceive social support as available or the ability to make use of it or both. An early family environment marked by harsh or conflict-ridden parenting is reliably associated with deficits in offspring psychosocial resources as well (Repetti et al., 2002) and with difficulty in managing challenging circumstances (Brody & Flor, 1998; Dishion, 1990; Repetti et al., 2002). Substantial research links economic adversity (low SES) to problems in the enlistment or use of psychosocial resources (Adler, Marmot, McEwen, & Stewart, 1999; Repetti et al., 2002; Taylor & Seeman, 1999). Deficits in psychosocial resources related to early family environment may appear in latent form in early childhood and contribute to a propensity for chronic negative affect and to a lack of psychosocial resources in adulthood (Repetti et al., 2002).

Intense, chronic, or recurring biological responses to stress represents a downstream pathway by which psychosocial resources may exert adverse effects on health across the lifespan (Repetti et al., 2002; McEwen, 1998). For example, a lack of supportive contacts in early childhood has been tied to higher HPA axis responses to stressors in both children and adults (Gunnar, Larson, Hertsgaard, Harris, & Brodersen, 1992; Taylor et al., 2004).

Neural Regulation of Stress Responses

Is there neural evidence to connect psychosocial resources directly to the regulation of biological responses to stress? Eisenberger, Taylor, Gable, Hilmert, and Lieberman (2007) examined the neural pathways that may link the experience of social support to reduced

physiological reactivity. Specifically, we examined the relation of daily experiences of social support to neural responses to social threat in the brain and to autonomic and HPA axis responses to laboratory stressors indicative of social threat. Thirty participants completed a daily experience sampling procedure over a 9-day period that assessed and averaged their experiences of social support. At the end of this 9-day period, participants took part in an fMRI investigation of neural responses to threat, specifically, the virtual social rejection task described earlier (Eisenberger et al., 2003). At a third time point, participants went through the Trier Social Stress Task (TSST) to assess autonomic and neuroendocrine activity to social stressors (Kirschbaum, Pirke, & Hellhammer, 1993). (The TSST is a standardized, widely used laboratory stress challenge known to produce social-evaluative threat (Dickerson & Kemeny, 2004). People who reported that they interacted regularly with supportive individuals showed diminished dorsal anterior cingulate cortex (dACC) and Brodmann area (BA8) reactivity to social rejection in the fMRI task; both are regions implicated in responses to social threat. People with strong social support also showed diminished cortisol reactivity to the TSST. Most important, individual differences in dACC and BA8 activity mediated the relationship between social support and cortisol reactivity. The results imply that social support may influence downstream biological stress responses by modulating neurocognitive reactivity to social stressors, which, in turn, attenuates neuroendocrine stress responses.

Do other psychosocial resources operate via these pathways? Two brain structures, the amygdala and, as noted, the dorsal anterior cingulate cortex (dACC), are consistently associated with threat detection, serving an alarm function that mobilizes other neural regions, such as the lateral prefrontal cortex (LPFC) and hypothalamus, to promote adaptive responses to environmental threats (e.g., Hariri, Tessitore, Mattay, Fera, & Weinberger, 2002). Once

activated, these neural threat detectors set in motion a cascade of responses via projections to the hypothalamus and LPFC (Botvinick, Braver, Barch, Carter, & Cohen, 2000), aimed at amplifying or attenuating the threat signal and preparing to respond to the threat. A neural region that appears critical for regulating the magnitude of these threat responses is the VLPFC (Hariri, Bookheimer, & Mazziotta., 2000; Lieberman, Hariri, Jarcho, Eisenberger, & Bookheimer, 2005).

We examined the relation of individual differences in psychosocial resources to neural responses in these regions to threat cues (fearful and angry faces) and to HPA axis and cardiovascular responses to the TSST stress tasks (Taylor et al., 2008). Specifically, participants took part in an fMRI investigation that examined 1) amygdala reactivity to threat-relevant cues, specifically observation of fearful/angry faces 2) amygdala and right ventrolateral prefrontal cortex (RVLPFC) responses to labeling emotions displayed in these faces and 3) the relation between RVLPFC and amygdala activity during the labeling task. Previous research had found that the face observation task evokes amygdala activity, that the labeling task evokes RVLPFC activity, and that activity in the amygdala and RVLPFC are (typically) negatively correlated in the labeling task (suggesting that RVLPFC may be involved in the regulation of limbic responses to threat cues) (Lieberman et al., 2005; Lieberman et al., 2007). Participants then completed the TSST described earlier.

High levels of psychosocial resources (a composite of optimism, control, and self-esteem) were associated with greater right ventrolateral prefrontal cortex and less amygdala activity during the labeling task in the fMRI component of the investigation and to lower cortisol responses and lower blood pressure during the TSST. Mediational analyses suggest that the relation of psychosocial resources to low cortisol reactivity was mediated by lower amygdala activity during threat regulation (i.e., the labeling task). Results suggest that psychosocial

resources are associated with lower cortisol responses to stress by means of enhanced inhibition of threat responses during threat regulation, rather than by decreased sensitivity to threat.

Taken together, these two studies suggest that social support may modulate biological stress responses by reducing emotional reactivity, whereas trait assessments of psychosocial resources (such as optimism and self-esteem) may modulate stress responses by augmenting regulatory capacity to manage stress. Whether those different patterns are a function of the particular tasks and methods used or whether they indicate that different psychosocial resources affect stress regulation in different ways remains to be seen.

Coping with Threat

Early environment, genetic factors, and psychosocial resources affect the coping processes that people use to manage stressful events. Coping processes include both actions taken (or not) to deal with stressors, as well as the regulation of emotional responses to threat. Although several frameworks for delineating coping processes have been advanced (see Skinner, Edge, Altman, & Sherwood, 2003, for a review), a particularly useful distinction is that between approach and avoidance coping. Reflecting a core motivational construct (e.g., Davidson, Jackson, & Kalin, 2000), the approach-avoidance continuum maps easily onto broader theories of biobehavioral functioning. Approach-related coping includes problem solving, seeking social support, and creating outlets for emotional expression. Coping through avoidance include both cognitive and behavioral strategies designed to tune out the implications of a stressor. For the most part, research suggests beneficial effects of approach coping and adverse effects of avoidant coping, although there are qualifications based on type and timing of stressor (e.g., Folkman & Moskowitz, 2004; Taylor & Stanton, 2007). Approach coping strategies have been reliably tied to positive affect and to beneficial health outcomes (Taylor & Stanton, 2007). Attempting to

avoid thoughts and feelings regarding stressors predicts elevated distress, physical health outcomes, chronic disease progression, and mortality (See Taylor & Stanton, 2007, for a review).

Research links a harsh family environment to the use of maladaptive coping strategies. Specifically, offspring from harsh family environments appear to overreact to threatening circumstances, responding aggressively to situations that are only modestly stressful (Reid & Crusafulli, 1990), but may also respond by tuning out or avoiding stressful circumstances when they can, as through behavioral escape/avoidance or substance abuse (e.g., O'Brien, Margolin, John, & Krueger, 1991). Genetic factors are also implicated in the propensity to use certain coping strategies. Using twin study methodology, behavioral genetics investigations have estimated moderate genetic contributions to problem solving, emotion-focused coping, use of social support, and avoidant coping, (e.g., Kato & Pedersen, 2005; Kendler, Kessler, Heath, Neale, & Eaves, 1991). Both shared and unshared environmental factors appear to contribute to these effects (Mellins, Gatz, & Baker, 1996).

Can poor coping resulting from a non-nurturant early environment be linked directly to the neural regulation of stress responses? To examine potential neural concomitants of coping deficits, we (Taylor, Eisenberger, Saxbe, Lehman, & Lieberman, 2006) explored neural reactivity to tasks involving threat detection and regulation of responses to emotional stimuli. Participants completed an assessment of early family environment (Taylor et al., 2004) and then completed the fearful faces task described earlier. Offspring from nurturant families showed expected amygdala reactivity to observing fearful/angry faces and expected activation of RVLPFC while labeling the emotions in the faces. Activity in these two regions was significantly negatively correlated, as expected. This pattern suggests that RVLPFC was effective in regulating emotional responses to the tasks. Offspring from harsh families, however,

showed little amygdala activation during the observation task, a strong amygdala response to the labeling task, and a strong positive correlation between RVLPFC and amygdala activation in the labeling task (Taylor et al., 2006). These patterns suggest potential dysregulation in the neural systems involved in regulating responses to threat.

Specifically, it appears that during the task that normally activates amygdala activity, participants from harsh families may instead have been tuning out the threatening stimuli, but when forced to confront the threatening stimuli in the labeling task, unexpectedly high amygdala activity was seen. Moreover, it appears that offspring from harsh families did not recruit RVLPFC effectively for regulating amygdala responses to threatening stimuli, given the strong positive correlation between amygdala and RVLPFC responses to the tasks. Thus, offspring from harsh families appear to experience deficits in threat detection and coping responses to emotional stimuli that are evident at the neural level. These processes, in turn, have downstream effects on autonomic, neuroendocrine, and immune responses to stress.

Autonomic, Neuroendocrine, and Immune Responses to Stress

As Figure 1 and the research described indicates, genetic factors, early environment, psychosocial resources, and neural and coping responses to threat have downstream effects on autonomic, neuroendocrine and immune responses to threat. These responses may represent the proximal contributors to both acute health disorders and, cumulatively, to chronic health conditions. Studies have shown connections between neural structures critical to threat detection and the hypothalamus, the origin of both sympathetic and neuroendocrine responses to threat. The amygdala has dense projections to the hypothalamus (Ghashghaei & Barbas, 2002), and the ACC projects to the paraventricular nucleus of the hypothalamus (PVN; Risold, Thompson, & Swanson, 1997), the specific region of the hypothalamus that triggers the cascade of events

ultimately leading to cortisol release. Stimulation of both the amygdala and the ACC has also been associated with increases in blood pressure and cortisol levels in both animals and humans (e.g., Frankel, Jenkins, & Wright, 1978; Pool, 1954; Setekliev, Skaug, & Kaada, 1961). Stress-induced proinflammatory cytokine activity (including interleukin-6 (IL-6) and tumor necrosis factor alpha (sTNFαRII)) are also implicated (Maier & Watkins, 1998).

We related aspects of the early family environment to autonomic and neuroendocrine responses to stress directly (Taylor, Lerner, Sage, Lehman, & Seeman, 2004). Young adults completed measures of early environment and participated in laboratory stress tasks. We found a strong relationship between childhood SES and a harsh family environment. Low childhood SES and harsh family environment were, in turn, related to an elevated and flat trajectory of cortisol across the stress tasks. For males only, those from the most harsh family environments had elevated heart rate and blood pressure during the challenges and throughout the post-challenge recovery. Because risk factors for CHD and CVD frequently show up earlier in life for males than females (Allen, Matthews, & Sherman, 1997), the fact that the results were significant only for males is not surprising. The model also significantly predicted self-rated health. This study, then, suggests that a legacy of having grown up in a harsh early environment includes the propensity to respond to new stressors with stronger biological threat responses.

Although stress-related multi-system changes such as these are protective in the short term, their chronic activation may negatively affect mental health over time, potentially elevating risk for depression and anxiety disorders and also enhancing risks for physical illnesses, including cardiovascular disease and Type II diabetes (e.g., Kiecolt-Glaser, McGuire, Robles, & Glaser, 2002; Seeman et al., 1997 for reviews).

Relating the Model to Risk Factors for Disease

Evidence linking variables in the model to specific health outcomes is substantial. Childhood SES (Cohen, Doyle, Turner, Alper, & Skoner, 2004; Galobardes, Lynch, & Davey Smith, 2004; Galobardes, Smith, & Lynch, 2006) and a harsh family environment (Repetti, Taylor, & Saxbe, 2007) have both been related to a broad array of risk factors for cardiovascular disease, immune-related disorders (e.g., Miller & Chen, 2007), diabetes, and some cancers. Chronic negative affect, especially hostility and depression, are tied to hypertension and CHD (Gallo & Matthews, 2003). Social support and social isolation have profound effects on all-cause mortality and risk of and progression of many chronic disorders (Cacioppo & Patrick, 2008). Individual differences of optimism, mastery, and self-esteem have been tied to health-related outcomes, which, in turn, been related to mental and physical health-related outcomes (e.g., Felitti et al., 1998).

This section highlights three specific examples from our laboratory that address (much of) the model detailed in Figure 1, specifically, early environment, social support, chronic negative affect, and health outcomes. In collaboration with investigators from the Coronary Artery Risk Factors in Young Adults investigation (CARDIA), we (Lehman, Taylor, Kiefe, & Seeman, 2005) used structural equation modeling to explore the relation of the model (Fig. 1) to metabolic functioning, which is a composite risk factor for diabetes, coronary artery disease, and several other chronic health conditions. Participants (N=3,225) completed our assessment of early family environment and participated in a physical exam that assessed cholesterol, insulin, glucose, triglycerides, and waist circumference (as indicators of metabolic functioning). Structural equation modeling indicated that low childhood SES and a harsh early family environment were associated with dysregulation in metabolic functioning via association with poor psychosocial resources and chronic negative affect, consistent with the model.

A second study assessed whether the model contributed to elevated C-reactive protein, a marker of inflammation and a risk factor for both mental (e.g., depression) and physical (e.g., heart disease) disorders in adulthood. Structural equation modeling supported a model whereby low SES and a harsh early environment contributed to elevated C-reactive protein via pathways involving poor psychosocial resources, chronic negative affect, and high body mass index (i.e., obesity). A third investigation explored the viability of the model for explaining variability in blood pressure as well as change in blood pressure over time (Lehman, Taylor, Kiefe, & Seeman, 2009). Again, the model was a good fit. Although the psychosocial variables included in these three tests of the model were restricted to chronic negative emotional states and social support, the results are encouraging evidence for pathways linking early environment through psychosocial variables to health outcomes.

Conclusions and Unresolved Issues

The picture of how genes and the early environment contribute to health risks via pathways implicating psychosocial resources, coping, and the neural regulation of stress responses is sketchy. Several directions for future work are evident. A first issue concerns the role of stress in the model. The guiding framework places a heavy burden on stress processes as a primary vehicle linking early environment, genes, and psychosocial resources to health risks. Is the damage actually done primarily during stressful times? Does damage accelerate as biological stress regulatory systems are compromised? Is the damage reversible? Answers to these questions are currently unknown.

Second, the guiding framework offered in this article is still evolving, and additional probable direct paths and feedback loops are not pictured. For example, environmental factors influence neural and endocrine functioning directly, as well as through psychosocial resources.

Stress hormones, cytokine responses, and environmental factors influence genetic expression. Thus, further research will add refinements, specificity, and complexity to the model.

At present, the model is a generic one that can be applied, albeit imprecisely, to a broad array of antecedents. As the specific genetic and experiential precursors of specific health disorders become increasingly well understood, it will be possible to build disease-specific models that integrate these multiple levels of analysis.

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Authors' Notes

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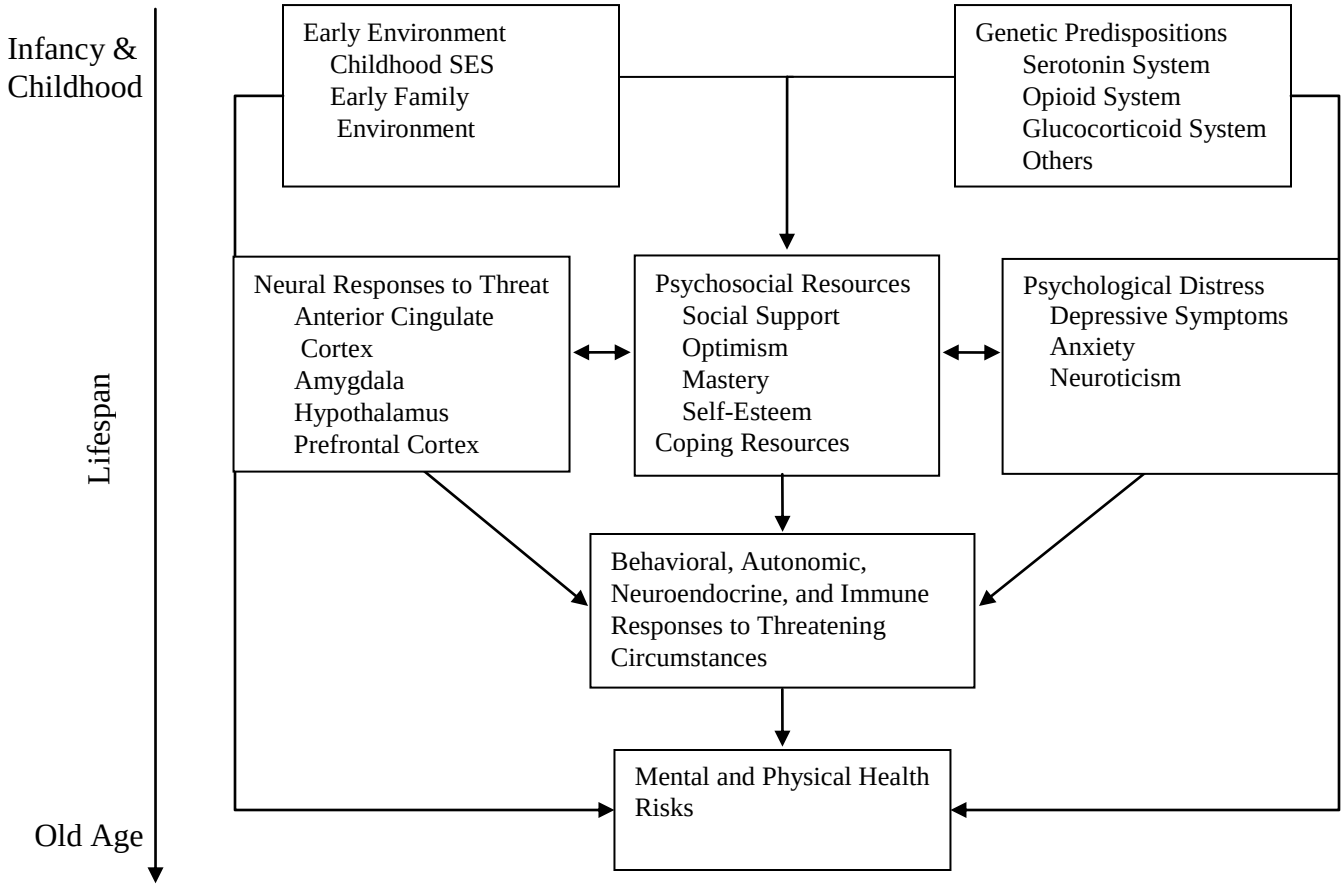
Figure Captions

Figure 1. A lifespan model of how early environment contributes to adult health risks.


Infancy &
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Opioid System
Glucocorticoid System
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Neural Responses to Threat
Anterior Cingulate
Cortex
Amygdala
Hypothalamus
Prefrontal Cortex
Psychosocial Resources
Social Support
Optimism
Mastery
Self-Esteem
Coping Resources
Psychological Distress
Depressive Symptoms
Anxiety
Neuroticism
Behavioral, Autonomic,
Neuroendocrine, and Immune
Responses to Threatening
Circumstances
Mental and Physical Health
Risks