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Early Life Stress, Physiologic Reactivity, and the Development of Control

By

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B.S. (Stanford University) 2001

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Early Life Stress, Physiologic Reactivity, and the Development of Control

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By Miranda Bik-Yin Ip

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CHAPTER 1:

A Review of the Control and Physiologic Reactivity Literature

Introduction

A widely established principle in health psychology is that stress can be a potential contributor to disease etiology [1]. Of the many factors implicated in stress, sense of control may be especially important among the psychological variables, whereas biologic reactivity may be particularly important among the physiological variables. Traditionally, stress research has examined these two factors independently of one another, and they each have been linked to various health outcomes, behavioral problems, and coping strategies. Both have been suggested to function as main effects, mediators, or moderators of various psychosocial factors. Despite the massive accumulation of data, there is still limited evidence for how these two aspects of the stress response may be related. Indeed, as knowledge about these two fields and their relationship to illness and behavior has moved deeper into their own respective definitions, constructs and mechanisms, our understanding of the psychological components of the stress response have now become largely divorced from our understanding of the physiological markers of the stress response. Reconnecting these conceptually distinct fields of research may highlight some important concepts for future public health interventions and clinical treatment strategies.

Control: basic definitions

Fundamentally, control is a desire to shape outcomes and make decisions and arises out of a human need to be a causal agent in the environment [2]. Control has been defined and operationalized in a variety of ways, either by emphasizing the behavioral outcomes, the emotional and cognitive processes involved, or the social and cultural circumstances that shape the way choices are made. Stress researchers have long been interested in this concept and have amassed significant data on how the controllability or perceived controllability of a stressful event affects coping styles, physiological reactions, and subsequent health and health behaviors. In health psychology, control has commonly been viewed as one key dimension of coping. Of all the psychological responses to stress within the human repertoire, a desire for a sense of control is invoked as the most common strategy for ending both the anxiety associated with a stressful event and the actual stressor itself.

There are many constructs related to control, and it will be useful to understand how they have been defined and used in prior research.¹ The numerous definitions that exist reflect the various ways researchers use and understand control. Some researchers recognize that individuals have the capacity to both control external events and internal processes. *Primary* and *secondary control* thus refer to a distinction between these two types of control [3], where primary control is the attempt to change objective conditions

¹ Control has been constructed in a variety of ways which will be discussed, but for the purposes of this paper, sense of control or control will refer to a combination of: 1) the confidence in one's ability to effect outcomes, 2) the ability to judge the contingency of an outcome, as well as 3) the intrinsic motivation and effort one musters to meet the demands of a task. This will be the definition used when describing developmental aspects of control, its hypothesized relationship to reactivity, and its general applications in future research.

as a way of solving problems and secondary control is the attempt to moderate the effect of those objective conditions on internal states. Primary control is sometimes referred to as problem-focused coping [4] and can involve a variety of strategies such as exerting effort, persisting, or changing one's approach. Secondary control is sometimes referred to as emotional-focused coping [4] and can involve psychological techniques such as accepting personal limitations, downgrading expectations, and changing the value of one's goals. More specific classes of secondary control have recently been outlined, including *selective secondary control*, which involves increasing the value of a goal to enhance one's focus and prevent distractions, and *compensatory secondary control*, which involves disengaging from one's goals and using self-protective causal attributions to buffer against the negative effects of failure or loss [5].

Much of the work in developmental psychology has shaped these definitions of primary and secondary control. Weisz's research suggest that primary control develops first and may even be present at birth [6]. Secondary control strategies emerge later in development as a function of cognitive maturation. As children learn that there is much more about the world that is beyond their control and learn about the internal world of others' thoughts and feelings, secondary control is used more often to cope with everyday stress [4]. However, younger children, not yet able to recognize that one way to deal with problems is to attempt to regulate their own thoughts, have no other option but to deal with the world directly.

Primary control and secondary control also seem to be related to health status through the life course. One study by Chipperfield and others shows that primary control strategies have more positive health implications in those aged 65-79 than in those aged

80 years or older [7]. In the older-old age group, those who employed secondary control strategies more frequently had better health status than peers in the same age group who used primary control strategies. Such findings suggest that primary control strategies are suited to the younger-old who possess the physical capacity to attain their goals, whereas secondary control strategies may be more adaptive for the older-old when goals are harder to achieve via direct physical manipulation of their environment or circumstances. Thus, both primary and secondary control both play adaptive roles throughout the life course in the appropriate social and physical context.

Other definitions of control recognize that the division between internal psychological states and external events is not so necessarily distinct. *Perceived control* has been defined as the expectation of having the power to participate in decision making in order to obtain a desirable outcome (an external event) and a sense of personal competence (an internal process) [2]. Perceived control, which is specific to a particular situation, is different from objective control and may be just as important, if not more important, than an individual's objective control over a situation. Usually there is not enough information available in the environment to make an objective assessment of a situation's controllability. Subsequently, individuals rely on their perception of control. Perceived control has been suggested to be a characteristic of adaptive human functioning: studies have shown that depressed people may have more accurate and realistic perceptions of personal control [8], indicating that perceptions of control, even when control is not objectively or entirely possible, may serve as a psychological buffer against the deleterious effects of negative cognitive-emotional states.

Related to this construct is *self-efficacy*. Developed by Bandura and colleagues, self-efficacy is an individual's belief in her capabilities to exercise control over her own motivations, behaviors, and environmental demands [9]. Four principles underlie the development of self-efficacy: direct performance accomplishments, vicarious experience, verbal persuasion, and physiological states. Experiences of success in all four realms help develop a greater sense of self-efficacy, whereas failures undermine it. Self-efficacy, in turn, can determine how much effort an individual will expend and how long she will persist in a behavior to overcome an aversive experience or challenge: the stronger the perceived efficacy, the greater or more active the effort.

Another related concept is *locus of control*, which was developed by Rotter and describes a global orientation to sense of control [10]. Individuals with an internal locus of control have the general belief that events are contingent upon one's own behavior. Individuals with an external locus of control believe that events are not contingent upon one's own actions but upon luck, fate, chance, etc. Unlike self-efficacy or perceptions of control, which are task- and situation-specific, locus of control is considered more of a global dispositional feature, stable over time like a personality trait. Locus of control has been widely used in health-related research and has often been considered a mediating factor between the health-related actions that individuals may pursue and cardiovascular health, myocardial infarction recovery, job strain, and other health outcomes.

A looser, more broadly defined construct than control that has also been used is Antonovsky's *sense of coherence*. Like loci of control, sense of coherence is defined as a general global characteristic, and it refers to the extent to which an individual has a pervasive, enduring though dynamic feeling of confidence that his internal and external

environments are predictable and that there is a high probability that things will work out [11]. Antonovsky's sense of coherence has been used in various studies as a predictor of psychosocial well-being in older adults, of diabetes management, of sickness absences, and has oftentimes been used as a marker of psychological well-being and adaptive coping [12].

Learned helplessness is another construct used to describe the sense of a complete lack of control. Experiments by Seligman with dogs undergoing uncontrollable shock demonstrated that dogs exposed to electric shock without any ability to control the shock and without any forewarning exhibited greater fear and anxiety [13]. These dogs eventually developed the expectation that their responses were independent of the aversive outcomes. They were then less able to learn to respond correctly in similar situations. Since then, studies in humans have shown that learned helplessness comes about after an individual develops the expectation that his actions have no consequence on his experiences and outcomes [14].

These various ways of defining control have been useful in understanding how it can possibly affect health outcomes. The process by which a sense of control exerts an effect on emotions, behavior and physiology has been hypothesized to operate through the process of *cognitive appraisals*. Folkman and Lazarus describe cognitive appraisals as a cognitive system for coping with stress [15]. In this two-step process, an individual first makes the primary appraisal of recognizing a threat, then secondly performs a complex evaluative process that reviews the available coping responses, evaluates a plan, and examines the potential costs and benefits of executing the plan. The primary appraisal comes in three forms: the first two, irrelevant and benign-positive, do not

require the initiation of a secondary appraisal process. Irrelevant suggests the encounter will either be irrelevant to the person's well-being, have no value or require no commitment from the individual, and benign-positive suggests the event will lead to a positive outcome. The third type of appraisal, the threat appraisal, does lead to a secondary appraisal. In threat appraisals, the individual can either anticipate an encounter to be one that will lead to harm or loss (harm appraisal), or the encounter may be construed more positively as a challenge (challenge appraisal) that can lead to the potential for gain or growth. Together, both primary and secondary appraisals shape the degree, strength, and content of an emotional reaction and coping response to a situation.

Folkman and Lazarus further suggest that challenge appraisals are more likely to occur than harm/loss appraisals when the individual has a sense of control over the situation. Beliefs about personal control—"feelings of mastery and self-confidence" [15] and the extent to which an individual feels she can control events and outcomes of importance—have the greatest influence over the appraisal process when the situation is ambiguous and novel. In other words, the less familiar the situation or the less information an individual has in a situation, the more her appraisal processes will be shaped by her sense of self-efficacy, perceived control, or a general sense of control. Thus, Folkman and Lazarus view cognitive appraisals as a process that incorporates self-efficacy, perceived control and other sense of control constructs that operate within particular situations or specific contexts.

One item to note, however, is that challenge appraisals will not occur if what must be accomplished does not require great effort. Effort of response has from early on been recognized as an important aspect of control [16]. However, while the cognitive

appraisal model suggests the lack of control and subsequent threat appraisal will generate a greater effort from the individual, the self-efficacy model posits that a greater sense of control—high self-efficacy—will lead an individual to invest a greater effort of responding. The findings on this will be discussed later in this paper.

Collectively, these definitions capture the dynamic quality of control as a construct that involves both the external effort to produce a desired outcome on the environment and also the internal cognitive capacity to moderate the psychological impact of a situation. However, another issue in the definition of control is whether or not it is a property of the individual or the situation [17]. On the one hand, control can reflect an individual's both internal and external capacity (or need) for shaping outcomes, and yet, on another, control may reflect the objective reality of his socioeconomic or cultural circumstances. Ann Foner points out the various ways in which social constraints limit individual autonomy and decision-making. She gives the example of the working mother: holding the multiple roles of homemaker and breadwinner may restrict her autonomy to perform some responsibilities to the extent she might wish [18]. Social networks, while sometimes enabling, can also be a restriction on the choices an individual can make. Jason DeParle, in a New York Times Magazine article points to the fact that the lack of fathers in inner-city black communities limits young boys' job networks. Furthermore, black males in the community have a narrow range of role models to choose from: rapper or drug dealer are the most appealing, the former being highly unattainable and the latter all too easily attainable [19]. Work by Dannefer supports the notion that disadvantages such as these accumulate over the life course and

those starting out at lower rungs of the SES ladder do not have the same freedom to make decisions about careers and institutional associations as those at higher levels [19].

Thus there exists a continuing debate over whether control reflects a quality of individuals or refers to an external availability of opportunities to exercise latitude and control. Still, other researchers suggest that control ought to encompass both, as Peterson has pleaded: "...it refers to the *relationship* between a person and his or her world, and isn't this the sophistication that all theorists eventually call for in the social sciences?" [20].

In sum, control can be understood as an orchestration of behaviors, coping activities, and physiological states that arises from cognitive-emotional processes and is influenced by external circumstances. Control is typically called upon in the event of a stressor and it is recognized as an important psychological component of coping. Although embracing a holistic definition of control, as Peterson suggests, is ultimately the most attractive option, understanding the more exacting definitions will serve us better in the later pages of this paper.

Origins and developmental aspects of control

Developmental psychology has taken on a great interest in how infants and children come to understand the personal significance of social interactions and events that lead to the development of certain control beliefs. Before a sense of control can be established, young infants must first acquire a sense of personal agency through understanding that environmental events can be the outcome of personally controlled actions. Action-outcome contingencies are initially affected by infants' exercise of

influence over their physical environment [21]. Children become more competent when parents are more responsive and when infant capabilities elicit greater parental responsiveness [2].

In exploring the ontogeny of control, John Weisz has recognized two distinct and important issues—the contingency of outcomes and personal competence [3]. One component of control is recognizing and accurately judging the contingent outcomes of an event. Furthermore, children need to develop a sense of the degree of contingency to expect from an event, ranging from high contingency events such as pushing a glass of water off a table and watching the glass break, to low contingency events, such as entering a state lottery and expecting to win. In studying school success, Skinner found that young children who have positive control beliefs experienced a high and consistent contingency between their actions and their successes [22].

Indeed, a large body of evidence supports the importance of early life experiences, which allow infants and children to learn about action-outcome contingencies. Children's expectancies of success from their actions are influenced in part by perceptions of caretaker (and other people's) attitudes and expectations for them [23]. Bandura suggested a similar framework for the development of self-efficacy beliefs: infants learn that they can influence and control their environment through experiences provided by parents and others that give them the chance to immediately control physical activities. Bandura further points out that self-efficacy cannot develop until children first gain a rudimentary self-concept and can distinguish the self as an individual. Gradually with age, children come to understand which types of events are high contingency and which are not.

The other component of control, personal competence, is an individual's capacity to manifest the behavior needed to bring about a contingent event [3]. Research in school underachievement, test anxiety and learned helplessness has also revealed that children who believe they can control their achievement outcomes feel more competent [6]. As in the case with contingency, children need to reach certain developmental milestones before competency is fully attained and accurately judged [24]. Factors such as direct and vicarious experience, the ability to take perspectives outside of oneself [25] and even affective state [26] all contribute to the development of competence.

There are other theoretical frameworks for how the family environment influences control beliefs. Antonovsky's sense of coherence model identifies four contributory characteristics of an individual's early life environment that help shape one's sense of coherence: 1) *consistency*, or clear rules and regulations and authority figures, 2) *load balance*, the extent to which demands are made beyond an individual's resources and family coping resources, 3) *autonomy*, or participation in shaping outcomes and having appropriate opportunities to learn about decision-making, and 4) *emotional closeness and a sense of belonging* to and being important within a family [11]. One retrospective study using semi-structured life history interviews explored the importance of these four factors in shaping sense of coherence and determined that the most relevant childhood experience contributing to sense of coherence was participation in shaping outcomes [27]. Again, this suggests that opportunities to make decisions, influence events, and learn from them, are important in shaping control beliefs.

The Perry Preschool Project provides the most compelling evidence to date on the importance of engaging children in play activities from which they can learn about

making choices and solving problems [28]. 123 children from lower SES families who were considered at high risk for failing in school were randomly assigned into either a group that received a high-quality preschool program or no preschool program. Data was collected on the cohort at various ages up into adulthood. Results showed that children in the preschool program group acquired a significantly higher level of schooling than did the no-program group, outperformed the no-program group on intellectual and language tests, reported better paying jobs, and averaged fewer arrests and crime-related activities than the no-program group. The causal model for this data suggests that the structured preschool experience improved their performance at school entry, which in turn improved their self-efficacy and motivation to perform well. The preschool activities involved having teachers who helped the children identify interest areas, who helped them maintain daily routines that allowed them to plan, execute and review their play activities, and who asked appropriate questions that helped them extend their thinking about their activities. Generally, this study and others provide critical evidence for the pivotal role that early education plays in fostering success. At a more fundamental level, the Perry Preschool Project demonstrates how early life experiences in making decisions and solving problems helps to shape individuals' sense of control.

A number of risk factors have been identified in the early family environment that lead to poor processing, control and regulation of emotions. A review by Repetti and colleagues [29] points out that high levels of conflict in the home sensitize children to anger, and children reared in these homes are found to react with greater distress, anxiety, anger and fear in novel situations. It has also been suggested that families with high negative affect engage in fewer conversations about emotions and emotional processing.

Evidence for this has been found in studies of abused children and children whose homes are marked by high levels of anger and distress: children from such backgrounds demonstrate a less accurate understanding of emotions compared to their peers. Work by Gottman and colleagues has suggested that parenting styles that encourage discussion of emotions and emotional-processing—coined a “meta-emotional philosophy” of parenting—have a significant influence on emotional and behavioral control in children [30]. Such meta-emotional parenting styles may be part of the experience children require to learn sufficient secondary control strategies. Repetti et al. also identify different developmental periods within which control beliefs may begin to take place: in infancy, insecure parent-child attachments have been associated with a wide array of maladaptive behaviors, and in adolescence, growing up in angry and aggressive homes has been associated with escape-type coping styles—these adolescents gradually abandon efforts to control difficult situations and focus instead on trying to escape them.

Non-human primate behavior studies have provided further evidence for the importance of early life experiences in shaping control beliefs, self-efficacy and mastery motivation. Studies by Champoux and colleagues of peer-reared infant macaques demonstrate that by giving subjects continuous opportunities to control their physical environment, they exhibit less reactive behavior in novel environments [31, 32]. “Master” subjects were given access to “operant manipulanda”—an apparatus that allows individual macaques direct control over treat delivery—whereas yoked subjects had no control over treat delivery and only received treats when their “master” partner pressed the lever to deliver the treat. Subjects’ reactions to a novel environment were tested and

“master” subjects were found to have more exploratory and fewer anxious behaviors than yoked subjects.

Other animal studies have provided evidence for the fact that controllability has profound consequences on health outcomes, despite limited evidence for its mechanism. In yoked-control studies of rats, Weiss and colleagues put groups of three rats into shock chambers: one animal served as an unshocked control, while the second animal was yoked to a third animal, who either received a warning tone or had the ability to prevent the shock by pressing a bar [14]. The second rat had no ability to control shock delivery, and received the shock whenever the third animal received one. The experiment demonstrated that rats given a warning tone before the impending shock had significantly fewer stomach ulcers than the yoked no-control rats. Giving the rats the option of preventing the shock further reduced the incidence of ulcers in the forewarned/controlling rat, but not in the yoked no-control rats.

Biologic reactivity: Basic Definitions

While the psychological construct of control has been widely conceived of as either a predictor of health and stress-coping behaviors or as a mediator between coping and health, biologic reactivity has been conceived of more as a marker for the physiological response we have to acute stressors. Reactivity has been operationalized as the difference between baseline arousal and stress-induced arousal; more specifically, it has been defined as the deviation of a physiological response parameter from a control value that results in an individual's response to an environmental stimulus [33]. It is quantified by measurable aspects of neuroendocrine and autonomic activation in response

to stressors, which in turn, mobilize metabolic resources to support fight/flight activities. However, since contemporary society provides few opportunities for true flight/flight responses, these autonomic and neuroendocrine responses to acute psychological stressors substantially exceed our metabolic requirements [34]. Given that the metabolic requirements posed by psychological stressors are relatively minimal, the differential responses that individuals exhibit towards stress may reveal possible underlying physiologic mechanisms for the effects of stress on health.

Much of the work on reactivity has been shaped by McEwen and colleagues' concept of *allostasis*. While homeostasis refers to an organism's ability to maintain physiological and behavioral stability in fluctuating environmental conditions, allostasis refers to an organism's achievement of stability through *change* [35]. It involves a continual process of minute-by-minute adaptation of multiple physiological systems to meet the demands of the internal and external environment, and it implies that "set points" and other such equilibrium states are constantly changing. *Allostatic load* is the cumulative process of allostasis and has been thought of as the "wear and tear" imparted on the body due to chronic physiological activation from frequent stress [36]. Constant or intensified exposure to unpredictable events, such as human disease, conflict, and other forms of psychosocial distress, can increase allostatic load. The consequence of carrying a high allostatic load is increased susceptibility to disease.

Reactivity may be a quantifiable measure of allostatic load in stress research. Its primary mediators include hormones of the hypothalamic-pituitary-adrenal (HPA) axis, catecholamines of the sympathetic-adrenal-medullary (SAM) axis, and the cells, cytokines and other inflammatory markers of the immune system. The two most

commonly studied systems of the stress response are HPA axis and the sympathetic division of the autonomic nervous system [35]. The most important feature of these mediators of reactivity to the concept of allostasis is their ability for both short-term protection and long-term damage. For example: glucocorticoids, the quintessential “stress hormone” released by the adrenal glands, help promote the immediate metabolic needs of the stress response by signaling for the conversion of protein and lipids into glucose, as well as initiating gluconeogenesis and blocking the action of insulin in peripheral tissues to prevent glucose uptake. Glucocorticoids also act on the brain to stimulate food-seeking behavior and increase appetite [37]. However, over long periods of time, chronic activation of glucocorticoids and chronically elevated glucose levels lead to the elevation of insulin levels. In combination, high insulin, glucose, and glucocorticoid levels leads to the deposition of body fat, the promotion of atherosclerosis, and hyperglycemia that can develop into diabetes mellitus. Glucocorticoids also have damaging effects in the hippocampus, which plays an important role in contextual memory, causing atrophy of dendrites and eventual neuron death [36, 38]. Thus, while allostatic mechanisms to sustain physiologic and behavioral activities in the face of stressful events are helpful in the short-run, continual activation of these systems are damaging over the long-run.

Reactivity has been useful for studying autonomic, endocrine and immune responses to stressors, where the same stressor can have profoundly different effects on physiological activation across individuals or across life circumstances. Large individual differences in reactivity have been found in animal models [39-41], adults [34] and children [42, 43]. These individual differences may serve both protective and harmful

purposes depending on context [33]. Highly reactive phenotypes are characterized by larger quantitative changes from baseline values in heart rate, blood pressure, cortisol levels, cytokine levels, and other reactivity measurements during stressful events. Low reactive phenotypes are characterized by less dramatic changes in these values. Most often, reactivity has been used as a marker to identify individuals with increased risk of cardiovascular disease [44], and increasingly, it has been associated with susceptibility to infectious disease and respiratory illness [42, 45] and with internalizing and externalizing behaviors and other psychological symptoms [43].

Origins and developmental aspects of reactivity

Researchers have suggested a number of psychological and biological pathways lead to reactivity differences among individuals. Lovallo and Gerin have identified three pathways that give rise to differences in reactivity, two of which suggest physiological and anatomical differences in brain structure, neurochemistry, and peripheral tissues, and one of which suggests differences at the cognitive-emotional level [44]. For the latter pathway, Lovallo and Gerin use temperament theory to explain how individuals integrate perceptions, cognitive evaluations, and affective responses to produce habitual stress response styles that are linked to individuals' reactivity profiles. While the authors do not suggest that cognitive-emotional functions are in and of themselves potential causes of disease, they do point out that because temperament theory has a strong biological basis, it may also be related to the origins of reactivity differences, which are, in turn, linked to potential disease outcomes.

Several animal studies point to the fact that temperament and stress reactivity differences are rooted in differences in early life experiences. Meaney and colleagues found that rat pups raised by mothers who engage in significant nurturing activities in the first ten days of life were less fearful and had reduced stress reactions compared to rats raised by non-nurturing mothers [39]. The nurtured rats were then later found to be nurturing mothers themselves. Another study by Meaney further consolidated evidence for the nongenomic behavioral transmission of individual differences in stress reactivity. In an experiment where offspring of low-nurturing rat mothers were cross-fostered to high-nurturing rat mothers and offspring of high-nurturing mothers were cross-fostered to low-nurturing mothers [40], the pups raised by high-nurturing mothers were significantly less fearful under conditions of novelty compared to the pups raised by low-nurturing mothers, including the biological offspring of high-nurturing mothers. The effects of maternal care also have profound and permanent effects on biology: the offspring of high-nurturing rats had increased benzodiazepine receptor density in the amygdala, increased α_2 adrenoreceptor density in the locus ceruleus, and decreased corticotropin-releasing hormone (CRH) receptor density in the locus ceruleus [39].

Other neuroanatomical features of the stress response system have been found to be influenced by repeated stress and other factors within early life. A review by McEwen cites various non-human primate and rat model experiments showing that repeated stress can cause cognitive impairment and altered behavior by compromising neuronal excitability, retraction of dendrites of neurons in Ammon's horn of the hippocampus, hypertrophy of dendrites in the amygdala, inhibition of neurogenesis in the dentate gyrus of the hippocampus, as well as significant and permanent loss of nerve cells in the

hippocampus after prolonged exposure to psychosocial stress [46]. Other studies have also confirmed that early life experiences can interact with biological traits to effect behavior: Suomi and colleagues have shown that early maternal deprivation in macaques reduced brain serotonin levels and increases alcohol preference and aggression [47, 48].

While there is no direct data indicating that early life experiences and caregiving influence the development of reactivity in human infants, cortisol reactivity in infants has been correlated with the security of attachment relationships between infants and mothers. Studies have shown that securely attached toddlers have no elevation of cortisol during novel situations, whereas insecurely attached toddlers have significant cortisol increases in the event of novel (i.e. stressful) stimuli [49].

A number of other human studies have described risks within the early family environment that contribute to both poor neuroendocrine responses to stress and poor emotional coping. A review by Repetti and others gathers evidence that constant exposure to stressful circumstances within risky families leads to alterations in the SAM and HPA axes responses and to disruptions in serotonergic functioning [29]. Studies have demonstrated that most children show increases in sympathetic arousal in response to exposure to angry adult interactions. Continual exposure to such conflict-type social interactions has been hypothesized to cause recurrent SAM activation, which can then lead to the development of high cardiovascular reactivity and poor cardiovascular health outcomes. Alternatively, poor cardiovascular health outcomes may be a result of children in hostile families developing a hostile interpersonal style, which in turn leads to more conflict-type social interactions that lead to recurrent SAM activation. Studies examining the HPA axis have shown that children in families characterized by low levels of warmth,

high levels of social control, anger, aggression, or abuse have disrupted patterns of HPA function, including chronically elevated corticosteroids, flattened daytime cortisol rhythms, and both lower morning cortisol concentrations and higher afternoon cortisol concentrations compared with children from healthy families [29, 49].

While much of the work on the developmental origins of individual differences in stress reactivity has assumed that high reactivity phenotypes lead to poorer health outcomes compared to low reactivity phenotypes, some more recent work has noted the more bivalent, nonlinear way in which high reactivity influences health outcomes. High reactivity may have both harmful and protective effects on health, depending on the levels of psychosocial stress within the environment. Studies by Boyce and colleagues have found that under conditions of high environmental stress, high reactive phenotypes have higher incidences of respiratory illness and physical injury compared to low reactive phenotypes. However, under conditions of low environmental stress, high reactive phenotypes have even lower incidences of respiratory illness and physical injury compared to low reactive phenotypes [42, 50]. Furthermore, low reactivity seems to moderate the effects of environmental stress on respiratory illness and injury in the opposite direction. These observations suggest that high stress reactivity may reflect a heightened “biological sensitivity to context” that, from an evolutionary standpoint, is a conditional adaptation to variable early childhood environments [33]. That is, high reactive phenotypes will typically emerge out of both highly stressful and highly protective early family environments. High reactivity in the context of highly stressful environments may function to increase the overall readiness of individuals to deal with the dangers of their environment even with the consequence of chronic over-arousal and

health problems. In contrast, highly reactive phenotypes in the context of low stress environments may function to “garner the health and survival benefits of highly supportive rearing environments” [51]. This hypothesis was then tested and confirmed by the same authors in a subsequent study [52].

Preliminary evidence is emerging in support of a curvilinear relationship between childhood stressful environments and the magnitude of stress reactivity. This work adds to a substantial body of data that details the genetic and environmental factors contributing to the development of stress reactivity early in life. Thus, variations in the early life environment, particularly variations in the intensity and quality of parental care, can alter the expression of genes that regulate the endocrine and behavioral responses to stress [41].

Convergences between control and reactivity: biological considerations

Research into the origins of control and reactivity have led to similar conclusions about the how factors in the early life environment, family and parental care, biological predilection and the interaction between genes and the environment play roles in shaping control beliefs and reactivity. As stated earlier in this paper, early life opportunities to manipulate the physical environment [9, 21, 22, 32], early exposure to decision making and problem solving activities [21], repeated opportunities to develop sense of contingency and competency [6, 22], low-conflict, nurturing family environments in which meta-emotional parenting styles are employed [29, 30], are all positively associated with sense of control. Parallels can be drawn between these early life conditions and the ones outlined for the development of stress reactivity profiles.

Amount and quality of parental care and interaction styles in the family environment are implicated in reactivity just as they have been in sense of control: in rats, low-levels of maternal nurturing lead to high levels of fear and an increased reactivity in response to novel situations [41]; in non-human primates, maternal absence or peer-rearing produces a constellation of behavioral, neuroendocrine and autonomic pathologies [53]; and in human children, families characterized either by high conflict, disorder, and stress or by nurturing, predictability, and low-stress produce high reactivity phenotypes [42, 49, 54].

Beyond developmental factors, there are neuroanatomical circuits that are physical evidence for the link between cognitive-emotional processes and physiological responses. Early research into emotion has provided some crucial evidence that conscious processes shape the character and strength of physiological and affective responses [55]. Central nervous system regions where cognitive evaluative processes are weighted with emotional significance include the premotor region of the frontal cortex, along with the anterior cingulate gyrus (part of the limbic system). Cognitive-emotional processing also occurs in the orbital prefrontal cortex, which is associated with the regulation of the hypothalamus and brainstem and which has extensive serotonergic and dopaminergic inputs. These higher cognitive-emotional processes then determine the descending inputs to the hypothalamus and brainstem, resulting in modifications of endocrine, motor, and visceral output patterns. A number of researchers have thus concluded that through this central nervous system circuitry there is great potential for individual differences in cognitive-emotional dispositions to influence and be linked to the physiological stress response [44]. Sense of control, which has been described both as a global dispositional

trait and a cognitive-emotional process specific to particular stressors, may therefore be generated in this neural system and implicated in the physiological stress response.

Having studied the circuitry of the autonomic and endocrine stress response, Lovallo proposes that much of what dictates reactivity and the coping response is rooted in higher cortical processes [14]. First: sensory inputs from the external environment are relayed through the thalamus to cortical sensory association areas and then to the prefrontal cortex. Second: the prefrontal cortex attaches meaning and significance to information about the ongoing experience, evaluating events and examining consequences of potential actions. In terms of cognitive appraisals, this can be thought of somewhat like the primary appraisal process. Third: this information is sent through the limbic system, which includes the amygdala, hippocampus, and insular cortex. Secondary appraisals, which involve complex evaluative processes that review the available coping responses and weight the potential threats or challenges in the situation, are believed to operate within this part of the neural circuitry. The functional anatomy of the limbic system seems well-suited for this purpose: the hippocampus is important for declarative memory, recalling specific events as opposed to abstract factual information; the amygdala enables emotions in connection with the present experience and allows for modification of actions based on those emotions and knowledge of past events as they are made available by the hippocampus; and the insular cortex allows the prefrontal cortex and amygdala to communicate and relate the present experience with cognitions and emotion.

Fourth: outputs are then sent from the central nucleus of the amygdala to the hypothalamus and brainstem. Regions of the hypothalamus and brainstem that receive

this outputs include: the pontine reticular formation, the nucleus of the solitary tract, the nucleus paragigantocellularis (PGi), and the brainstem aminergic nuclei (AMN), which are all part of systems that regulate autonomic outputs. The AMN is also responsible for sending dopaminergic, noradrenergic and serotonergic projections back to the rest of the cortex in a central feedback loop to modulate emotional experience and various brain states. Fifth and finally: hypothalamic and brainstem activation leads to the generation of physiological outputs to the periphery. This culminates in the typical cascade of stress response events: in the HPA axis, corticotropin releasing hormone (CRH) from the hypothalamus triggers the release of ACTH in the anterior pituitary, which triggers cortisol release from the adrenal glands, which exerts its multitude of regulatory and metabolic activities in response to stress. In the SAM axis, the brainstem, the nucleus PGi, the nucleus of the solitary tract, and other centers send sympathetic efferents to the adrenal medulla to release epinephrine, the catecholamine responsible for activation within the sympathetic nervous system.

Although the central nervous system circuits described above are not specific to particular cognitive-emotional processes or particular patterns of physiological response, it can very well serve as a neuroanatomical basis for how sense of control influences stress reactivity. If sense of control is shaped by early life experiences, these experiences must be evaluated and acquired through cognitive-emotional processes within the limbic system and prefrontal cortices. The emotional valence and cognitive associations attached to these experiences are then retrieved from hippocampal memory during later events and continue to influence an individual's appraisal of a situation's potential for threat or challenge. What is considered an individual's "sense of control" is a

dispositional trait, a belief, or in more operative terms, a part of the cognitive-emotional process that is invoked to help appraise the immediate event and determine the most appropriate coping strategy. As already discussed, there are a number of neuronal outputs from the amygdala to the hypothalamus and brainstem, which in turn, modulate the physiological response to stress. Although the number, quality, and strength of these neural inputs are in part determined by heritable variations, these neuroanatomical components of reactivity are also calibrated over critical periods of development to become the stress response system distinctive to each individual.

Lovallo also points out that a crucial feature of the neural circuitry for this integrated cognitive-emotional-physiological stress response system is its capacity for regulation and feedback. Cortisol not only has permissive effects on fight/flight functions, but it also has regulatory effects on the circuitry that released it, inhibiting the release of ACTH and CRH and also influencing neural activation within the amygdala, hippocampus, and other regions of the limbic system. More recent evidence also supports the fact that CRH acts as a neurotransmitter upstream of HPA axis events, with CRH-containing neurons projecting up into the cortex and limbic system and serving as an integrator of sensory information with emotional, behavioral, autonomic and hormonal responses. These physiological mechanisms of regulation are accompanied by behavioral mechanisms of regulation as well: the behaviors and actions generated through the cognitive appraisal process are coping behaviors, and coping essentially works to reduce emotional agitation associated with limbic activity. Lovallo postulates that these reductions may serve as a sort of reward on the neural circuitry, and as long-term

behavioral tendencies, coping behaviors can contribute to the improved maintenance of homeostasis.

Such feedback and homeostatic regulation may, in fact, be integral to how reactivity and sense of control are calibrated through early life experiences. As previously discussed, “handling” and high levels of maternal care in rats reduces levels of fear and stress reactivity in novel situations. This has also been accompanied by physiological evidence of permanent down-regulatory changes in the CRH system in the amygdala, leading to decreased exposure to the adrenocortical effects of stress [41]. Long-term periods of maternal care deprivation have produced the opposite effects, including chronically upregulated activity in the HPA axis, amygdala and locus ceruleus [51]. These data suggest that protective aspects of early life parental care have a soothing effect on limbic system activation; that there is a “ratcheting-down” of fear-related emotional stimulation of the entire system via external influences such as caregiving and other early environment influences.

Similar conclusions can be drawn about the importance of feedback from the external environment in the development of control. Caregiver responsiveness to infant emotional needs and capabilities has been implicated as a factor in children’s development of their own physical and symbolic self-soothing strategies against emotional distress [56]. As children develop increasing linguistic and play capacities, parents who employ strategies of active engagement, distraction with play, and physical and emotional reassurance have children who are more capable of self-control and self-monitoring of emotional distress as they grow older. Integral to the concept of development is the process of internalization, which is how regulatory processes that are

originally external become part of the personal repertoire of the child. Again, these data suggest that control strategies learned from the early life environment are integrated into children's own individual sense of control and become effective ways of reducing psychological distress and regaining emotional homeostasis.

Convergences between control and reactivity: Current studies

Recent work attempting to delineate the relationship between control and reactivity has typically treated control as the primary independent variable with reactivity as the outcome variable. However, evidence for the directionality of this relationship is mixed. While some studies have found that high control has been linked to lower cardiovascular reactivity, others have found high control to be linked to high cardiovascular reactivity. Still, other studies have qualified these findings by pointing out that the level of effort involved in addressing the challenge or stressor also moderates the relationship between control and reactivity. Other research highlights self-efficacy, incentive value, or other personal traits or psychological factors as potential moderators of control and reactivity. Comparison across findings is further complicated by poor consensus about the specific dimensions or subtypes of control and by the fact that constructs with similar names oftentimes have different meanings across studies.

Research by Sanz and Villamarin has examined the role of self-efficacy and incentive as regulators of cardiovascular reactivity [57]. Self-efficacy was defined as an expectation of competence regarding a specific task. Their work shows that high or low *incentive value* – a cognitive anticipation of the appetitive or aversive value of success or failure in the stressful task – moderates the relationship between self-efficacy and

cardiovascular reactivity. In studies using arithmetic task stressors, high self-efficacy predicted higher reactivity under conditions of high incentive value, namely, when subjects perceived the consequences of their success (or failure) at the task to be substantial. However, when the incentive value was lower—when subjects felt that the personal consequences of failure at the task were insignificant—high self-efficacy no longer had a strong effect on reactivity.

Predictability of an event has also been shown to be a factor influencing reactivity. In a study by Baker and Stephenson, predictability was defined as the likelihood of an event's occurrence, whereas control was defined as an individual's ability to influence that event's occurrence. Predictability therefore shares a similar meaning with contingency and control shares a similar meaning with competence. The authors demonstrated that while predictability and control are independent of one another, they each separately have mixed effects on cardiovascular reactivity that were inconclusive [58].

Still, others have suggested that *effort of responding* may moderate the relationship between control and the physiologic stress response [16]. That is, an increased effort of response to the stressor may accompany increased control, leading to greater reactivity. Recognizing effort and control to be separate yet related entities allowed Gerin and colleagues to then outline a mechanism for how perceived control, self-efficacy, and effort affect reactivity. In the first of two studies, they first determined that how much actual control an individual has over a situation affects reactivity such that low actual control leads to greater changes in reactivity and high actual control leads to smaller changes in reactivity. However, self-efficacy—a confidence in one's ability to

produce a particular outcome—moderated that effect, so that, holding effort constant, under conditions of high actual control, high self-efficacy lowered reactivity but low self-efficacy increased reactivity [59].

In the second study, perceived control, a perception of the available responses to a situation regardless of one's skill or actual control, was then determined to be a precondition for self-efficacy to have an effect on reactivity [60]. Perceived control, combined with self-efficacy, determines the amount of effort one invests in accomplishing a task, which then determines the level of reactivity. For example: under conditions of high perceived control and high self-efficacy, one will put a greater amount of effort into a task, leading to high reactivity. Under conditions of high perceived control and low self-efficacy, one will expend less effort, leading to a smaller change in reactivity. Low perceived control, despite any self-efficacy condition, was found to lead to decreased effort of response and lowered reactivity. The definitions of perceived control and self-efficacy used in these studies are not unlike contingency and competence, suggesting that: 1) all the various components of control have some sort of effect on reactivity, yet 2) difference combinations of these components of control can differentially effect reactivity.

Cognitive appraisals have also been examined in relation to reactivity. In a study by Waldstein and colleagues on the associations between cognitive appraisals, cardiovascular reactivity, and affect, threat/challenge appraisals were associated with increased diastolic blood pressure reactivity, especially threat appraisals. However, negative affect was found to be of even greater predictive value for reactivity, suggesting that emotion and motivation are more proximal influences on reactivity than cognitive

appraisal [61]. One limitation of this study may have been the nature of the laboratory stressor: subjects were asked to perform computer-generated mental arithmetic tasks, a stressor which may be limited in its ability to fully engage the cognitive appraisal process. As outlined by Lazarus and Folkman, cognitive appraisals are called upon to execute a coping strategy against a psychological stressor that requires a particularly great effort of response, and further, control beliefs influence the appraisal process only when the task is ambiguous or novel. Mental arithmetic tasks may not require as great of a coping effort as a more personally relevant stressor, nor are such tasks seemingly unfamiliar terrain for most psychology student test subjects, which were the type of subject used here.

A more recent study of cognitive appraisals and reactivity also seems to support the notion that negative emotion may seem to play a more prominent role in reactivity than threat/challenge appraisals. Cohen and colleagues measured levels of negative emotion, threat/challenge appraisal processes, and reactivity during anticipation of a stressor—the five minutes of preparation prior to having to deliver a speech [62]. The study found that although threat appraisals could not explain the effect of stress on cardiovascular reactivity during speech preparation, negative emotion accounted for over half the effect. However, the authors do point out limitations in the way appraisals were investigated in their study and further postulate that such negative emotion may be the outcome of negative appraisals, leading to increases in reactivity.

Ultimately, interest in the relationship between control and reactivity is for the goal of understanding how they impact health. A large assumption is that control may be able to moderate the effects of reactivity on health status. Connor-Smith and Compas

found that coping strategies that employ control do indeed moderate the relationship between reactivity, health status and internalizing problems. High use of primary control coping buffered the relationship between heart rate reactivity and health status, whereas high use of secondary control coping buffered the relationship between heart rate reactivity and internalizing problems. Thus, both primary and secondary control strategies were beneficial in different contexts. However, disengagement—a form of secondary control involving cognitive and behavioral avoidance and denial—seemed to be the most harmful in the long run.

Although this by no means is a complete review of the literature on control and reactivity, it does provide a picture of the mixed results, the multiple definitions of control, and the limitations of laboratory-designed stressors that have challenged researchers trying to elucidate the mechanism by which control exerts its effects on reactivity. Despite this, it is important to recognize that the impetus for all these studies is the consistent evidence that both psychological factors such as control and physiological markers such as reactivity are pertinent to a wide array of disease pathologies. Conventional thinking about the neural circuits involved in the cognitive-emotional-physiological stress response would suggest that researchers should approach the control-reactivity relationship by assuming that psychological control dictates downstream physiological events. However, given the possibility for feedback within these systems, and given the nonlinear developmental trajectory of reactivity, the effect of control on any health-related outcome may not necessarily be linear, either.

Convergences between control and reactivity: Proposal

Thus far, control has had a variable relationship with reactivity, with some studies suggesting that a greater sense of control is associated with lower reactivity, others suggesting that a greater sense of control is associated with higher reactivity, and all studies using different definitions of control. However, few of these studies have taken into consideration the contextual effects of psychosocial stress: control, like reactivity, most likely exerts its effects on health in context-dependent ways. Just as highly reactive profiles may reflect a heightened biological sensitivity to context, a lower sense of control may be the product of a psychological sensitization to early cognitive-emotional influences. In Boyce and Ellis's hypothesized model of reactivity development, the vast majority of children are exposed to early environments that are "neither entirely threatening nor universally safe." These are the environments that down-regulate children's biological sensitivity to context and buffer individuals against chronic stressors by lowering their reactivity profiles. Such environments may also be the context for the development of a greater sense of control. If "sense of control" implies a combination of the belief in one's ability to control a potential stressor (i.e. competence and self-efficacy) as well as an accurate assessment of the degree of controllability of an outcome (i.e. contingency and predictability), this may be the level of control necessary and sufficient for effectively dealing with moderate levels of psychosocial stress. Like Antonovsky's concept of load balance, early life experiences that are stressful yet not beyond an individual's available coping resources are the ones that have been considered most instrumental in facilitating a greater sense of control and self-efficacy in children.

Low sense of control, on the other hand, may be a product of either high or low stress early life environments. Lack of stimulation or low levels of challenge and stress

may have just as harmful consequences as environments filled with aggression, chaos and conflict. Early life environments with a paucity of stimulation and engagement may rarely require children to call upon cognitive appraisal processes or coping strategies, and through lack of use, children will fail to develop the emotional-cognitive capacity for control in the event of emotional distress and will lack the intrinsic motivation to seek out novelty. A lack of opportunity to make decisions, solve problems and generally influence events will hinder the development of a greater sense of agency or self-efficacy. At the other end of the spectrum, continuously conflict- and anger-filled circumstances can also prevent children from developing adequate control beliefs and coping behaviors if such circumstances are far beyond any objectively controllable means. High levels of conflict and distress in the home sensitizes children to fear and anxiety and provides obstacles which children may never be able to overcome with any modicum of control. These early failures will frustrate children and eventually force them to abandon all attempts at primary control. Thus, such overwhelming or underwhelming early life environments cannot provide the growth-promoting experiences that lead to greater confidence in one's abilities to shape outcomes, accurate judgment of contingency, or to greater motivation and effort of response.

Although evidence to substantiate this hypothesis is not yet available, the literature has yielded a number of models that treat both reactivity and control as mediators or moderators of the effects of psychosocial stress on health outcomes. Control has typically been conceived of as a mediator of the environmental and socioeconomic factors that influence health. Syme has used *control of destiny* as a factor in understanding how lower SES affects health outcomes. Syme's control of destiny

theory postulates that the degree of control an individual has over life choices and living circumstances is well correlated with one's SES [17]. A number of studies have shown that low job control and high job demand show a strong correlation with coronary heart disease risk [63, 64]. Syme furthermore identifies lack of control as the common feature in all major social epidemiology studies that cite factors such as social support, mobility, type A personality, and stressful life events as major contributors to poor health outcomes.

Control can also serve as a moderator of the effects of psychosocial factors on health. If those highest on the SES ladder have more opportunities, training, skills and resources to cope with stressful life problems, it can be postulated that the situation of those at a lower SES could be improved by creating opportunities to learn new and varied problem-solving skills, creating access to more coping resources, and essentially developing the competence required to harbor a sense of control. Control can thus serve independently as a buffer against detrimental psychosocial factors; it need not be causally preceded by and dependent on psychosocial predictors of health. Such factors would suggest that control be treated as a moderator in some contexts. [65].

Although there have been few rigorous attempts to identify how sense of control specifically influences disease pathogenesis have been few, Sheldon Cohen has suggested that control be considered either as a main effect or a stress-buffering moderator [66]. As a main effect, control may imply having access to good sources of health information (an information-based model), access to tangible economic services that result in better healthcare, or it can imply that the positive affect, sense of self-worth, predictability, and stability generated by control can lead to increased motivation to care for oneself. In a

stress-buffering model, control is more of an integral component of coping. Having access to information about a stressful event or more ways of coping with the event reduces the evaluation of potential threat or harm, and such a reduction of a stress appraisal can lead to an improved affect, reduced negative health behaviors and a concomitant improvement in health outcomes. As a buffer against stress, control can also imply a perception of having access to tangible and economic resources, even if those resources objectively aren't available; such a perception, again, can reduce a stress appraisal and lead to improved health outcomes.

The role of reactivity as a mediator or a moderator has also been debated. While many of the popular conceptualizations of the mechanisms linking SES and health outcomes involve access to healthcare, diet, and compliance to medical advice, another observation has been that individuals from low SES backgrounds experience more day-to-day stress than do individuals from higher SES. Such a differential exposure to stress along the SES gradient means that reactivity may either be viewed as a moderator or mediator of the relationship between SES factors and health outcomes. If reactivity during stress is a consistent physiological characteristic of an individual, then highly reactive individuals living in high stress environments will have poorer health outcomes than individuals who are neither highly stressed nor highly reactive [67]. In this case, reactivity serves as a moderator. Another possibility for the role of reactivity as a link between SES and health outcomes is that exposure to a more threatening or challenging environment by lower SES individuals results in greater reactivity across physiological systems. Over time, individuals chronically exposed to more threatening environments

may also begin to experience threat even in benign situations, leading to overall greater stress load. In this case, reactivity plays more of a mediating role.

Much of the research examining reactivity's role in the etiology of cardiovascular disease has conceptualized it as a potential mediator of the relationship between psychosocial factors and disease risk [68, 69]. However, Boyce and colleagues have used reactivity as a moderator between psychosocial factors and both respiratory illness and externalizing behavioral problems [42]. Although the question of whether control and reactivity serve as mediators or moderators between psychosocial factors and health outcomes remains unresolved, it is still important to carefully specify a model.

Reactivity as a moderator has accounted for the observation that poor health outcomes can be a result of both high stress and low stress environments, depending on the magnitude of one's reactivity profile. Because the associations between psychosocial factors and health outcomes are stronger in this model, stronger associations between psychosocial factors and health outcomes may be revealed if control is also treated as a moderator. If low sense of control can be a product of both highly conflict-filled, stressful early life environments *and* exceedingly impoverished and challenge-deficient early life environments, it could function like reactivity to moderate the relationship between psychosocial factors and health outcomes. That is, in high stress environments, a low sense of control will predict greater risk of illness and injury and poorer behavioral outcomes. However, in low stress environments, a low sense of control will predict lower rates of illness, injury and behavioral problems, since a low stress environment will neither require an individual to call upon a strong sense of control nor demand too much in the way of coping. In contrast, a higher sense of control in low stress environments

may predict higher rates poor health and behavioral outcomes, since the individual's urgency or desire for control may be in excess of what the situation objectively demands.

Conclusion

The primary objectives of this paper have been to justify the use of control as a moderator between psychosocial factors and health and behavioral outcomes and articulate the neurophysiological and developmental reasons for why control and reactivity may be parallel processes. The purpose of this paper was not to create a authoritative definition of control, although the multifaceted dimensions of this construct were addressed. While this by no means is an exhaustive review of the literature relating control to reactivity, this paper does highlight the mixed results and numerous definitions of control that researchers have used.

CHAPTER 2:

A Study of Psychosocial and Physiologic Predictors of Sense of Control

Background and Significance

The concept of control has been a sensitizing concept across disciplines because of its power in explaining various behavioral, psychological, sociological and epidemiological phenomena. The psychologist Robert White argued in 1959 that an innate yearning for competency and mastery was one of the fundamental drives of human behavior, and labeled this motivation *effectance*, the purpose of which is the "feeling of efficacy." In the 1970's, Albert Bandura developed the concept of *self-efficacy*, which

focused on an individual's beliefs in his capacity for exercising control and which has been useful in predicting subsequent behavior. At the sociological level, control has been useful for understanding the damaging effects of low social class. In the 1980's Melvin Kohn and colleagues determined it was through SES correlations with *occupational self-direction*—the opportunity to exercise initiative, judgment and creativity in one's work—that social class exerted its effects on personality. Subsequent studies by Marmot and colleagues have shown that health and SES are highly correlated, and have lead researchers to postulate that it is the exposure to opportunities to exercise latitude and control that accounts for good health [17, 63, 64]. Regardless of how control has been defined or used, it is an enduring concept that explains, at multiple levels of analysis, the ability to mitigate the stress associated with environmental threats or challenging situations.

Early work has suggested that control may not so much an inborn “trait” as a characteristic acquired through experience. Investigations by Seligman and colleagues demonstrated that animals can learn the degree to which they can control an outcome [13, 70]. Dogs exposed to uncontrollable shock exhibited greater fear and anxiety even in novel situations in which control was possible [13]. In infant rhesus macaques, researchers found that “master” infant macaques who learned to control an appetitive reinforcer through the use of operant manipulanda demonstrated less emotional reactivity than infants who were delivered the same appetitive reinforcer noncontingently [31, 32]. Research in children has also shown that repeated exposure to noncontingent and uncontrollable events produces expectancies of noncontingency and uncontrollability [24]. Different developmental periods have been identified within which issues of

control become important in regulating emotion and behavior. In infancy, insecure parent-child attachments have been associated with a wide array of maladaptive behaviors: less securely attached infants are known to have less effective coping strategies during novel arousing stimuli [29], and less securely attached children demonstrate less understanding of negatively valenced emotions such as anger, sadness and fear [29]. In adolescence, growing up in angry and aggressive homes has been associated with escape-type coping styles; that is, these adolescents gradually abandon efforts to control difficult situations and focus instead on trying to escape them [29]. A large body of research in school achievement and mastery motivation suggests that children develop positive control beliefs through the internalization of experiences in which they are successful at controlling an outcome [6, 24].

Thus, at the behavioral and psychological level, control has been identified as a salient feature of coping with stress and challenge. Responses to stress at the physiological level, however, are less controllable. Physiologic stress reactivity, while demonstrating plasticity in early life, is considered a trait unalterable by adulthood [71]. Indeed, stress-induced activations of the hypothalamic-pituitary-adrenocortical (HPA) and the sympathetic-adrenomedullary (SAM) systems have been found to be relatively stable in adult individuals across time and across different stressors [71]. Attempts have been made to modify cardiovascular reactivity through strategies such as biofeedback and hypnosis but few studies have shown these techniques to impart long-lasting modifications to reactivity. Meditative relaxation strategies, cardiac education and visual feedback, and muscle relaxation and thermal biofeedback have been effective in reducing cardiac reactivity only when subjects had positive expectancies about the technique or

received a monetary reward for the anticipated outcome, and the results were not consistent across a variety of stressors [72-74]. A meta-analysis of biofeedback techniques to reduce hypertension pointed out that the effects of biofeedback on reducing cardiac reactivity are effective only in comparison to non-intervention controls but not to sham or other non-specific behavioral intervention controls [75]. Thus, while biofeedback and hypnosis appear to induce a general relaxation response, there is little evidence to support the idea that stress reactivity phenotypes are continuously modifiable through life.

Reactivity phenotypes, like control, appear to be calibrated in response to early life stressors. Investigations by Meaney and colleagues have shown that variations in the level of maternal care by rats alter the neural circuitry responsible for behavioral and endocrine responses to stress in their offspring [41]. One study showed that high levels of maternal licking and grooming and arched-back nursing led to reduced fearful behaviors by rat pups in response to novelty. These rat pups additionally showed significantly increased central benzodiazepine receptor density in the amygdala and locus ceruleus and decreased corticotrophin-releasing hormone (CRH) receptor density in the locus ceruleus. Given the anxiogenic influence of CRH projections from the amygdala to the locus ceruleus and the anxiolytic actions of benzodiazepines, these findings suggest that maternal care during infancy may “program” behavioral responses to stress in offspring by altering the development of neural circuits that mediate stress reactivity [39]. Work with non-human primates has also demonstrated the effect of early life experience on stress reactivity and behavior. A study by Suomi and colleagues showed that rearing conditions for infant macaques interacted with serotonin transporter genotype to yield

different adrenocorticotrophic hormone (ACTH) levels during a stressful separation period [48]. It was found that peer-reared macaques who also possessed a genotype for low levels of serotonin transporter ribonucleic acid exhibited marked increases in ACTH release after exposure to social separation [48]. Because peer-rearing produces a constellation of pathologic behaviors compared to mother-rearing [53], and since serotonin neurotransmission is involved in activation and feedback control of the HPA axis, the authors suggested that stressful early life experiences may predispose those carrying gene variants for low serotonin transporter towards developing heightened cortisol reactivity.

Studies of human children have also shown that aspects of early life experience, particularly parent-child interactions and family stressors, play a significant role in shaping biological reactivity. In a study examining the effect of early childhood exposure to highly protective or acutely stressful environments on the development of reactivity, Boyce and colleagues found that children in either very low-stress environments or very high-stress environments showed evidence of heightened autonomic reactivity, pointing to a curvilinear relation between the level of childhood environmental stress and magnitude of stress reactivity [76]. The authors hypothesized that individuals who experience acutely severe stressors in early childhood tend to develop highly reactive adrenocorticotrophic and adrenergic systems to increase overall readiness and capacity to deal with dangers in their environment. Furthermore, there is an extensive literature supporting the notion that insecure and neglectful early life environments shape highly reactive HPA and SAM systems. A review by Gunnar indicates that insecure infant-parent attachments and insensitive or unresponsive caretaking heightens cortisol

reactivity in response to stressful, novel situations [49]. Work by Taylor et al. demonstrated that children from risky family backgrounds—characterized by cold, conflict-ridden or neglectful parenting—exhibited signs of HPA dysregulation in both baseline cortisol measures and cortisol responses through the course of a stress challenge [77].

Given that both psychological sense of control and physiologic reactivity are influenced by similar aspects of the early life experience and given that both are, at the psychological and biological levels, important response mechanisms to stress, associations between the two would provide confirmation of consilience across multiple levels of analysis. However, the relationship between control and physiologic reactivity is complex and poorly understood. While some studies have found that a greater sense of control has been linked to lower reactivity, others have found just the opposite association. Early studies documented that increased self-efficacy in coping with a specific phobia produced a reduction in sympathetic activity when the effective coping behavior was carried out [78] and that increased control over outcomes reduced blood pressure responses [79]. However, research by Sanz and Villamarin found that high self-efficacy predicted greater cardiovascular reactivity when subjects were highly invested in the stressful task at hand [57]. Gerin and colleagues further support this notion by demonstrating that high self-efficacy leads to greater cardiovascular reactivity because of the greater effort of response, but low self-efficacy leads to lower levels of physiological arousal [59, 60]. Yet another study found that threat appraisals, which are experiences of stress that are assessed as aversive because the individual expects harm or loss, were associated with increased diastolic blood pressure reactivity, suggesting that a lack of

control is linked to increased reactivity [61]. Thus, there little consensus in the literature to support a positive or negative correlation between sense of control, in the various ways it has been defined, and physiologic reactivity, in the various ways it has been measured.

A large challenge in understanding the association between control and reactivity has been in establishing a definition for control that provides integration across many different research findings. This study presents two ways of conceptualizing control that may be useful in understanding its biological underpinnings. First, *emotional control* may be defined as the process of regulating one's emotional reactions to stressors. Because emotions are "our perceptions of autonomic and somatic response systems," [80] the acquisition in early life of cognitive and behavioral strategies to regulate emotional experiences may serve to also modulate autonomic responses to stress. Studies have shown that risk factors, such as high levels of conflict in the home, families with high negative affect, and families where emotions or emotional issues are rarely acknowledged or discussed, lead to poor processing and recognition of emotions and increased sensitization to anger, anxiety and fear [29, 30]. Perry and colleagues have hypothesized that exposure to high levels of family conflict or violence are a form of chronic stress that affects neurobiological development and creates a sensitized stress-responsive system that influences arousal and emotional regulation [81].

Second, *behavioral control* may be defined as the process of regulating one's behavioral reactions to stress. Developmental psychology has long been interested in how children acquire the skills necessary to regulate their behavior in challenging situations [82, 83]. Internalizing and externalizing behavioral problems in children have been associated with a wide array of factors, including parental controls that constrain or

invalidate children's psychological and emotional experience [84], family conflict and violence [85, 86], chronic illness in children [87, 88], and learned helplessness and other control-related beliefs [89]. Behavior is a complex aggregate of responses that is explained by an array of motivational, social, emotional, cognitive, and biological factors. Although there are few parsimonious explanations for behavioral regulation that assemble evidence across disciplinary boundaries, biological reactivity to stress may provide integration to seemingly disparate neurobiological and psychosocial findings.

Thus, given that behavioral control, emotional control, and physiologic reactivity are all processes related to regulation and adaptation at different levels of abstraction, integration between these concepts would provide a much needed interdisciplinary bridge across multiple levels of analysis. As outlined above, physiologic reactivity can be viewed as the most visceral form of regulation in response to stressors, over which we have little control once it is "hardwired." Higher on the neurophysiological axis, emotional control may be somewhat more malleable through the influence of cognitive associations. Behavioral control may be considered a process influenced by myriad cognitive, social, emotional and biological factors, with an even wider range of predictors than emotional control. Furthermore, the similarities in the early life experiences that shape control and physiologic reactivity may also point to a shared neurophysiologic and developmental trajectory. Therefore, the purpose of this study was to examine biological reactivity and early life stress as joint predictors of emotional and behavioral control in children. While separate investigations have shown that poor sense of control and heightened physiologic reactivity may each individually be moderators of the stress-

illness relationship in children [42, 90], few studies have examined how physiologic reactivity and emotional and behavioral control actually may be interrelated processes.

Previous studies of sense of control or physiologic reactivity have documented that children with chronic illnesses, such as sickle cell anemia, cystic fibrosis, asthma, and HIV, are at a particularly increased risk for emotional, social, and behavioral difficulties [91-94]. Understanding how chronically ill children manage illness-related and typical childhood stressors will provide insight into how these processes are related to well-being and resiliency. In this study, subjects who carried the burden of chronic illness were either children who were HIV-positive themselves or HIV-negative with HIV-positive mothers, since chronic illness may have an indirect impact via caregiving that is compromised by symptomatic periods. Improvements in diagnosis and treatment of pediatric HIV have led to greater numbers and longer survival of HIV-positive children [91]. As a consequence, pediatric HIV can now be viewed as a chronic illness characterized by acute symptomatic periods and periods of relatively stable health. The HIV-affected children in this study were compared to controls unaffected by the HIV epidemic and matched by gender, age, and race.

Another important parameter of this study was to be able to examine emotional and behavioral control and reactivity accompanying a normative stressor, such as school entry. Starting school is a universally recognized childhood stressor that involves a range of emotional and behavioral challenges [95, 96], and which also has been associated with changes in adrenocortical, sympathetic, and immune reactivity [54, 97]. For these reasons, adrenocortical reactivity and cardiovascular reactivity were measured, in addition to markers of psychosocial stress including family conflict, school entry stress,

caretaker health and depression, and HIV status. We hypothesized that children with both high levels of environmental stress and high physiologic reactivity would show poorer emotional and behavioral control. In contrast, children with low levels of psychosocial stress and less dramatic cardiovascular and adrenocortical reactivity profiles would demonstrate more adaptive emotional and behavioral control. The study's procedures were approved by the University of California, San Francisco Committee on Human Research and the University of California, Berkeley Committee on Protection of Human Subjects, and informed consent was obtained from the caretaker of each child before enrollment.

Method

Participants

The sample for this study consisted of one hundred thirty-seven children entering kindergarten or first grade recruited over four successive years, from 1997-2000. The enrollment of the study sample over four consecutive years reduced the logistical burden of the project in any single year, allowing the investigators to maintain close contact with each study family. As a consequence, the remaining sample consisted of 132 children: 75 boys and 57 girls, all between the ages four and six (mean = 5.31), which included 18 white, 69 black, and 45 other race or biracial children. The cohort comprised three groups: group A, which consisted of HIV-positive children of HIV-positive mothers (n = 38); group B, which consisted of HIV-negative children of HIV-positive mothers (n = 29); and group C, which consisted of HIV-negative children of HIV-negative mothers

matched for race, gender and grade to subjects in groups A and B (n = 65). See Table 1 for complete demographic breakdown of study subjects.

Subjects in groups A and B were identified through the patient registry of the Northern California Pediatric HIV Surveillance Study and were recruited from the Pediatrics AIDS Clinics of five affiliate institutions. Group B children were recruited from siblings of HIV-positive children attending the Pediatric AIDS clinics of Bay Area institutions or were identified through care and service providers for HIV-positive mothers. Group C children were recruited from kindergarten and first grade classrooms in schools demographically similar to those of groups A and B. The three group design allowed investigators to examine the specific effects of HIV-positivity in the child in contrast to HIV-positivity of the mother. Children with advanced HIV illness (CD4 count < 200) or other chronic medical conditions were excluded in order to have a sample which was healthy enough to be transitioning to a new school year and in which decrements in health status could be monitored.

Study Design

Each child was followed for six months, but for the purposes of this analysis, only data collected four weeks prior to school entry and four weeks after school entry were used. Four weeks prior to school entry in the fall, children completed cardiovascular reactivity testing as well as baseline salivary cortisol sampling in the first laboratory session. Four weeks after the start of school, children participated in a second laboratory session for testing of school readiness, developmental status, and psychiatric morbidity. Salivary cortisol sampling was again completed for assessment of adrenocortical response to school entry stress. Questionnaires assessing demographic information,

family context, child resilience, vulnerability and behavior were completed by the primary caretaker. For all questionnaires, children's mothers were preferentially used as the source of data, and when the mother was unavailable or the child was in foster care, foster mothers, fathers or closest living related caretakers were asked to fill out the questionnaires. All statistical procedures on these data were performed using SPSS 12.0 for Windows.

Questionnaires

Demographic data. A parent-completed questionnaire was developed for this study to obtain information about the child's background. Background questions identified the child's ethnicity, parent's ethnicity, parent's education, family income, number of relatives and non-relatives living in the same household, and religious background.

Family stress. Psychosocial child stressors were assessed through four surveys completed by the primary caretaker, which included:

(1) The Major Life Events Questionnaire (MLEQ), a modified version of the Coddington Life Events Questionnaire [98, 99], which is a checklist of major stressful events in the family over the preceding twelve months. The MLEQ is an expanded version of Coddington's 30-item questionnaire that allows primary caretakers to assess the number of event occurrences for 37 major life events plus space for additional life events to be added by the respondent. Events include items such as loss of a job by a parent, death of a loved one, increase in number of arguments by parents, or birth of a sibling. Composite life event scores were computed as the sum of event occurrences. Scale-level reliability statistics (e.g., coefficient alpha, split-half reliability) usually are

not reported for this scale since individual items would not be expected to covary with one another [100, 101].

(2) the Moos Family Relationship Index (FRI), a multidimensional measure of the social environment and functioning of the family [102]. This version of the Moos FRI consists of 36 items rated on a 4-point likert scale (e.g. 0 = “very false, 1 = tends to be false, 2 = tends to be true, 3 = very true”) addressing the amount of openly expressed anger, aggression, and conflict among family members (e.g. “we fight a lot in our family,” “family members sometimes get so angry they throw things.”) Scores were summed separately for four subscales, including conflict, control, cohesiveness, and expressiveness. For the purposes of this analysis, only family discord was assessed using the conflict subscale, and Cronbach’s alpha for this subscale was 0.89, suggesting a high level of internal consistency.

(3) the Beck Depression Inventory (BDI), a measure of the severity of affective, cognitive, motivational and psychological symptoms of depression in the primary caretaker [103]. Parents completed a questionnaire of 21 items rated on a 4-point likert scale (e.g. “0 = I do not feel sad, 1 = I feel sad, 2 = I am sad all of the time and I can’t snap out of it, 3 = I am so sad or unhappy that I can’t stand it.”) A total score was summed for the entire scale. Cronbach’s alpha was 0.89, suggesting a high level of internal consistency for the BDI.

(4) the Chronic Health Conditions Questionnaire (CHCQ), which was designed for the purpose of this study and evaluated self-reported chronic health conditions for the caretaker. The CHCQ consisted of a checklist of 14 health problems that the caretaker may have had in the past six months, including common ailments such as asthma,

diabetes, arthritis, anemia, heart disease, or back problems, and included two spaces for additional problems to be added by the respondent. A total score was summed for the entire scale. Scale-level reliability statistics were not reported for this scale since individual items would not be expected to covary with one another.

Principle components analysis was used to derive a single factor, family stress. Based on the strong correlations between measures, family stress was determined to be a regression factor based on the Major Life Events scale, the Beck Depression Inventory and Chronic Health Conditions questionnaire for the primary caretaker, and the conflict subscale of the Moos Family Relationship Index.

Child Measures

Biological reactivity. Subjects were tested for both cardiovascular and adrenocortical reactivity in the first laboratory session four weeks preceding school entry.

Cardiovascular reactivity has been defined as “the deviation of a physiologic response parameter from a comparison or control value that results from an individual’s response to a discrete, environmental stimulus” [104]. A protocol for the laboratory measurement of reactivity in children was designed and standardized in a previous kindergarten entry project [42]. A 30-minute test was administered to subjects in a quiet, private room. Measurements of heart rate (HR) and mean arterial pressure (MAP) were taken using an automatic, oscillometric Dinamap monitor (model 1846 SX/P, Critikon, Inc., Tampa, FL), the validity of which has been previously established [105]. The blood pressure cuff remained on the child’s nondominant arm for the duration of the testing period. To minimize the potential aversiveness of the monitoring equipment itself, children were given the opportunity to see, touch, and operate the equipment during a

group meeting held in each childcare setting approximately one week before reactivity testing. The reactivity protocol was administered by a female examiner not known to the child, and consisted of four tasks: 1) a child interview taken from the Gesell school readiness screening test [106]; 2) number recall, involving recitation of a series of digits; 3) lemon juice tincture, in which a small drop of pure lemon juice was placed on the child's tongue; and 4) two emotion-evocative video clips, during which the child was prompted with verbal descriptions of the video clips. Seven measures of MAP were collected throughout the challenging tasks. Four baseline cardiovascular measures were collected during one resting period prior to the set of tasks, resting periods between tasks, and at the end of the set of tasks when a final, calming, neutral story was read to the child. The MAP variability scores for individual study children were used as the final measure of cardiovascular reactivity.

Adrenocortical reactivity has been assessed with measurements of salivary cortisol because it can be non-invasively collected and reflects the plasma concentration of the non-protein bound active fraction [107]. Salivary cortisol was measured with samples collected during the first and second laboratory sessions. All samples were frozen and stored at -20° C for later transport and analysis in a single batch in order to avoid error from interassay variation. Each sample was assayed in duplicate using a previously developed modification of the Amersham International Amerlex Cortisol radioimmunoassay kit procedures [108]. This assay is highly sensitive and specific to cortisol, with inter- and intra- assay coefficients of variation of 7% and 4%, respectively. Adrenocortical reactivity to school-entry stress was measured as the change score computed by subtracting the cortisol measure of the first session from the cortisol

measure of the second session. Circadian influences on cortisol levels were controlled by collecting saliva samples between 9:00 AM and 12:00 PM, with both samples obtained at the same time of day, plus or minus 30 minutes.

Measures of control. Subjects' *behavioral control* was assessed through a series of 13 questions selected from the Child Behavior Checklist (CBCL) that identified behavioral issues most closely associated with sense of control (e.g. "Impulsive or acts without thinking," "temper tantrums or hot temper," "doesn't get along well with other children," "disobedient at home." See table 2). The CBCL is a caretaker-completed checklist that produces subscores for problem behaviors in aggression, depression, attention, social withdrawal, delinquency, internalizing and externalizing, and somatic complaints [109]. Cronbach's alpha was 0.769 for this set of 13 items, suggesting a moderately high level of internal reliability. While a number of these items are related to attention or obsessive-compulsive problems, they were selected because they reflected at least one or more component of the working memory, response inhibition and attention allocation required to control behavioral responses to external stimuli [110].

Emotional control was measured through the emotional control subscale of the National Institutes of Health Diagnostic Q-sort [111]. After testing sessions lasting approximately one and one-half hours, a psychologist conducted the NIH Diagnostic Q-sort, which assesses the social, emotional and motivational behavior of pediatric subjects and which produces subscores for four factors: depressed behavior, hyperactivity and attention deficits, autistic behavior, and low frustration threshold or poor emotional control. Three items were scored for the poor emotional control subscale (see table 2). Cronbach's alpha was 0.722 for this set of three items, suggesting a moderately high level

of internal reliability. Intraclass correlations for Q-sort ratings completed by a psychologist, social worker or primary caretaker/parent have ranged from .71 to .98, indicating strong interobserver reliability [111].

Statistical Analyses

Preliminary analyses included descriptive statistics and univariate correlations. The studies hypotheses were tested via two sets of multiple linear regressions to determine the combined influence of the predictor variables on each outcome of interest, behavioral control and emotional control. For each of these two models, five independent variables were used, including: HIV status, family stress, MAP variability and cortisol difference, and the interaction variable between MAP variability and cortisol difference. This last interaction variable was included since the relationship between sympathetic reactivity and adrenocortical reactivity may provide further explanation for the outcome variables of interest.

Results

Table 3 summarizes the descriptive characteristics for the independent and outcome variables. As can be seen from the table, there was a wide range in scores for behavioral control (range, 0.00-18.00), suggesting that the population selected contained a wide distribution of children with either few behavioral problems or many behavioral problems. This range cannot be compared to the criteria for normative populations established by Achenbach et al., since only a subset of questions was selected from the CBCL [109].

Next, Pearson correlations were conducted among the predictor variables (family stress, HIV status, cortisol difference, and MAP variability) and between the predictor variables and the outcome variables (emotional control and behavioral control) (Table 4). Correlations between predictor variables and outcome variables indicated that poorer outcomes in behavioral control were associated with increases in family stress ($r = .344, p \leq .01$), greater MAP variability ($r = .203, p \leq .05$), and greater cortisol differences ($r = .179, p \leq .05$). In addition, poorer outcomes in emotional control were associated with HIV status only ($r = -.193, p \leq .05$).

Two sets of linear regressions models were computed to test the hypothesized associations between the independent variables and the outcome variables. Another regression was also performed for each outcome variable using the interaction term between MAP reactivity and cortisol difference as an additional independent variable. These analyses allowed for an investigation of how the proposed predictors independently related to behavioral control or emotional control when the other predictors were taken into consideration. Results of the regressions for behavioral control and emotional control are summarized in Table 5.

The models for behavioral control were highly significant (Regression 1: R-square = 18.5%, $F(4,118) = 6.489, p < .001$; Regression 2: R-square = 20.2%, $F(5,118) = 5.712, p < .001$). Several independent variables including family stress, cortisol difference and MAP variability were highly significant and moderately associated with behavioral control (family stress: $\beta = .324, p < .001$; cortisol difference: $\beta = .206, p < .05$; MAP variability: $\beta = .184, p < .05$). As hypothesized, poorer outcomes in behavioral control were predicted by high levels of family stress (see Figure 1) and high reactivity.

The second regression for emotional control was significant (R-square = 15.9%, $F(5,112) = 4.034, p < .05$). Several independent variables were highly significant and moderately associated with emotional control, including HIV status, cortisol difference, and the interaction term between MAP variability and cortisol difference (HIV status: $\beta = -.275, p < .05$; cortisol difference: $\beta = .846, p < .005$; MAP variability \times cortisol difference: $\beta = -.888, p < .001$). As hypothesized, poorer outcomes in emotional control were predicted by being HIV-affected (see Figure 2), cortisol difference, and the interaction between the two reactivity variables, MAP reactivity \times cortisol difference.

The interaction for MAP reactivity \times cortisol difference is illustrated in Figure 3. Emotional control—adjusted for HIV status, family stress, cortisol difference and MAP reactivity—is shown as a function of low versus high cortisol difference, within low-(1 SD below the mean) and high-(1 SD above the mean) reactivity subgroups of child subjects. Subjects are further divided into subgroups exhibiting low-(1 SD below the mean) and high-(1 SD above the mean) MAP reactivity. It was noted that poorer emotional control was experienced by children who exhibited asymmetries in the two axes of their reactivity profiles. That is, children with either low cortisol difference combined with high MAP variability or children with high cortisol difference combined with low MAP variability demonstrated the poorest outcomes on emotional control. On the other hand, children whose reactivity profiles were low in both cortisol difference and MAP variability or high in both cortisol difference and MAP variability demonstrated comparatively better outcomes on emotional control. Tests for differences in slopes among children experiencing high v. low MAP variability confirmed interactions for cortisol difference.

An important question in regard to this result is why asymmetries in the reactivity profiles of children—as opposed to overall low or high reactivity—were associated with poor emotional control. It has long been assumed that the sympathetic and adrenocortical systems work together to generate the physiological changes associated with the stress response. For example, glucocorticoids of the HPA system and catecholamines of the SAM system both increase blood glucose levels. However, the precise coordination of the SAM and HPA systems still remains a topic of empirical investigation. It has been suggested that the SAM and HPA systems are activated differentially depending on situational demands and individuals' perceptions of events, which could lead to dissociations between the two systems [112]. This theory is supported by Sapolsky and colleagues, who suggest that glucocorticoids function to both augment and suppress sympathetically mediated changes in the cardiovascular system [37]; that is, glucocorticoids serve initially as an activator of the stress response and then as a suppressor to return the body to homeostasis. Dissociations between the two systems—such that sympathetically-mediated actions are no longer responsive to glucocorticoid effects at the appropriate moment—may be part of the etiology of behavioral and emotional problems in children. Thus, optimal functioning occurs when sympathetic and adrenocortical activities are balanced, and maladaptive functioning occurs when the adrenocortical system fails to coordinate with the sympathetic response to stress.

Discussion

The goal of the present study was to identify psychosocial and physiological predictors of emotional and behavioral control during the stress of school entry in

children who are chronically ill. Results indicate that children with considerably high levels of family stress, greater school-entry related adrenocortical activation, and high MAP variability during a cardiovascular reactivity protocol had poorer scores on behavioral control. In addition, children affected by HIV (either HIV-positive or HIV-negative with HIV-positive mothers) who had asymmetries in their adrenocortical and sympathetic reactivity systems had poorer scores on emotional control. From these two primary results, we speculate that both emotional control and behavioral control are influenced by early life psychosocial stress and physiologic reactivity, but each is responsive to specific influences at different critical points along the developmental time course. While the chronic illness of HIV-positivity may have bearing on early infant-parent attachment security and the subsequent development of emotional control, family stressors such as caretaker depression and inter-family conflict may not influence the development of behavioral control until a child attains the cognitive capacity to “absorb” such stressors. Furthermore, physiologic reactivity’s influence on control may manifest itself more clearly in emotional control than in behavioral control. This may be because the myelination and neural wiring of limbic structures involved in emotion occurs earlier than the myelination and wiring of higher cortical structures which provide cognitive and associative inputs into behavior [110]. The SAM and HPA systems therefore may exert more salient effects on more proximally situated brain structures such as the limbic system. The reason to consider the developmental time course in the relationships between psychosocial stress, reactivity, emotional control and behavioral control will now be explained in the following sections.

HIV, Infant-parent attachment, and emotional control

Correlations and regressions indicated that HIV status significantly influenced emotional control. Specifically, children who were either HIV-positive or HIV-negative with HIV-positive mothers scored significantly poorer on emotional control than children who were not affected by the HIV epidemic. The effects of HIV on emotional control may make sense in the context of the host of psychosocial factors involved in HIV infection. The poverty of many HIV-infected women increases the likelihood of many risk factors, including depression, poor physical health, poor nutrition and substance abuse, which then creates obstacles to nurturing and attentive parenting [113]. One study of HIV-infected Ugandan mothers and their infants detected no differences in the security of infant attachment in HIV-positive mothers versus HIV-negative mothers [114]. However the study did find that HIV-positive mothers with AIDS had less securely attached infants than HIV-positive mothers without AIDS, indicating that the presence of AIDS symptoms may affect the quality of infant attachment. More relevant for HIV-positive mothers without AIDS symptoms is the high rate of depression, which is associated with less emotionally responsive parental care [115]. Because of the importance of maternal responsiveness to children's socioemotional development, maternal depression has been considered a risk factor for insecure attachment [116, 117]. Insecure attachments have been associated with a range of emotional regulatory dysfunctions in both human and animal models [77, 118], and insufficient maternal nurturing and responsiveness in early development has been known to cause disruptions in the development of infant self-soothing techniques, which are a basic step in emotional self-regulation [29]. Insecure attachments in toddlers were found to cause less

understanding of negative emotions [119], and the identification of different types of emotions may be a significant part of the process of emotional control.

Although this study did not directly assess the quality of infant-parent attachment, it should also be noted that less than half of the HIV-positive children lived with their biological mothers (45%), suggesting that a number of these children had already suffered from “caretaking casualties” [120]. While relatively few studies have explored the security of non-biological maternal and infant attachments, one study suggests that infants placed in foster care already experience substantially disorganized attachments with primary caregivers [120]. Thus, the lack of continuity or security in primary attachments, the chronic physical illness and depression of HIV-afflicted mothers, and the impoverished socioeconomic circumstances of many HIV-affected women may all have a negative impact on the development of emotional regulation in children.

Physiological reactivity and emotional control

Children who had greater school entry-related adrenocortical responses also had poorer scores on emotional control. Furthermore, children with asymmetries in their reactivity profiles—that is, children who exhibited either high cortisol differences but low MAP variability or low cortisol differences but high MAP variability—had poorer emotional control scores than their peers who exhibited either low or high scores on both measures of reactivity. The effect this interaction had on emotional control may be explained by a theory put forth by Bauer and colleagues that dissociations in children’s HPA and SAM systems can contribute to a number of childhood psychopathologies [112]. Sapolsky and Munck have postulated that the glucocorticoids of the HPA axis have multiple influences on the SAM system, functioning to both suppress and augment

sympathetically-mediated changes in cardiovascular function, metabolism, and fluid homeostasis at the appropriate times [37]. This suggests that optimum functioning following induction of a stressor leads to two potential sets of coordinated activity within these systems. One response would involve a rise in sympathetically-mediated cardiovascular activity in response to stress leading to a concomitant increase in glucocorticoid activity that provides negative feedback to cardiovascular activity. Alternatively, a rise in catecholamines in response to stress may initiate an increase in glucocorticoids that serves to augment or maintain SAM activity. In contrast, dissociations between the two systems may occur in one of two ways. First, a rise in catecholamines in response to stress may not induce a subsequent rise in glucocorticoids, and sympathetically-mediated cardiovascular responses to stress could go unchecked. Second, the SAM system itself may not respond adequately or appropriately to stressors, and the slow elevation of glucocorticoids in response to the stressor may have a much more delayed effect on catecholamine-induced physiological stress responses.

Either of these two forms of dissociation between the SAM and HPA systems may be the picture of what occurs in children with poor emotional control. How these two stress response systems become uncoupled is unclear, but evidence generally points to repeated early life stressors disrupting essential homeostatic processes that are crucial to behavioral and emotional responses to stress. Also known is the fact that there are distinct adrenocortical and sympathetic outflow tracts that affect brain structures involved in emotion processing and regulation [41]. Corticotropin-releasing factor (CRF) neurons in the central nucleus of the amygdala project to the locus ceruleus and increase the firing rate of locus ceruleus neurons, resulting in norepinephrine release across the entire

ascending noradrenergic system. CRF overproduction is associated with increased fearfulness in rats [41], and dissociations in these neuro-hormonal pathways may mediate maladaptive emotional responses to stress.

Although scant evidence exists for how neural circuits involved in stress reactivity and emotional processing develop in human infants, there appears to be a biological basis for the emergence of fearfulness and other anxiety emotions in infants. Across almost all cultural settings, infants around 7-10 months of age exhibit signs of anxiety when they are separated from their primary caretakers or approached by strangers [121], and this parallels the dramatic increase in synaptic density in the prefrontal cortex and the increased differentiation of glutamic pyramidal cells and GABAergic interneurons in the prefrontal cortex at this age [121]. The prefrontal cortex is responsible for combining inputs from sensory cortices (e.g., allowing the child to perceive that her mother is leaving) and the amygdala (which contributes emotional significance to the event). The prefrontal cortex then sends a signal back to the amygdala to stimulate the basal ganglia, hypothalamus, and the HPA axis, leading to a physiologic stress response. Experiential factors in early life may shape the neural circuitry of the stress response to emotionally charged stressors. Thus, the consequences of repeated exposure to very early stressors, interacting with developing neuro-hormonal stress responses patterns, can lead to the large differences observed in susceptibility to stress over time.

Behavioral control, family stress and physiologic reactivity

Correlations and regressions indicated that higher levels of family stress predicted poorer behavioral control. In this study, family stress was assessed as a combination of multiple factors, including level of inter-family conflict, chronic health and depression in

the caretaker, and major life events for the child. A review by Repetti has shown that various aspects of family discord—such as marital conflict, quarreling or fighting between parents or between parents and children, physical harm and parental aggression—create deficits in children’s social competencies and are associated with a disproportionate number of internalizing and externalizing behavior problems that begin appearing in childhood and progress through adolescence [29].

Although it is difficult to assess when behavioral problems first start to appear, it is important to note that behavior changes and becomes more complex as children age and acquire greater cognitive capacities. The neurophysiologic basis for this lies in the development of the prefrontal cortex, one of the last brain regions to mature and which plays a pivotal role in cognitive development [110]. Cognitive processes that have been attributed to the prefrontal cortex include working memory, response inhibition and attention allocation [110]. All of these processes appear to be part of the execution of specific behaviors—for example, memory, attention and inhibition are all involved in recalling certain information, attending to it, and inhibiting competing representations or memories to allow for the selection of an appropriate response. Inhibitory control appears to be at the center of cognitive and social learning throughout childhood, as this allows children to select from a range of internally-derived and externally-derived inputs and competing response alternatives [110, 122]. The acquisition of greater inhibitory control through childhood and adolescence coincides with the prolonged development and organization of the prefrontal cortex: the gradual loss of synaptic connections through childhood presumably indicates a strengthening of remaining synapses, which ultimately represents the neurophysiological suppression of competing, irrelevant behaviors. At the

same time, myelination of the remaining fibers takes place, which can account for the increased speed of information processing and behavioral responses that are observed throughout childhood and adolescence [110]. Thus, assuming that high family stress is representative of a number of complex information sources that disrupt the formation of inhibitory control and undermine the reinforcement of appropriate behavioral responses, it is plausible that distressing family environments cause the derangements in prefrontal cortical function that mediate behavioral control psychopathologies.

Results from this study also indicated that there was a linear association between the two reactivity measures and behavioral control such that children who had greater school-entry related adrenocortical reactivity or higher cardiovascular reactivity during the laboratory protocol had poorer scores on behavioral control. One possibility may be that the inability of children with highly reactive phenotypes to cope with stress manifests itself externally through poor behavioral control. However, given the interaction observed between cardiovascular and adrenocortical reactivity on emotional control, a more complicated relationship between physiologic reactivity and behavioral control ought to exist. As outlined above, behavioral responses become more complex with age, and an increasing demand is placed on cognitive inputs such as memory, attention allocation and response inhibition. The effects of physiologic reactivity may be more distal to the effects of cognitive associations on behavioral control. In other words, dissociations between the SAM and HPA systems may have less of an observed impact on behavioral control.

Limitations

Although this study offers new insight into predictors of children's emotional and behavioral control, several caveats need to be mentioned. First, the data from the original study was not designed to test these hypotheses. As a consequence, emotional control and behavioral control were measures created for the purpose of this analysis. Other previously validated measures are available to assess constructs such as planned behavior [123] and emotional regulation [124]. However, the questions selected for assessing emotional and behavioral control in this study were derived from previously validated and commonly used surveys and within this study had a high internal statistical validity. Another limitation derived from the fact that the data was not intended for this analysis is that the study methodology did not allow for full consideration of the developmental trajectory of control-related psychopathologies nor did it allow for empirical testing of causality. While this study suggests that physiologic reactivity and environmental stressors may both influence the development of emotional and behavioral control, children's emotion and behavior also exert an influence on the family environment and also may impact physiologic reactivity in this early developmental period.

Another limitation was that the number of participants in this study was small, limiting the power to detect other meaningful predictors of control. Since one of the main purposes of the study was to study children under the severe stress of chronic illness, limited conclusions can be drawn about emotional and behavioral control among a normative population. Nonetheless, these findings indicate that children affected by the HIV epidemic and children with dissociations in their physiologic reactivity systems are likely to experience difficulties with emotional control.

Conclusion

Despite these limitations, important evidence emerged from this analysis to demonstrate how family context and physiologic factors both contribute to the development of control. While multiple disciplinary fields generally recognize the importance of early life contextual factors and biology as primary influences on emotion and behavior, these results elucidate a more sharply carved path for the development of distinct emotional and behavioral regulatory dysfunctions. This study further highlights the need for adequate psychosocial support for families burdened with the chronic illness of HIV. It is from this basic knowledge that researchers can advocate for improvements in preventive health services designed to lower the risk of future emotional and behavioral psychopathologies in children.

Table 1. Subject Characteristics

	Group A (HIV+ child, HIV+ mother)	Group B (HIV- child, HIV+ mother)	Group C (HIV- child, HIV- mother)
Sample size	38	29	65
Sex	M: 53% (19/38) F: 47% (17/38)	M: 57% (17/29) F: 43% (12/29)	M: 58% (38/65) F: 42% (27/65)
Age (mean in years)	5.16	5.21	5.45
Grade	K: 76% (29) 1st: 24% (9)	K: 55% (16) 1st: 45% (13)	K: 59% (38) 1st: 41% (27)
Race	White: 18% (7) Black: 53% (20) Other: 29% (11)	White: 10% (3) Black: 45% (13) Other: 45% (13)	White: 12% (8) Black: 55% (36) Other: 33% (21)
Lives with biological mother	45% (17)	93% (27)	92% (60)

Table 2. Items Measured for Behavioral Control and Emotional Control

Behavioral Control

1. bowel movements outside the toilet
2. Can't get his/her mind off certain thoughts
3. can't sit still, restless or hyperactive
4. disobedient at home
5. disobedient at school
6. feels he/she has to be perfect
7. impulsive or acts without thinking
8. physically attacks people
9. picks nose, skin, other parts of body
10. repeats certain acts over and over
11. temper tantrums or hot temper
12. too concerned with neatness or cleanliness
13. screams a lot
14. showing off or clowning
15. stubborn, sullen or irritable
16. acts too young for his/her age

Items were rated by the primary caretaker on a 3-point scale: 0 = not true, 1 = somewhat/sometimes true, 2 = very true/often true.

Emotional Control

1. Resists change, i.e. upset or distressed when change occurs
2. has frequent temper tantrums or is irritable
3. is easily frustrated

After a testing session lasting 1.5 hours with each subject, psychologists completed the Q-sort procedure, producing subscores for four factors, including emotional control.

Table 3. Descriptive Statistics for Predictor and Outcome Variables

Variables	Mean	SD	Range
Behavioral control	4.70	3.70	0.00 – 18.00
Emotional control	3.35	0.97	1.67 – 7.00
MAP variability	6.07	2.44	2.33 – 13. 83
Family stress	0.00	1.00	-1.76 – 4.22
Cortisol difference	-0.03	0.30	-1.15 – 1.60

Table 4. Pearson Correlations Among Predictor Variables and Between Predictor and Outcome Variables

	Predictor Variables			
	Family Stress	HIV status	MAP variability	Cortisol difference
Family Stress	—			
HIV status	-.117	—		
MAP variability	.032	-.033	—	
Cortisol difference	-.047	-.004	-.002	—
Behavioral control	.344**	-.116	.203*	.179*
Emotional control	.152	-.193*	.120	-.040

* $p \leq .05$; ** $p \leq .01$

Table 5. Multiple Linear Regressions Predicting Behavioral Control and Emotional Control

	Behavioral Control		
	b	β	t
Family stress	1.182	0.324	3.786**
HIV status	-0.232	-.052	-0.610
Cortisol difference	2.625	0.206	2.436*
MAP variability	0.291	0.184	2.176*
R ²		0.185	
F _{4, 118}		6.489**	
<hr/>			
Family Stress	1.213	0.332	3.898**
HIV status	-0.111	-0.025	-0.289
Cortisol difference	-1.723	-0.135	-0.564
MAP variability	0.289	0.183	2.175*
MAP variability x cortisol difference	0.779	0.367	1.518
R ²		0.202	
F _{5, 118}		5.712**	
<hr/>			
	Emotional Control		
	b	β	t
Family stress	0.060	0.067	0.709
HIV status	-0.235	-0.209	-2.219*
Cortisol difference	0.053	0.017	0.185
MAP variability	0.036	0.094	1.008
R ²		0.062	
F _{4, 112}		1.790	
<hr/>			
Family Stress	0.043	0.047	0.526
HIV status	-0.309	-0.275	-3.001*
Cortisol difference	2.576	0.846	3.347**
MAP variability	0.037	0.096	1.084
MAP variability x cortisol difference	-0.445	-0.888	-3.502**
R ²		0.159	
F _{5, 112}		4.034*	

* $p \leq .05$; ** $p \leq .001$

Figure 1. Main Effect of Family Stress on Behavioral Control

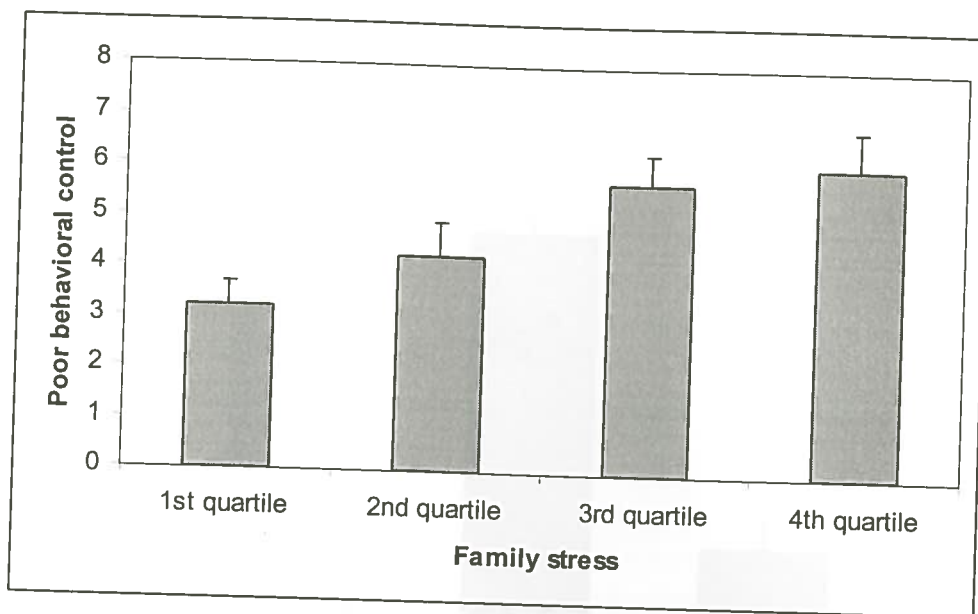


Figure 2. Main Effect of HIV Status on Emotional Control

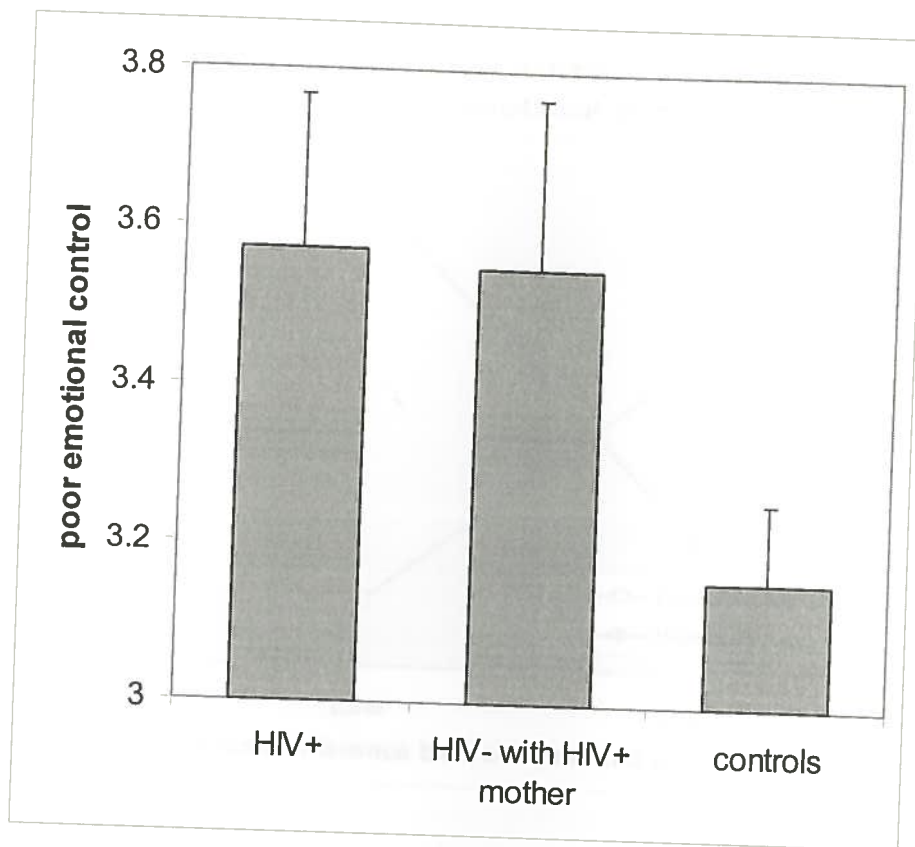
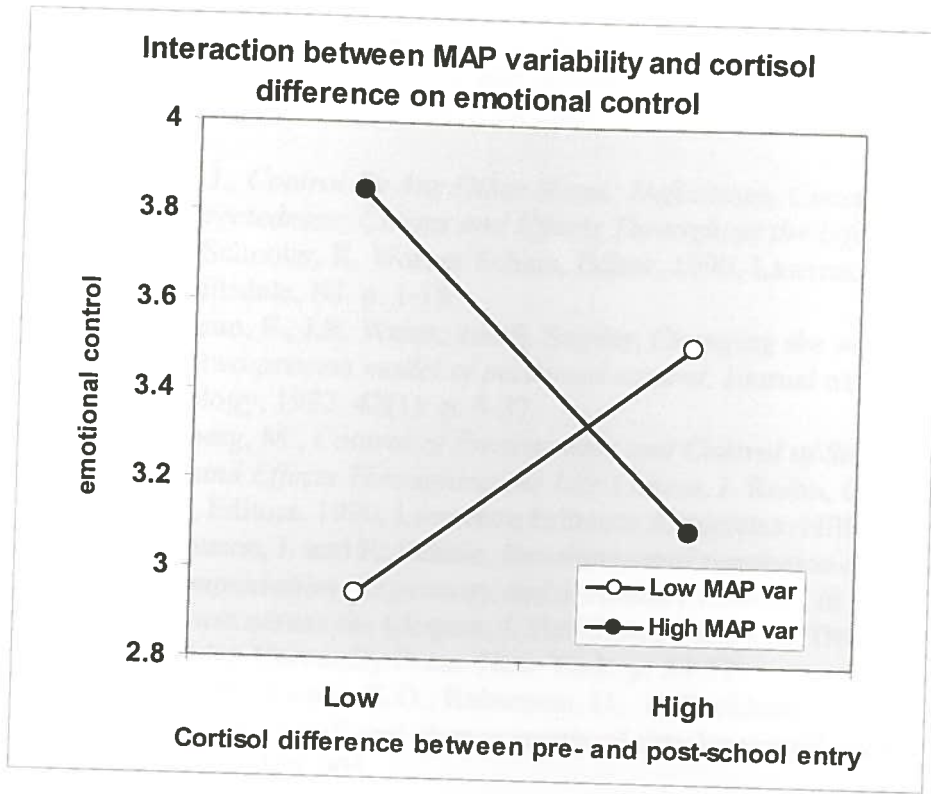


Figure 3. Interaction between MAP Variability and Cortisol Difference on Emotional Control



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