Psychophysiology of Chronic Stress: An example of Mind-body Interaction

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ABSTRACT

We present an example of mind-body interaction through the psychophysiology of chronic stress. We show the dynamic pattern of effects on the mind and body associated with chronic stress response and recognize how the mind coordinates the body systems to sustain internal equilibrium for optimal function. In fact, many other bodily illnesses are caused by an interaction of mental and physical subtleties. It is important to note that these psychophysiological disorders bring actual physical damage. This review provides a clear direction in understanding how the mind controls the stress response, facilitates positive change, and improves the ability to cope with stress that can be the key to successful healing for overall physical and mental health.

Key Words: mind-body, allostasis, anxiety, depression, stress, homeostasis, hpa axis, physiology of stress responses, chronic stress on the brain, stress-related disorders, stress hormones, cortisol, psychophysiology

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Introduction

Stress is how the brain and body respond to any pressure, demand, or upsetting change that can lead to psychosomatic dysfunction. Stress arises when the demands exceed the adaptive resources required to cope with maintaining homeostasis. Homeostasis is a vital and automatic process by which the physiological system maintains dynamic stability necessary for optimal body functioning despite disturbances from external demands (Segerstrom et al., 2017). Stress manifests in several forms that could be physical and mental reactions to protect oneself from potential threats from either external demands (i.e., psychosocial situations) or internal demands (i.e., sickness, negative thoughts) causing bodily and mental strains that exceed the ability to preserve homeostasis (Deckers, 2018; Segerstrom et al., 2017). Although a little bit of stress can be healthy as it motivates the mind to act quickly and focused, in effect, it can help sharpen the mind and improve the ability to remember details about what is happening. This particular stress is termed “eustress” and has a positive effect on health and performance that keeps the mind vital and excited about life even as stress increases.

Conversely, a negative stress “distress” is harmful under which health and performance deteriorate. A natural state of equilibrium, “allostasis” refers to the body’s attempt to sustain homeostasis by continually reacting to external forces that attempt to disrupt the balance. The body attempts to maintain this equilibrium through physiological or behavioural change to ensure that the brain can still manage when life stressors jolt the mind into instability (Gibbons, 2012; Sterling, 2012; Selye, 1983). Maintaining a stable condition of bodily functions and its internal environment is key to overall health. Sterling (2004) described that allostasis is the process of achieving homeostasis through physiological and behavioural change. It represents the adaptation process of complex...
physiological systems to physical, psychosocial, and environmental challenges. In essence, while homeostasis describes a specific condition, allostatic is a process of achieving stability. However, when the stress response continues to act, it can be detrimental, something negative causing anxious feelings as though the brain has no control over the situation because the brain does not possess the appropriate repertoire to cope with such stressors. Gradually it could put health at risk, and the more adverse and stressful the situation becomes. Exposure to repeated stress contributes to “allostatic load” (McEwen et al., 2015) as demonstrated in Figure 1, the frequent disruptions of biological processes resulting from chronic stress can be harmful to both physical and mental health. Allostatic load pathology stemming from dysregulation of any one of these systems will also produce a vulnerability to other allostatic pathologies (Fig. 1 and 2).

Stress reactivity is better understood as the result of intertwined psychological and biological processes that ultimately ensure the body's more optimal functioning. Stress is a perceived demand or threat (Stressor) to our mind, body, value system, or emotions and its associated reactions in these same systems. Strong evidence indicates that the core emotional regions of the brain constitute the primary mediator of the well-established association between stress and health, as well as the neural focus of “wear and tear” due to ongoing adaptation (Ganzel et al., 2010). The allostatic load supposedly accumulates throughout life and affects multiple bodily systems. What the mind thinks and feels can affect what happens to their body, conversely what happens in their body can affect the mind and how they think and feel. What is happening in the body continuously changes the mind. The synergy of this relationship is that the mind, in response, also directs and changes the body. The mind-body interaction is the relationship between human thoughts, emotions, and bodily responses. That is why the psychosomatic disease is a physical illness or disorder that is caused or aggravated by emotional stress.

The Stress Response System: Hypothalamus Pituitary Adrenal Axis

The brain is the organ of stress response because it determines what is threatening, and therefore stressful (McEwen, 2007). It also regulates the behavioural and physiological responses to potentially stressful experiences. The stress response begins when the amygdala perceives danger. It determines how the body should respond emotionally by using input from brain’s stored knowledge. The hippocampus and the amygdala regulate the hypothalamic-pituitary-adrenal (HPA) axis, which mediates fight or flight response (Heim et al., 2008). The hypothalamus, a tiny region at the base of the brain, functions like a control tower, communicating with the rest of the body through the nervous system so that the body has the energy for fight or flight (Jansen et al., 1995). Stress triggers the HPA axis, a neuroendocrine system that regulates central and peripheral homeostatic adaptive responses to stress (Freberg, 2015; Bale and Vale, 2004). The HPA axis regulates various bodily processes and is a vital component of the body’s neuroendocrine response to stress.

Figure 1. A schematic representation of the brain and hormonal mechanisms responsible for hyperactivity of hypothalamic-pituitary-adrenal (HPA) axis in response to stress. When the brain receives stress signal, the hypothalamus activates the release of CRH (corticotrophin releasing hormones) and funnels them to activate the pituitary glands found below the hypothalamus, which ultimately control the other endocrine glands and body’s hormonal response to stress. The CRH activation triggers the release of adrenocorticotropic hormone (ACTH), which is carried by the blood to the adrenal glands located on top of each kidney. ACTH in turn stimulates the adrenal glands to produce the stress hormones cortisol, adrenaline and noradrenaline and releases them into the bloodstream to assist the body to handle stress better. Cortisol and other stress hormones are carried via blood stream to relevant organs and muscles mobilizing the body’s resources by increasing energy and decreasing inflammation, especially in injuries. However, high levels of cortisol due to unrelenting stress can wear down the brain’s ability to function properly including metabolism. Healthy body functioning can be disrupted when cortisol is released in excess due to prolonged activation of stress response systems in the body and brain. So when high amounts of cortisol interact with the hypothalamus, the HPA axis will slow down its activity to maintain hormonal balance within appropriate levels.
During stressful situations, the body reacts by secreting stress hormones into the bloodstream. Hormones are complex chemicals that convey messages to organs or tissues throughout the body via the bloodstream and trigger specific responses. The hypothalamus triggers the pituitary gland, which causes secretion and synthesis of another hormone called corticotrophin-releasing hormone (CRH) that enables the body to continue to resist the stress until homeostasis returns (Aguilera 2011). As outlined in Figure 1, the CRH stimulates the pituitary gland to secrete adrenocorticotropic hormone (ACTH) into the bloodstream. The anterior pituitary gland controls the secretion of ACTH in response to CRH from the hypothalamus. The adrenal gland receptors detect the high levels of ACTH, which stimulate its secretion of cortisol. Often called the stress hormone, cortisol regulates energy-controlling blood sugar levels, mobilizes energy to target tissues and muscles, and reduces inflammation in the body. Cortisol concentration plays a vital role in the body's stress response as an indicator of stress level (Cook 2002). As illustrated in Fig. 1, when cortisol levels rise, the HPA axis starts to slow down the release of CRH from the hypothalamus and ACTH from the pituitary gland. Having the right cortisol levels is essential for proper body functioning.

As an adaptive response to stress, the level of various hormones also changes. When stress goes high, so does cortisol level (Ebrecht et al., 2004; Mavoungou et al., 2005). Correspondingly, the ACTH levels start to fall when cortisol is high. Sustaining a stable secretion in these brain hormones improves the ability to maintain a healthy, balanced mood which is mutually supporting physical health. As detailed in Fig. 2, the end-product of the HPA axis is cortisol and other stress hormones norepinephrine and epinephrine, which contribute to the inflammatory response. Cortisol, an essential glucocorticoid, has many significant functions in the natural processes of the body, involved in regulating metabolism, immune response, and general homeostasis. (Morey et al., 2015; Adam et al., 2006). Cortisol puts the body into a general state of arousal, giving that hyperactive feeling when stress starts to have an effect. Further, cortisol by tapping into proteins stored in the liver provides the body with high amounts of glucose in the bloodstream, enhances brain's use of glucose and increases the availability of substances that repair tissues and reduce inflammation (Otmishi et al., 2008; Gunnar and Quevedo, 2007).

While stress itself is not necessarily problematic, the build-up of cortisol in the brain can have long-term harmful effects (Pawelec et al., 2005). The mechanisms of hormonal release involved in response to stress can impact human behaviour and more negative effects on health. In moderation, the cortisol hormone is perfectly normal and healthy (Fig. 1). However, when chronic stress goes on, the body is in a state of continuous physiological provocation that can lead to health problems (Pasquali et al., 2006; Otmishi et al., 2008). As a result, a high amount of cortisol leads to severe fatigue, difficulty concentrating, irritability that leads to anxiety and depression (Schneiderman et al., 2005; Ebrecht et al., 2004). Eventually, with long-term stress or constantly repeating triggers such as with the repeated experience of symptoms, the cortisol hormone release does not shut down, leading to increase blood sugar levels (Hucklebridge et al., 1999). Consequently, continuing activation of the stress-response system and the overexposure to cortisol and other stress hormones that follow can disrupt almost all body's processes and homeostasis.

Figure 2. Illustrates that sustained or repetitive stress can increase vulnerability to certain diseases due to some maladaptive changes. If the resistance reaction fails to overcome the stress, eventually, the body reserves are exhausted, and the resistance reaction (adaptation) cannot sustain. The duration and severity of a stressful situation can sometimes be out of proportion to the original trigger or stressor – a situation where the mind feels the demands outweigh the resources to cope appropriately. Allostasis is essential to enable the body to maintain stability amidst change. Defending the body against the challenges of internal and external stressors can also contribute to allostatic load, which results from being stressed out.
Anxiety is a physiological and psychological response to something destructive that might happen in the future. Thus, it is always future oriented, fear-based and focused on worrying over what is about to come, and conceivably one may become excessively apprehensive about the outcome of routine activities. Anxiety is a problem when it becomes pervasive and intense, resulting in helplessness and isolation. It is important to note that the entire process begins with negative thoughts due to stressful events and constant threats that intensified over a long period, escalating until panic attacks set in.

The anxious mind scantly protected against these threats becomes vulnerable to negative emotions. An affected mind feels a sense of insecurity and helplessness, becoming withdrawn and isolated. It is important to note that the entire process begins with negative thoughts due to stressful events and constant threats that intensified over a long period, escalating until panic attacks set in. Even with the absence of actual danger, panic attacks are associated with overwhelming anxiety and fear, more severe and intense than anxiety. As schematized in Fig. 3, intrusive thoughts build-up recurring concern of situations involving harm or danger and bring about the onset of anxiety and panic disorder. Feelings of extreme apprehension of impending doom occur even in the absence of actual danger.

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extends beyond logical worry in an unreasonable, unwarranted, uncontrollable way. A diffuse apprehension that is vague and is associated with feelings of uncertainty and helplessness. An earlier investigation of Monroe and Simons (1991) reported desparate stress reaction, untreated anxiety disorder, and difficulty controlling it - precipitate and intensify the actual onset of depression. While depression and anxiety are two different conditions, their symptoms, causes, and treatments can often overlap. As the stress and anxiety escalate, apprehension builds up, compounded with poor coping strategy, exhaustion sets in, and this can trigger depression. Chronic anxiety can increase the risk of depression.

**How does Stress Trigger Depression?**

Stressful experience and chronic stress typically precede the onset of depression and are associated with symptoms of depression. Research suggests that continuing difficulties, (e.g., long-term unemployed, death of a loved-one, uncaring relationship) are most likely to cause depression than recent life stresses. Early clinical observations have documented that deficiencies of certain chemicals in the brain lead to depression (Gold et al., 1985). Subsequent studies have shown that the depressed person has hypersecretion levels of CRH and cortisol (Epel, 2009). The body thus stays revved up and on high alert (Fig. 3 and 4). Symptoms can be much more intense such as a constant feeling of sadness, and loss of interest. It is loss based, an accumulated sense of frustration either physical or psychological, a condition in which the mind feels discouraged, sad, hopeless, unmotivated in life. Depression is a normal temporary reaction to life events, such as the loss of a loved one (Heim, 2008). Anyone experiencing too much pressure can become emotionally exhausted, overwhelmed, and unable to concentrate. It affects self-esteem, decision making, all of which make it hard to feel positive and progressive (Schlotz et al., 2011; Kendler et al., 1999; Segerstrom and Miller, 2017). If such symptoms of stress and anxiety carry...
on long enough, then depression is often a logical outcome (Kindler, 2004).

Depression is a real, pathological condition with many emotional and mental difficulties due to earlier psychological trauma that can resonate throughout life, eventually manifesting themselves as depression (Storr et al., 2007; Phillips, 2015; Lewinson et al., 2000). Minds that go through those traumatic events have direct personal experience outside the usual range of human involvement of uncontrolled threat, events that challenge the limits of the brain's capabilities and self-concept while confronting challenges or internal conflicts (Ridley, 2003). Evidence derived from observational studies claim these conditions can occur after triggering a distressing event (Carlson et al., 2001), or usually begin at a young age which can be perceived differently since the brain rewires in a way around the trauma (Gee et al., 2013; Jeronimus et al., 2013; Crews 2008). Comparative studies revealed that children raised in orphanages showed neuropsychological deficits and lower IQ scores than those children who grew up with their parents (Van Ijzendoorn and Juffer, 2006; Sonuga-Barke et al, 2010). Also, other studies consistent with those observations and natural experiments indicate that childhood adversities such as bereavement, parental separation, mental and physical abuse in particular, significantly correlates with the likelihood of experiencing depression (Lindert et al., 2014; Pillemer et al., 2010; Short, 2002; Twenge, 2000). Exposure to nonresponsive environments and the absence of good early care impact physical, biochemical, and mental responses inside the body and may also affect mental function and performance (Schneiderman et al., 2005; Lowenthal, 1998, Peterson and Seligman, 1984).

Figure 4. Demonstrates depressed mood ultimately develops when the mind with negative outlook experiences repeated stress. Depression is a whole mind-body illness, involving the moods and thoughts. One of the manifestations of depression is the presence of automatic negative thoughts about self and the future, which in turn perpetuates and increases depression. The body's activity levels decrease, one may become even less motivated and more lethargic. The mind then reacts to anxiety, which creates added symptoms, and the cycle continues until exhausted, fatigue sets in leading to more depression. Depression involves feelings of despair, hopelessness, which in turn lead to a lack of motivation and energy, and thus inactivity and isolation incline to more depressed feelings. Along with a persistent overall low mood, other symptoms can include tiredness, low self-esteem, difficulty concentrating, self-harm, and in more severe cases, suicidal thoughts.
The depressed mind is wandering full of self-condemning desperate thoughts, always preoccupied with unpleasant worries as though it is hopeless (Phillips et al., 2015; Kendler et al., 1999). Depression is not merely a sudden change in mood, laziness as a sign of weakness, or character flaw. It is more than the feeling of sadness that brings intense feelings of hopelessness and dejection to a point where the mind cannot take part in everyday life and normal functioning (Kingston et al., 2016). Hence, depression is a health condition that needs understanding, treatment, and care. Studies pointed out that depression is a wide range of mental health problems characterized by feeling down or sadness, social withdrawal, loss of interest, feelings of guilt, low self-worth, disturbed sleep, loss of appetite, severe fatigue and poor concentration (Andrew et al., 2009; Cassano and Fava, 2002). Categorically if there is no support, these negative feelings can spiral into destructive thoughts and strong enough to disrupt critical bodily processes completely. In this context, the depressed mind does not worry much about the future. At its most severe, depression can be life-threatening and the mind constantly jump to the worst, often assume a terrible future and do not expect anything else or think there is anything worth preventing. Unfortunately, the chronic and devastating nature of depression makes the prognosis of many chronic diseases complicated and aggravates the situation of disease and disability (Krishnan and Nestler 2008; Horwitz 2010).

Stresses of modern life are more likely to be chronic from adverse interpersonal and psychological consequences in subtler ways that exacerbate depression (Shaw et al., 2015; Park et al., 2015). Normal pressures with the endless demands of work and family responsibilities can leave the body feeling over-burdened and stressed out. Over time, with continuous exposure to stress, the body runs down, triggering both anxiety and depression (Shalev et al., 2017; Hammen 2005). In essence, the frantic schedule of modern living creates stress, and the brain registers stress as the threat, danger or loss (Hostliner et al., 2014; Hersen and Rosqvist, 2008). These SAD reactions start in the brain and spread through the body to make adjustments for the best defence (Uncapher and Wagner, 2018). Whether or not the mind has any “valid reason” for feeling depressed, the brain interprets reaction to stress as a significant loss, and quite often, the threat or impending danger (Shalev et al., 2017; Hostliner et al., 2014; Kemeny 2003). Unreasonable and negative thinking patterns dominate; as a result, negative emotions arise - coax into expecting the worst outcome in any situation will occur. Ultimately, this can also leave the mind vulnerable to intense anxiety feelings and depression (Ballenger, 2000), which may explain why anxiety and depression go hand in hand since both stem from the same vulnerability.

**Physiological Effects of Chronic Stress and Anxiety Disorder**

Fronting a chronic stressful situation can engage in different behavioural expressions - especially if the body remains in high stress, a range of physiological responses occur (Moroz et al., 2005) that can lead to many health disorders through various behavioral and physiological pathways due to some essential biochemical, metabolic, and hormonal pathways (Epel, 2009). The body’s responsiveness to hormonal activity is susceptible to flare up at times of persistent stress and threat. A series of physical manifestations that can include increased blood pressure, muscle tension, slowed digestion, shaking, accelerated breathing and heart rate, flushed skin, dilated pupils, tunnel-like vision and the senses become sharper (Gu et al., 2010; Brownley et al., 2000). In the process, higher reasoning and language structures of the brain virtually shut down, and executive functions crash – one is now on red alert (Arnsten 2009). This process referred to as the fight-flight reaction, which is automatically triggered when the mind perceives a threat or perplexing change. The muscles tense up ready for emergency action, the body’s way of guarding against injury and pain.

When the brain perceives pressures, immediately it sends a distress signal to the hypothalamus (Arnsten 2009). Thus the body stays more active and on high alert. The strength of the stress response is related to the level of perceived threat rather than the actual threat. The body responds to threat by releasing more substantial quantities of hormones and chemical messengers in the brain, which in turn triggers these anxious reactions in a process often referred to as ‘fight or flight’ response. The body's stress response induces a collection of physiological changes that activated in times once the mind perceives stress or threat (Aguilera 2011). Stress is responsible for slowing down normal bodily functions, such as the digestive and immune systems, so that energy and resources can then be concentrated on alertness, rapid breathing, blood flow, and muscle use (Figure 5). Outward physical reactions prepare
the body to respond by increasing heart rate, blood pressure, heightened senses, increase more-in-depth intake of oxygen, and the rush of stress hormones, such as cortisol, adrenaline (Fig. 2). These hormones accelerate heartbeat and send blood rushing to areas that need it most in an emergency, such as the heart, and other vital organs, heighten muscle preparedness and improve the ability to respond to a risky or challenging situation.

Although stress responses developed as adaptive processes, Selye (1956) observed that severe, prolonged stress responses could impact negatively on health. It acts as a trigger for mechanisms that leave the state of mind at increased risk of mental illness or changes in certain brain regions. Although stress responses developed as adaptive processes, Selye (1956) observed that severe, prolonged stress responses could impact negatively and lead to tissue injury, infection, or disease. In this stage, the body’s capacity to respond to both continuous and new stressors has severely compromised the physical and mental health (Mariotti, 2015).

Figure 5. The illustration above presents the micro and macro stress in the minds with genetic vulnerability and its relationship to psychophysiological symptoms. Accumulation of micro stresses has harmful effects in the mind and acts in multiple ways to undermine health. It acts as a trigger for mechanisms that leave the state of mind at increased risk of mental illness or changes in certain brain regions. Although stress responses developed as adaptive processes, Selye (1956) observed that severe, prolonged stress responses could impact negatively and lead to tissue injury, infection, or disease. In this stage, the body’s capacity to respond to both continuous and new stressors has severely compromised the physical and mental health (Mariotti, 2015).

Conclusion

It is essential to realize that the mind is the work done by the brain which is the organ that processes stress and trauma. We have identified that SAD affects the body’s response mechanism and affects the brain in similar ways. Too much stress, ineffectively coped with over some time, becomes problematic. With long-term stress or constantly repeating triggers, hormone release does not shut down causing accumulating harmful effects. When the stress response fails to shut off and reset after a stressful situation has passed, it can trigger depression in vulnerable minds. Stress impacts the course of many health conditions, and is a significant risk factor that can escalate into anxiety and depression. Both are described as the two main psychophysiological response patterns to stress. When physiological response becomes maladaptive, the stress system activates repeatedly giving rise to chronic stress that can result in allostatic load due to dysfunctional coping mechanisms. Stress left unchecked can contribute to many different health outcomes that can lead to further damage to bodily and mental health (Andrews and Thomson 2009). In a situation of chronic stress, the HPA axis is overstimulated and associated with lasting changes in these brain areas. Chronic stress can alter the brain – impacts are reversible, but health is crucial.

Herbert and Cohen (1993) have expressed that stress hormones can harm the body’s organs, mental functioning, and immune system. A persistently stressed mind can get locked into these responses, massively increasing the allostatic load, meaning that the body and brain stay “worn and torn” without the energy to repair. Over time, the allostatic load can accumulate, and the overexposure to neural, endocrine, and immune stress mediators can have adverse effects on various organ systems, leading to disease or mental breakdown (McEwen et al., 2015). The body cannot stay in this state for long without serious health consequences as too much stress hormones can be even more dangerous. Understanding these effects will ensure an accurate discretediasnosis and determine the most appropriate natural-based remedies for treatment and other possible levels of care. Part of the impact of stress is our view of how it affects our lives. That framing is crucial for mind’s health. Regulating the mind’s own emotions and helping people regain a sense of positive control is really critical. By understanding the causes, symptoms, and treatment options of common mental disorders, we can help those affected
to regain control over their incapacitating symptoms and discover long-term techniques for conquering their anxiety and depression to maintaining a sense of well-being. Selye (1983) indicated, “Every stress leaves an indelible scar, and the organism pays for its survival after a stressful situation by becoming a little older.”

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