Neurobehavioral Adaptations to Psychosocial Stress in the Context of Human Evolution

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**Introduction**

The negative health consequences of stress are well documented. The human response to psychosocial stress is directly implicated in hypertension and subsequent vascular diseases. It is also implicated in reduced immune function, complicated pregnancies, reduced fertility, gastrointestinal disease and psychiatric conditions (Ader and Cohen, 1993; Bohus, 1984; Facchinetti and Ottolini, 2004; Fielding, 1989; Leidy, 1989; Rabin et al., 1986; Schneiderman and Baum, 1992; Selye, 1976). The negative impact on human health begs the question of whether human biological stress responses have an adaptive purpose and, if so, exactly how this adaptation occurs and how has it been favored by natural selection. Though there is some agreement of an adaptive function of this response, the totality of the adaptive qualities has been overlooked, as research has focused primarily on stress related pathologies (Heuther, 1996; James and Brown, 1997; Selye, 1976).

This paper will discuss the adaptive nature of the human biobehavioral responses to stress in the context of neurophysiologic, cognitive and behavioral changes at the level of the central nervous system. These changes will then be discussed in the context of natural selection. Cannon’s (1914) familiar “Fight or Flight” response and Selye’s (1976) General Adaptations Syndrome will be discussed in the historical context of stress research. Their limitations for the study of stress responses in humans will also be addressed. A review of more recent literature will demonstrate not only an adaptive mechanism in response to repeated and/or long-lasting controllable stressors, but also the possibility of positive adaptation in the response to uncontrollable stressors (Heuther, 1996).
For the purposes of this paper stress or stressor will be defined as an external psychosocial stress unless otherwise specified. Though other forms of stress such as altitude, climate, physiological stress and nutritional stress can result in adaptations in the body and in behavior, these adaptive mechanisms are beyond the scope of this paper (Frisancho, 1993). Also this paper assumes some rudimentary knowledge of neuroanatomy and neurophysiology on the part of the reader.

**Literature Review**

The study of the biological and behavioral response to stress has been greatly influenced by the contributions of Selye. Building on the identification of the “Fight or Flight” response by Cannon (1914), Selye (1976) developed a model, over several decades, to describe the general stress responses and their effects on the body called the General Adaptation Syndrome (GAS). Selye’s model is based on his years of research of the effects of artificially induced stress, including physical stress, in rats. The GAS is composed of three stages: the alarm reaction, the stage of resistance and the stage of exhaustion (Heuther, 1996; Leidy, 1989; Selye 1976).

The alarm reaction stage is the first part of the body’s response to stress. It is characterized by the activation of the peripheral sympathetic-adrenomedullary system (SAM) with the secretion of norepinephrine and epinephrine, otherwise known as the catecholamines. These hormones prepare the organism for a behavioral reaction, which Cannon (1914) referred to as “Fight or Flight.” Also, during the alarm reaction the hypothalamic pituitary-adrenocortical (HPA) system is activated. The activation of the HPA system begins the cascade that eventually releases the stress hormone cortisol. This alarm reaction stage, and its release of catecholamines, prepares the body for action by
increasing heart rate, decreasing blood flow to the organs not needed for immediate 
action, mobilizing energy stores and increasing blood pressure (Heuther, 1996; James and 
Brown, 1997; Selye, 1976).

The stage of resistance is characterized by the biological changes in the organism 
that cause the tissues of the body to build resistance to the stressor. The last stage of the 
GAS is the stage of exhaustion, and it is characterized by the gradual decline of the 
resistance of the tissue’s resistance to the stressor resulting in disease (James and Brown, 
1997; Selye, 1976).

According to Heuther (1996), the GAS model has driven stress research 
throughout the twentieth century, and the focus has primarily been in the context of 
stress-induced pathologies. Heuther (1996) calls this as “a reductionistic-mechanistic 
view of stress induced pathology.”

Heuther argues that research on artificially induced stress in rats is not sufficient 
to the answer the questions about the adaptive nature of stress in humans. He calls for a 
more complex evaluation of the stress response in humans in the context of evolution. 
The central stress response systems and their peripheral effector systems in lower 
vertebrates are not highly differentiated. The response is poorly controlled by regulatory 
feedback systems, and this stress response in these animals does not result in long-term 
adaptive reorganization of the brain or modification of behavior (Heuther, 1996). These 
animals have a limited and predictable behavioral response to stressors; it is “fight or 
flight” (Cannon, 1914). The lower vertebrates’ behavioral responses are innate and 
inflexible; Heuther refers this to as the archaic stress response (1996).
Further research into the central stress response of lower vertebrates to any type of stress has revealed that afferences from only a few key brain structures are involved in the activation of the neuroendocrine stress response and the mechanisms involved are rather simple. Different kinds of stressors elicit the same behavioral responses in the lower vertebrates, and repeated exposure to the same stressor does not attenuate the activity of the neuroendocrine response (Heuther, 1996).

The archaic stress response can be elicited in higher, socially organized vertebrates under extreme conditions. The activation of this response and the subsequent “fight or flight” (Cannon, 1914) behavior can, no doubt, serve an adaptive function favored by natural selection to some extent. However, the study of higher vertebrates in their natural environments demonstrates that a complex central stress response is triggered more frequently by social conflict, rather than by life threatening scenarios. In short, the response is triggered most frequently by psychosocial stress (Heuther, 1996; James and Brown, 1997; Vermetten and Bremner, 2002).

Not only are the triggers different and more frequent in the higher vertebrates, the physiology of the stress response is much more complex than in lower vertebrates. In higher primates stress can act as a trigger for that adaptive modification of the brain structure and function. This serves to adjust or change the behavior of the individual in response to the stress (Heuther, 1996; Vermetten and Bremner, 2002). Heuther (1996) argues that it is the higher associative brain structures in which stress is recognized and the response is initiated. Subsequently, these are the structures that are acted upon by the stress response and where adaptation occurs. It is not the protective nature of the single response and the subsequent behavioral action that is adaptive, as in the archaic response,
but it is the modifications to the brain and changes in behavior that are more adaptive in the context of psychosocial stress (Heuther, 1996; Vermetten and Bremner, 2002). The brain is the key target of the stress response; there are complex feedback and feed forward systems, which cause modification of the brain and subsequently cognitive and behavioral modification with repeated exposure to psychosocial stress (Heuther, 1996; Vermetten and Bremner, 2002).

The repetition of the short-lasting stress responses caused by controllable stressors is generally considered a positive adaptive event. When controllable stressors have been studied in higher mammals, a complex activation system for the SAM and HPA systems has been identified. This activation system involves afferences from the prefrontal cortex and the amygdala, as well as other cortical and subcortical memory storage areas. It has also been demonstrated that different controllable stressors elicit different central stress responses, which translates into different patterns of activation of the HPA and SAM systems. The central and the subsequent behavioral responses of an individual to repeated controllable stressors are dependent on past experiences with that particular stressor. The central response is also attenuated with repetition of the stressor. Interestingly, a large degree of variability of the central stress responses exists among individuals exposed to the same stressor (Bear et al. 2001; Heuther, 1996; Vermetten and Bremner, 2002).

A neuroendocrine stress response, the central stress response, will only be activated if the individual does not possess an efficient enough system of mechanisms and strategies to control the challenge presented by the stressor. Successive attenuation of the central response occurs with repeated exposure to the potentially controllable stressor via
the facilitation of those mechanisms, which adapt themselves to control the stressor. The result of this repetition of exposure and the successive facilitation of coping strategies is adaptive behavioral specialization. These strategies allow the individual to act as opposed to simply reacting to the stressor. With the increased success of each action in response to the stressor comes the increased involvement of more neuronal pathways and synaptic connections associated with the action. A behavioral response is learned and stored. This increases the positive adaptive nature of the response to controllable psychosocial stress. These specialized responses to controllable stress are much more adaptive than the archaic stress response in the context of psychosocial stress in socially organized animals (Heuther, 1996). What about uncontrollable stress?

Uncontrollable stress occurs when these specialized coping strategies for controllable stress are used in an ever-changing social environment where they are not suited to the rapidly occurring new stressors. Generally the long-lasting activation of the central stress response resulting from severe, uncontrollable stressors is attributed to disease processes (Heuther, 1996; James and Brown, 1997; Vermetten and Bremner, 2002).

Heuther (1996), not discounting the resulting pathologies, offers an argument for a positive adaptation of brain reorganization triggered by uncontrollable stress. Heuther proposes the possibility that the behavioral, neurochemical and neuroanatomical consequences of exposure to uncontrolled stress may result in a neurological reorganization that serves as a positive adaptation. He supports this with several points.

First he states that, in socially organized higher vertebrates, uncontrollable psychosocial stress is an essential feature of their lives particularly during developmental
periods. He also states that even uncontrollable stress need not be associated with life-threatening events. Secondly, Heuther (1996) argues that the reorganization of the neuronal circuits in the associative brain is the result of a reaction to uncontrollable stress. Next, he states that neuroendocrine stress response preferentially targets and influences brain structures involved in emotional and motivational behavior. Lastly, Heuther proposes that those genotypes which allowed their phenotypes to experience severe and long-lasting activations of the stress response systems and subsequent reorganization of the associative brain structures would be favored by natural selection (1996).

For these changes to occur in the brain there must be a certain level of neural plasticity. Though it has been previously believed that neural plasticity is severely reduced or even eliminated in adulthood, this has been demonstrated to be incorrect in numerous studies of neural adaptations to stimuli in adults. The plasticity of the brain allows for that adaptation to stress as well (Dowling, 2004; Huttenlocher, 2002).

To better understand the response to and the processes of adaptation to uncontrollable stressors per Heuther’s (1996) argument, as well as the adaptation to controlled stressors, the physiology of the central stress response in humans must be discussed in more detail.

The associative cortex of the brain is implicated in the interpretation of threatening stimuli. Once the threat is recognized, the activation of the limbic system occurs. The limbic system is involved in the processing of emotions, and its activation results in the arousal of fear and anxiety. At almost the same time in the sequence of events the central noradrenergic system, the corticotrophin releasing factor (CRF) system,
then the hypothalamic hyposeotropic system are activated. This results in the general 
neuroendocrine response (Bear et al., 2001; Heuther, 1996; Vermetten and Bremner, 
2002).

The arousal of the limbic system and the associated fear and anxiety is a 
prerequisite to the activation of the stress response. The limbic system is composed of 
several anatomical structures of the brain, each with a specialized function to serve the 
system. They are the hypothalamus, septum, hippocampus, ventral striatum and the 
amygdala. The hypothalamus is associated with the expression and/or the organization of 
motivated behavioral responses and endocrine responses. The amygdala is a primary 
player in the arousal of fear and anxiety and the unleashing of the neuroendocrine stress 
response (Bear et al., 2001; Heuther, 1996; Vermetten and Bremner, 2002).

The amygdala is crucial in the acquisition of conditioned fear as well as the 
consolidation and expression of conditioned fear. It is also involved in attention and 
social behavior. The amygdala is allows for the retrieval and the emotional analysis of 
information about the stressor. The activation of it is essential for the stimulation of the 
HPA and SAM systems if the stressor is emotional in nature. The connection of the 
amygdala to other brain structures and regions implicated in the integration of autonomic 
and endocrine responses to stress further demonstrates its critical role in the central stress 
response. The central nucleus of the amygdala holds many CRF containing neurons, 
which project into the hypothalamus and brainstem. Originating in the central amygdala 
are extensive descending pathways, which terminate at the levels of the midbrain, pons 
and medulla, which includes the serotonergic and catacholaminergic nuclei. It is thought 
that along these efferent pathways the amygdala coordinates the behavioral, autonomic
and endocrine aspects of the stress response (Bear et al. 2001; Heuther, 1996; Vermetten and Bremner, 2002).

The amygdala receives afferences from the prefrontal cortex, hypothalamus, hippocampus, brainstem (pons and medulla) as well as inputs from the memory storage regions at the cortical and sub-cortical levels. The prefrontal cortex’s activity is controlled by the mesocortical dopaminergic system. There are ascending noradrenergic projections to the frontal cortex to the mesolimbic and mesocortical dopaminergic systems to the amygdala and to the hypothalamic nuclei. These projections exert a potentiating and reinforcing effect on the activation of the HPA system as well as the generation of fear and anxiety (Bear et al., 2001; Heuther, 1996).

Psychosocial stress and fear activate the noradrenergic cell groups of the brainstem. This occurs via the descending fibers, which contain CRF, primarily from the amygdala. These fibers project into the medullary noradrenergic cell groups and release CRF. During extended or intense activation further release of CRF is provoked via efferences back to the amygdala. In the course of the central stress response the release of both CRF and noradrenaline is escalated via this positive feedback loop (Heuther, 1996; Vermetten and Bremner, 2002).

The locus coruleus, which is located bilaterally in the pons, contains about one-half of all the noradrenergic neurons in the brain. It has a dense efferent network, which covers most of the forebrain. The locus coruleus is integral in the control of arousal and vigilance reactions to environmental stimuli. It also acts as a relay station for peripheral autonomic inputs into the brain. Since there is similarity between the sympathetic
neurons and noradrenergic neurons in forma and function, the locus coruleus is thought to be a central analog of the peripheral sympathetic ganglia (Heuther, 1996).

The activation of both the central and peripheral noradrenergic systems via acute stressors indicates that these two components operate as a single, extended noradrenergic system. This single, extended system with innervations to both central and peripheral targets participates in the body’s global response to perceived threats/stressors. Evidence suggests the central noradrenergic component of the system is controlled by mechanisms similar to those, which control the peripheral, sympathetic activity (Bear et al., 2001; Heuther, 1996).

The increased biochemical indices of central noradrenergic activity in extensive areas of the brain are well documented. These areas include the hypothalamus, the amygdala and the cortex. Individual brain regions are affected to differing degrees by the stress-induced activation of the central noradrenergic system, depending on the origin of their noradrenergic innervations. GABA-ergic and opioid peptidergic inhibitory neurons control the activity of the central noradrenergic cells. The secretion of adrenal corticosteroid is the final step in the neuroendocrine response beginning in the thalamus (Heuther, 1996; Vermetten and Bremner, 2002).

According to Heuther (1996) the activation of the central stress response serves and adaptive function. The central stress response is only triggered if a stressor cannot be controlled by a behavioral response to the threat. He argues that the central stress/neuroendocrine response is not a necessary, but a possible response of the activation of the cortical and limbic brain structures involved in evaluating and reacting to the stressor. Triggering of the full-blown response is dependent on the efficiency in
which the initial activation of the system will be propagated to the central effector systems of the neuroendocrine stress response. Several built in feedback and feed forward loops exist (see Figure 1.) at the levels of the cortical, limbic, central noradrenergic, HPA and SAM systems. These loops are activated during the central stress response and serve to either suppress or enhance further propagation of the central stress response and can facilitate reorganization of the brain (Heuther, 1996).

For example, noradrenaline regulates the effectiveness of other excitatory or inhibitory inputs into a given neuron. The increase of biochemical indices of central noradrenergic activity in various structures and regions throughout the brain occurs in response to stressors. The locus coeruleus has a large efferent network of projections throughout the brain. Major input from the locus coeruleus into the cortex and hippocampus occurs via the dorsal noradrenergic bundle. Specifically, noradrenaline promotes the target neurons’ responses to other strong afferent inputs while reducing the neuron’s spontaneous activity (Heuther, 1996). In short, it shapes the firing of the target cells in favor of a specific type of response. Activation of the central noradrenergic system translates into the facilitation of a behavioral output in response to stimuli. The interaction of noradrenergic system with the various structures of the brain helps to facilitate a behavioral response for that same or a similar stressor. The activation of this system by an uncontrollable stressor results in a neurophysiological modification. This modification facilitates the acquisition and retention of sensory information and behavioral responses, which make the stressor controllable (Heuther, 1996). This is an example of changes that result in attenuation of the central stress response and
subsequent reorganization of the brain to adapt to the stress. The response can also be perpetuated by the intricacies of the system.

The noradrenergic system operates in a feed forward mode to perpetuate the central stress response at the levels of the cortex, the amygdala, the hypothalamus and the mesolimbic and mesocortical systems. Its impact on the amygdala during acute stress results in the stimulation of CRF release in the noradrenergic nuclei and potentiates the firing of these neurons. This same kind of potentiating effect occurs in the prefrontal cortex, which is also affected by the mesocortical dopaminergic system. One will recall that the mesocortical system is also stimulated by the afferences of the noradrenergic system (Heuther, 1996).

The various feedback and feed forward mechanisms provided by Heuther (1996) in support of the neurobehavioral adaptation to uncontrollable stress are convincing. Also, the generally accepted adaptive mechanism to controllable stress is valid in regard to its function (Vermetten and Bremner, 2002). However the question at hand is whether or not either or both of these are adaptations that could have been selected for in humans by the forces of natural selection, especially in light of the known health consequences of stress seen in modern humans.
Numerous studies have demonstrated the negative effects of the psychosocial stress of modern lifestyles on the human body. For example, hypertension is a significant risk factor for cardiovascular disease (Andre-Petersson, et al., 1999). Increased arterial blood pressure resulting from catecholamine release triggered by the central stress response has been implicated in response to psychosocial stress in populations experiencing rapid modernization throughout the world (Dressler and Bindon, 1997;
Dressler et al., 1987; James and Brown, 1997). Other studies addressing job related psychosocial stress have demonstrated correlations between increased stress level and hypertension (Garruto et al., 1999). Vascular disease is not the only negative effect of exposure of humans to stress.

Stress has been attributed with decreased immune function, which can have immediate implications regarding and individual’s survival at any age, especially during childhood (Ader and Cohen, 1993; Flinn and England, 1997). Altered immune function makes the individual susceptible to infectious diseases.

The negative health effects of stress on fertility, in men and women, and during pregnancy are also well established. Stress has been demonstrated to be a factor in pre-term delivery and other complications at birth and during pregnancy. This includes the effects of decreased immunity during pregnancy, which can adversely affect the chances of delivering a healthy offspring (Facchinetti and Ottolini, 2004; Rabin et al., 1986). With these adverse consequences of the exposure to stress in modern humans in mind, one has to wonder how the central stress response could have served as a positive adaptive mechanism that was selected for by the forces of nature.

Discussion

There is an obvious, potentially positive adaptive purpose for behavior elicited by the primitive “Fight or Flight” response (Cannon, 1914). This may have been perpetuated by natural selection, as it can still be elicited in humans, but it is less functional in socially organized animals than other more specialized and useful responses (Heuther, 1996). What of the more common responses to psychosocial stress in the context of the long-term health consequences? What could the adaptive nature of these responses be?
Naturally it would appear that, at least in the present, the effects of stress on humans are maladaptive given the extensive list of stress-related, potentially fatal ailments. However, if one considers the age at which stress related vascular disease is usually fatal, one quickly realizes that it may not reduce an organism’s chances of producing offspring. So, in this sense it is not particularly maladaptive when viewed in the context of natural selection. Also the amounts, intensities and lengths of exposures to psychosocial stress in early human hunter-gatherers could probably be assumed to have been much less. Therefore the chronic diseases, such as vascular disease, observed as a result of modern stressors have little bearing on the effects of natural selection in early humans’ responses to stress.


Increased risk of contracting infectious disease associated with decreased immune function could have been a selective factor in those who were not genetically equipped with the neurobehavioral mechanisms to adapt to stress (Heuther 1996). The same stressors would have more adversely affected some individuals than those who were equipped with a more adaptive neurobehavioral system. This could have been a pivotal selection factor as human populations grew, as people became sedentary and infectious diseases became more prevalent (Cockburn, 1977). Changes in population, subsistence and settlement also resulted in more socially complex cultures, possibly increasing the amount and frequency of psychosocial stress. The demands on the stress
response systems of humans would have been taxed, and those who were more adaptive would have staved off infection and subsequently been more likely to reproduce. The same selective pressure against those poorly equipped to adapt to psychosocial stress could also have occurred as a result of decreased fertility and decreased ability to deliver a healthy viable offspring (Heather, 1996).

Looking at the pathological results of decreased ability to adapt to stress is only looking at one side of the coin. Given the likely existence of psychosocial stress in early human societies, albeit probably much less than in the present, a neurobehavioral mechanism to adapt to such stress could conceivably have been favored by the forces of natural selection in a much more subtle way. The demands of living in social groups and managing subsequent psychosocial stress could potentially impact an individual’s ability to compete for mates or otherwise function as a member of the social group. It could also impact the ability to rear children effectively and/or impact the number of offspring that could be successfully reared.

Conclusions

Given the evidence for positive neurobehavioral adaptations in response to stress and what is known about stress related pathology, some conclusions may be drawn. The adaptive mechanisms in the central nervous system’s response to psychosocial stress are complex and highly specialized, much more so than the archaic stress response (Heather, 1996). It could also be argued that they are more highly evolved. In spite of the diseases associated with long-term exposure to chronic stress, the central stress response is likely an evolutionary adaptation favored by the forces of natural selection. In fact, some of the ill effects of exposure to stress provide evidence for ways in which the central stress
response could have been selected. The focus of the study of stress primarily in the
context of stress related pathological conditions has limited the knowledge about and the
consideration of the neurobehavioral stress response as a positive adaptation. Further
investigation of the stress response in the context of evolution and natural selection may
be able to shed light on some of the propositions discussed here in regard to the forces
selecting for such a stress response in early humans.
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