The Neural Correlates of Cognitive Reappraisal Stress Resilience

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Abstract

Resilience refers to the fact that some individuals cope well with stressful experiences. Many factors contribute to this sort of resilience, such as the early environment, the serotonin transporter gene (5-HTTPLR), the hypothalamic-pituitary-adrenal (HPA) axis, the sympathetic-adrenal medullary (SAM) axis, and emotion regulation techniques. The aim of this thesis is to investigate which factors contribute to resilience, with a particular focus on the emotion regulation technique of cognitive reappraisal. The results show that the prefrontal cortex (PFC) and amygdala each play a crucial role when it comes to stress regulation. Studies have found that the PFC inhibits the amygdala response, but that the PFC is vulnerable to exposure to chronic stress. As a result, the PFC might fail to inhibit the amygdala response. Individuals who use cognitive reappraisal techniques – which has been associated particularly with frontal and parietal brain activity – seem to be less prone to this sort of problem, and, as a result, more resilient to stress.

Keywords: Stress, resilience, coping, emotion regulation, cognitive reappraisal
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1. Introduction

According to the Swedish Social Insurance Agency, 36,552 Swedish people took sick leave due to stress-related illnesses in January 2016 (Försäkringskassan, 2016). This compared to 2011, when only 6,237 people took sick leave due to stress. Stress-related illness is a big health issue nowadays, which leads to the following question, although some people seem to be more resilient to stress than others. The question then is: why, neurobiologically speaking, are some individuals more resilient to stress?

Resilience is a dynamic concept, which refers to the fact that some people “bounce back” after stressful, traumatic experiences (Hornor, 2016). One of the first longitudinal studies in resilience research was done with children that grew up with schizophrenic mothers. This study found that even though these children had both a genetic and an environmental risk to develop stress-related disorders, some of the children still thrived in life as adults (Werner, 1989). In the studies on resilience to stress, results suggest that there are many factors that could contribute to an individual’s capacity to cope with a stressful situations in this manner. Some of the factors that seem to contribute to an individual’s stress resilience include the interplay between the prefrontal cortex (PFC) and amygdala, the hypothalamic-pituitary-adrenal (HPA) axis, the sympathetic-adrenal medullary (SAM) axis, and the individual’s genetics, such as the serotonin transporter gene (5-HTTPLR) (Buschman & Miller, 2007; Gaffey, Bergeman, Clark, & Wirth, 2016; LeDoux, 2007; Rutter, 2006).

The interplay between the PFC and amygdala seems to be of particular importance, since the PFC is responsible for decision-making, impulse control and the inhibition of the amygdala (Arnsten, 2009; McEwen, 2016). In regard to chronic stress, elements of PFC activity can shut down, and this can result in an over-activated amygdala, which is also a feature of many psychiatric disorders (Arnsten, 2009; Roozendaal, McEwen, & Chattarji, 2009).

A related factor that can contribute to an individual’s capacity for stress resilience is the use of emotion regulation techniques. The purpose of using emotion
regulation techniques is to reframe a stressful situation to a more positive view, and it has been shown to enhance positive emotions and well-being (John & Gross, 2004).

Cognitive reappraisal is an emotion regulation technique that can be used in many different contexts. One part is to either up- or down-regulate positive or negative emotions (Gross & Thompson, 2007). Studies have found that cognitive reappraisal is associated with well-being if used appropriately (John & Gross, 2004). In relation to the study of stress resilience, cognitive reappraisal can be used to down-regulate the negative emotions that are associated with stressful experiences (Troy, Wilhelm, Shallcross, & Mauss, 2010). Appraisal theories of stress and emotions state that it is not the event itself that makes an individual stressed, but the evaluation of the perceived stressor (Lazarus & Folkman, 1984). Therefore, cognitive reappraisal techniques may be a tool to enhance resilience, by re-evaluation of the perceived stressor (Gross & Thompson, 2007).

The aim of the thesis is to investigate some of the factors that contribute to stress resilience. Therefore, this thesis investigates the following questions:

- What are some of the more important factors that contribute to an individual’s stress resilience capacity?
- Can emotion regulation techniques such as cognitive reappraisal be used to strengthen an individual’s stress resilience?
- What are the neural correlates of cognitive reappraisal, related to stress and resilience?

This thesis will begin with an introduction to the history of stress research and some of the main theories of relevance to the topic, which is needed to gain a greater understanding of the relationship between stress and resilience. The chapter will also introduce the primary neural correlates that are activated by stress. In the following chapter, the thesis will investigate what resilience and its neural correlates consist of. In the subsequent chapter, the thesis will investigate what emotion regulation is generally, what cognitive reappraisal consists of more specifically, and how cognitive reappraisal might be used to enhance stress resilience. Because stress and resilience are broad topics, the thesis focuses on the neuroscientific perspective of these areas.
2. Stress

Stress is a broad topic in science. This chapter will focus on briefly presenting some recent definitions of stress. It will also provide an overview of the history of stress research, and then go introduce the relationship between stress and resilience. Since the topic of stress is so broad, the emphasis will be on the psychological and biological perspectives of stress.

2.1 What is stress?

In 1936 a physician from Hungary with the name Hans Selye published an article with the name “A syndrome produced by diverse nocuous agents”. In this article Selye described that some mice were treated with extract from the ovary, consequentially this resulted in that the mice suffered from stomach ulcer, magnified adrenal cortex, and disruption in the immune function. With this publication, Selye helped form the phenomenon that in subsequent articles would be called stress (Selye, 1936).

Selye stated that anything such as hunger, heat or psychosocial problems could be a stressor if it triggers the stress response (Währborg, 2009). However, Selye found out that there is a common response to different types of stressors, which he named the non-specific response (Bright & Jones, 2001; Nicolaides, Kyratzi, Lamprokostopoulou, Chrousos, & Charmandari, 2014). The primary focus of his research was on the possible physiological explanation to this response, which he later constructed a theory from known as general adaptation syndrome (GAS; Rice, 2012). GAS has three stages and is associated with changes in the nervous system. The first stage is an alarm reaction, which is activated in front of a serous threat. The next stage is the stage of resistance, which means that the body is saving energy to fight against the threat. The last stage is the stage of exhaustion when the body is overloaded with all the effort (Bright & Jones, 2001). Seyle’s stress theory only focused on the autonomic nervous system. Contradictory, current research postulates that stress can be defined according to what consequences it causes, and factors that lead to these consequences are missing from Seyle’s research (Währborg, 2009).

In fact, stress can be defined in many different ways (Bright & Jones, 2001; Lazarus & Folkman, 1984; McEwen, 2007; McGrath, 1970; Rice, 2012). According
to McGrath (1970) stress is “a substantial imbalance between demands (physical and/or psychological) and response capability, under conditions where failure to meet that demand has important consequences” (p. 20). Other important names in the history of the concept of stress are Claude Bernard and Walter Cannon (Filaretova, 2012). Both Bernard and Cannon devised some of the most important aspects of present-day stress research. Claude Bernard was the first system-biologist and he coined the term *milieu intérieur*, referring to the fact that the body is trying to maintain a constant inner stability even if there are external changes (Filaretova, 2012; Nicolaides et al., 2014). Walter Cannon was a professor in physiology and he coined the term *fight-or-flight response* at the beginning of the 20th century. This refers to the response that is taking place when an individual perceives a threat and the body is ready to fight against the threat or to run away from the threat (Nicolaides et al., 2014).

Furthermore, according to Lazarus and Folkman’s *cognitive transactional model* of stress, an individual’s appraisal of a specific situation is important for the stress response (Folkman, Lazarus, Gruen, & DeLongis, 1986). If an individual perceives a situation as stressful, then the stress response is activated. Lazarus realized that when individuals are confronted with stressful situations, different thoughts, or *appraisals*, are used. Depending on which type of appraisal that is used during challenging experiences, there can be either a positive or a negative effect for the individual (Folkman et al., 1986; Speisman, Lazarus, Mordkoff, & Davison, 1964). The cognitive transactional model of stress was developed further during the 1990s, when Lazarus collaborated with another researcher, Smith, and realized that emotions affected the stress response. This model was named the *cognitive appraisal theory* and posits that, depending on which appraisal that is used, an emotional response will be elicited (Morrison & Bennett, 2012).

Stressors that are perceived as a threat are associated with anger, fear, jealousy, and anxiety. Stressors that are perceived as loss or harm are associated with sadness, depression, hopelessness, and despair. On the other hand, stressors that are seen as challenges are associated with hope and confidence (Morrison & Bennett, 2012). If an individual believes that they have resources to cope with the stressor, a *challenging mindset* is made. Contrariwise, if an individual believes that they don’t have the capability to cope with the stressor, the situation is more likely to be
perceived as a threat (Blascovich & Mendes, 2010; Jamieson, Mendes, & Nock, 2013). The sympathetic nervous system, which is activated during the fight-or-flight response, is greater during a challenging mindset and enhances performance and effective coping, compared to a threat mindset (Dienstbier, 1989; Jamieson et al., 2013). However, the criticism against Lazarus and Folkman’s cognitive appraisal theory of stress claims that it only focuses on the individual’s appraisal of the situation. This model does not focus on the objective resources that could cause stress to an individual such as socioeconomic factors, cultural aspects and poverty for example (McLaughlin, Doane, Costiuc, & Feeny, 2009).

Additionally, a more recent definition of stress is given by McEwen (2007), who defines it as “a word used to describe experiences that are challenging emotionally and physiologically” (p.874). According to him, stress can be divided into different subcategories such as good stress, tolerable stress, and toxic stress. Good stress refers to the fact that it enhances performance in a positive outcome and is called "eustress" (McEwen, 2016). To feel eustress, it is important to have healthy brain architecture, this means that an individual has a well-developed brain that enables them to have good impulse control, healthy self-esteem and good decision-making capability. Tolerable stress refers to the fact that an individual with healthy brain architecture is able to cope with a stressor, this often with help and support from family and friends (McEwen, 2016). This is called “distress” and refers to the feeling when it is uncomfortable to not have control over the stressor. Toxic stress refers to the situation when an individual does not have resources to cope with the stressor, such as social support, and the brain architecture could have been damaged in early brain development so the individual has poor impulse control and cognitive ability (McEwen, 2016).

Another way of explaining stress is homeostasis, allostasis and allostatic load (Cooper & Dewe, 2008; McEwen & Stellar, 1993; Sterling & Eyer, 1988). Walter Cannon who introduced the fight-or-flight response also introduced the term homeostasis about 70 years ago (Cooper & Dewe, 2008). Homeostasis means that the body is trying to get all the body organs in balance even if an external trigger causes stress to an individual (McEwen, 2000a). An example of this is that the body is able to change blood pressure and heart rate when needed, to variegate hormones and to fluctuate cytokines to the immune system (McEwen, 2000a). Moreover, Sterling and
Eyer (1988) introduced the term allostasis, which refers to the process when the body is trying to keep inner stability through change. The concept allostasis describes that the body adapts to different things that happen in the environment, for example, loud noise, hunger, isolation, and threats to safety (McEwen, 1998b). When the autonomic nervous system, the HPA axis, the immune system and the metabolic system work together, subsequently a healthy brain and body could adapt to the environment even when facing a supposed stressor (McEwen, 1998b). All individuals perceive their environment differently so that these systems can be precipitating in different situations (McEwen, 1998b). Both homeostasis (the process of maintaining balance in the body through change) and allostasis (the process of keeping stability) are good for health if they last for a short-term period i.e. minutes to hours (McEwen, 2003). When these systems (HPA axis, autonomic nervous system, immune system, metabolic system) are overused it can lead to chronic stress and a model for explaining this is the allostatic load that McEwen and Stellar (1993) developed. The allostatic load could, in turn, lead to wear or tear on the body and brain and refers to the cost of adaptation (McEwen, 2003). Remarkably, it seems that activation of the allostasis systems depends on how the individual perceives his or her environment according to historical (stressful environments, trauma, major life events), behavioural (health habits and coping) as well as genetic factors (Juster, McEwen, & Lupien, 2010; McEwen, 1998b).

Furthermore, research has identified how allostasis can lead to allostatic load (Korte, Koolhaas, Wingfield, & McEwen, 2005). It depends on the four following stages; to iterate challenge, failure to handle this challenge, failure to turn off the stress response after the challenge and failure to have a moderate response (Korte et al., 2005; McEwen, 2003). Allostatic load or chronic stress damages the brain in the form of suppressed neurogenesis (difficulty with building new neurons), synaptic and dendritic remodeling and structural atrophy (Juster et al., 2010). The function of allostasis and allostatic load can be regulated through the behavior of the individual. Exercise, sleep, and healthy diets promote allostatic balance and health whereas alcohol, cigarettes and a high-fat diet promote allostatic load. The neuroendocrine, cardiovascular and the immune system are working together to get the body in balance (McEwen & Gianaros, 2010).
However, much criticism against the allostasis model subsists. The allostasis model explains how energy consumption can be overused and in that way leads to allostatic load, on the other hand, it does not take into account the early environment and how the brain develops inappropriate mechanisms for coping with stressful situations (Romero, Dickens, & Cyr, 2009). An inappropriate brain development can make an adult more sensitive to stressors. Therefore, the allostasis model takes little account of the cognitive aspect of stress which makes an individual perceives an environment as either a threat or not (Romero et al., 2009).

2.2 Stress and the brain

This section will go more in depth and explain some central parts of the brain, which are especially involved in stress regulation. These parts are the PFC that is responsible for higher-order functions, the amygdala that is especially involved with affective stimuli, SAM axis that is involved with the fight-or-flight response and the HPA Axis that is activated in front of acute danger.

2.2.1 Prefrontal cortex

The PFC is activated in form of regulating thoughts, actions and inhibits inappropriate behavior (Arnsten, 2009). These processes work in combinations with other brain areas. PFC is responsible for detecting inputs from both the external and the internal environment and chooses what to focus on. This process is also called top-down regulation (Arnsten, 2009). The ventromedial PFC is responsible for detecting emotional stimuli and connects with nucleus accumbens, amygdala, and hypothalamus. The right inferior PFC is associated with inhibiting inappropriate motor responses. The dorsomedial PFC is responsible for reality testing. In the healthy brain where an individual is not exposed to traumatic stress, these PFC regions, which were mentioned above, work together when involved in processes such as decision-making and higher order function to make the best possible solution to everyday problem. When an individual is exposed to traumatic stress, however, these functions are working differently (Arnsten, 2009). The PFC has a direct connection with the brainstem and the locus coeruleus that is releasing Norepinephrine. PFC also connects with substantia nigra, that is a part of the brainstem and is located in the midbrain. PFC also connects with ventral tegmental
area, that is a group of neurons that is located next to the floor of the midbrain. The substantia nigra and ventral tegmental area are major dopamine projectors. Norepinephrine and dopamine are regulating catecholamine. The release of catecholamine in optimal dose enhances PFC regulation and this lead to a healthy cycle (Arnsten, 2009). On the other hand, when an individual perceives acute stress the amygdala activates the brainstem and hypothalamus pathways, which release high doses of dopamine and norepinephrine. This leads to an unhealthy cycle in the long term by enhancing the amygdala activity and diminish the PFC regulation. The PFC is then more activated in bottom-up regulation which means that sensory organs and motor pathways get more attention than top-down regulation when the focus is on problem-solving for example (Buschman, & Miller, 2007).

2.2.2 Amygdala

The amygdala is located bilaterally in the medial temporal lobe (LeDoux, 2007). Amygdala means in the Greek language almond, which is corresponding to the shape of the structure of the amygdala. Amygdala has strong connections to the hippocampus, which is a brain area that is associated with memory (Nyberg, 2009). Amygdala has also strong connections to cortical regions of the brain (Nyberg, 2009).

The amygdala is activated during emotional processing. Both for negative and positive stimuli. Amygdala is especially involved with fear and fear conditioning. Lesions in the amygdala can lead to the ability to not recognize fearful stimuli (Gupta, Koscik, Bechara, & Tranel, 2011). Functional and structural alterations in the amygdala can lead to posttraumatic stress disorders (PTSD), major depressive disorder (MDD), schizophrenia, autism, phobia or anxiety disorder (LeDoux, 2007).

When individuals are confronted with acute stress the amygdala induces their activation. This has an evolutionary perspective, in the form of scanning the environment and remember dangerous situations and places to enhance survival (Workman & Reader, 2014). The memory consolidation is active in perceived acute danger together with other stress-sensitive brain areas such as hippocampus and PFC (Roozendaal et al., 2009). In longstanding, this process is good for the long-term memory of the perceived situation, but it destroys working memory and memory retrieval. Perceived traumatic experiences, which enhance amygdala activation and
memory consolidation, can make an individual develop PTSD because of the re-experiencing the traumatic experiences (Roozendaal et al., 2009).

**2.2.3 Hypothalamic-pituitary-adrenal axis**

When individuals perceive acute danger, the HPA axis is activated (Gazzaniga, Halpern, & Heatherton, 2013). The stressor can be anything from not being able to pay the bills or to having a fight with a friend. The HPA axis takes longer time than the SAM axis to be activated. When the HPA axis is activated, the hypothalamus sends a chemical message to the pituitary gland, which is located below the brain. The hormone adrenocorticotropic hormone (ACTH) is then released from the pituitary gland (Gazzaniga et al., 2013). After this, ACTH then reaches the adrenal glands via the bloodstream. Cortisol is then released from the adrenal glands. From here, Norepinephrine and epinephrine are released from the adrenal glands and the sympathetic nervous system is activated (Gazzaniga et al., 2013). Forward, the sympathetic nervous system is activated, blood pressure is increased and the body is now ready to fight against a threat or to run away from it.

The HPA axis is involved in the diurnal rhythm and in the face of both acute and chronic stress. Individual’s cortisol levels are regulated by sleep and wake cycles (Gaffey et al., 2016). The HPA axis regulates negative feedback of glucocorticoid. Corticotropin-releasing hormone (CRH) and ACTH cause the production of glucocorticoid levels, so the negative feedback loop is important because it turns off the glucocorticoid levels by down-regulating CRH and ACTH (Gaffey et al., 2016). Cortisol is decreasing the levels of CRH and ACTH and it down-regulates the HPA axis (Gaffey et al., 2016). This process is different from individual to individual. Therefore, the form of HPA axis activity is important in the research of resilience and stress. A dysregulated HPA axis can be a cause of genetics and an early environment with maternal neglect or abuse (Szyf, Weaver, Champagne, Diorio, & Meaney, 2005). Chronic stress with prolonged levels of glucocorticoid can also lead to a dysregulated HPA axis (Nelson, 2011). By which a dysregulated HPA axis can lead to PTSD or MDD (Gaffey et al., 2016).
2.2.4 Sympathetic-adrenal medullary system

The SAM axis is the human’s defense system that prepares the body for either fight against a perceived threat or to run away from a threat (fight-or-flight response) (Lundberg & Wentz, 2012). The signal goes from the hypothalamus to the SNS that affects the adrenal medulla to release catecholamines such as norepinephrine and adrenalin. In the time of only less than one minute the catecholamines are released into the bloodstream (Lundberg & Wentz, 2012). The catecholamines travel through the body organs to make them ready for a fight. The norepinephrine enhances the blood pressure and the adrenaline release goes to inner organ and diminish the activity to the digestion area and enhances the activity of muscles, heart and the brain (Lundberg & Wentz, 2012).

2.3 Stress and coping

There are many ways to cope with a stressful event (Compas, Connor-Smith, Saltzman, Thomsen, & Wadsworth, 2001; Folkman & Lazarus, 1988; Skinner, Edge, Altman, & Sherwood, 2003). The most famous way to cope with a stressor is either problem-focused coping that motivates someone to deal with the stressor and take action to solve the problem or emotion-focused coping that is used for reducing the emotional distress of a perceived stressor (Folkman & Lazarus, 1988). When individuals perceive stressful situations both problem-focused and emotional-focused coping are usually used in combinations to some extent (Folkman & Lazarus, 1988). Also, these techniques vary, this because emotion-focused coping can involve denial or reinterpretation of a situation. According to Compas et al. (2001), coping can be defined as “conscious volitional efforts to regulate emotion, cognition, behavior, physiology, and the environment in response to stressful events or circumstances” (p. 89). A review by Skinner et al. (2003) found over 400 categories of coping strategies. Many reviews were about top-down processes of higher order functions that are used in coping strategies and different forms of emotion regulation strategies. One model that is included in many of the articles was a three-factor model of coping by Connor-Smith, Compas, Wadsworth, Thomsen and Saltzman (2000).

The first factor was; primary control engagement coping, which refers to that an individual is taking action to either problem solve, use emotional expression or emotional modulation to act directly on the source of stress. Secondly, secondary
control engagement coping, which refers to an individual that uses positive thinking, cognitive restructuring, distraction or acceptance to adapt to the sources of stress. Thirdly, disengagement coping, which refers to an individual that uses avoidance, wishful thinking and denial to behaviorally or cognitively withdraw from the sources of stress (Andreotti et al., 2013). The form of coping styles affects both cortical and subcortical pathways (Puglisi-Allegra & Andolina, 2015). Secondary control engagement coping is associated with working memory (Andreotti et al., 2013). Working memory is a part of executive functions, which are associated with multitasking and organize activities or thoughts. Working memory is associated with memory retrieval, processing and manipulating information from the environment. Deficits in working memory are associated with poor interpersonal functioning and problems to use secondary control engagement coping and emotion regulation (Campbell et al., 2008).

According to Puglisi-Allegra and Andolina (2015) there are two types of general stressors. The first type is the systemic stressors that challenge the body’s homeostasis by different sensory pathways (spinothalamic tract or spinocerebellar tract for example). The second type is the psychogenic/neurogenic type that requires appraisals. Effective coping strategies are needed for an individual to adapt to stressful experiences. If the individual has problems to adapt to a specific stressor the stress response can be prolonged which can lead to psychopathology in the long term (Puglisi-Allegra & Andolina, 2015).

If an individual experience psychological stress, the appraisal of control can help the individual to cope with the stressor in an effective way and the body can adapt to the situation in form of effective allostasis. From the perspective of psychogenic stress the interaction between the individual and the form of appraisal used in the context of the environment, have a large effect of what effect the stress has on the body and the brain. Because how an individual perceives a specific environment affects their brain (Puglisi-Allegra & Andolina, 2015). The perception of control seems to be important in the form of dealing with stressful experiences (Amat et al., 2005; Maier, Amat, Baratta, Paul, & Watkins, 2006). Findings from rat studies have shown that the perception of control is associated with ventral medial PFC activity in the experience of perceived stress (Maier et al., 2006). One study by Maier et al. (2006) measured controllability by putting rats in small boxes. There were two
groups of rats; the first group got their tails extended from a rear of a box with a wheel in front of them. These rats got electric shocks at their tail, but they had behavioral control of the termination of the shocks if they pulled the wheel with their paws. The second group also got electric shocks to their tails but they did not have any control over the shocks, because when they pulled the wheel, nothing happened. These rats were located in the same box as the rats that had control over their shocks.

The findings show that these two groups got the same electrical shocks, but one group had control over the perceived stressor (the electrical shocks) and the other did not. Since the experience to have control over a perceived stressor is kind of subjective, this is a way to measure what happens in the brain when these rats do not have control over a situation. From this study, they found that the rats that had control over the perceived situation had more activation in the ventral medial PFC compared to the other rats with no control over the electrical shocks. This study also found that the ventral medial PFC had a connection to the dorsal raphe nucleus, which is an area that is located in the medial temporal lobe that is rich in the neurotransmitter serotonin (Maier et al., 2006). The study found that when the rats perceived control of the electrical shocks, the ventral medial PFC inhibited the dorsal raphe nucleus neurons.

Another study with rats by Amat et al. (2005) is in line with the study above because when the dorsal raphe nucleus neurons were blocked by a serotonergic agonist the rats that were exposed to uncontrollable stress did not show any freezing behavior that is associated with uncontrollable stress. Therefore it seems that the dorsal raphe nucleus and the ventral medial PFC are especially important when it comes to taking control over a perceived stressor. Moreover, the dorsal raphe nucleus is an area that is rich in the neurotransmitter serotonin and serotonin has a crucial role when it comes to resilience research that this thesis will explain further in the next chapter.

However, these studies show that the perception of control affects the dorsal raphe nucleus that in turn affect the serotonin transporter. So can the way of thinking affect the brain and in that way makes individuals more resilient against stress?

Another study has shown that vmPFC are especially involved in eliminating the fear response (Phelps, Delgado, Nearing, & LeDoux, 2004). This finding is important because when individuals experience acute stress, the fear response and the
fight-or-flight response is on. Prolonged stress is not healthy and therefore to reevaluate a stressful situation can be a way to build resilience.

The stress response is important for humans and animals because in that way we can respond to danger and either fight against it or run away from it to enhance survival. Coping strategies can help us build resilience after threat and provoke allostasis in our body, but ineffective coping strategies can make us develop psychopathology by that our body is developing allostatic load (Puglisi-Allegra & Andolina, 2015). In the form of stress appraisals, cortical and limbic structures in the brain are activated. For example, when an individual is studying for an exam and believes that the exam is above his or her knowledge, the amygdala and the fear-pathway in the brain will be activated and the stress response is on. The individual will probably perceive anxiety. If the person instead had used another stress appraisal, for example by thinking that "I am not in control right now, but I will when I have read a lot, and then I will pass the exam", the threat-pathway will probably not be activated (Puglisi-Allegra & Andolina, 2015).

A history of many uncontrollable stressful events for an individual can lead to learned helplessness. On the other hand, many stressful situations from the past, which the individual has coped with and have taken the control over, can lead to a resilient individual (Puglisi-Allegra & Andolina, 2015). Uncontrollable events can also lead an individual to develop a passive coping style.

In this chapter, the thesis has investigated what concepts that can be found in stress research and how stress affects the brain. The next chapter in this thesis will focus on what resilience is. Stress and resilience are integrated because how an individual perceives a situation will affect the stress response (Olff, 1999). Therefore, this thesis will in the subsequent chapter investigate emotion regulation techniques that can change an individual’s appraisals to cope better with stress. Ineffective coping styles or prolonged periods of negative affect can make the HPA axis become dysregulated. This makes the cortisol inhibit the sympathetic nervous system and thereby decline correct homeostasis (Olff, 1999).
Resilience is a dynamic concept with no clear definition (Rutter, 2013). Most of the articles about resilience are about how people overcome adversities in relation to stressful or traumatic experiences (Bowes & Jaffee, 2013). Resilience can also refer to an individual experiencing positive psychological outcomes despite aversive risk environments (Rutter, 2006).

Resilience research is multidisciplinary, because research involves everything from health epidemiology, through neuroscience to psychology (Greenberg, 2006). Research also focuses on how risk environments in early childhood, for example, affect development and the brain (Greenberg, 2006). Adverse childhood experiences such as sexual abuse, neglecting parents, a household with drug or alcohol dependence, poverty or child maltreatment are factors that can lead a child to experience toxic stress (Felitti et al., 1998). The concept is difficult to measure because there need to be a genetic risk and an environmental risk to measure if individuals will be resilient or not (Rutter, 2006). The three hit model of resilience investigates the interaction of genetic disposition with the early life environment and the later life environment. This model states that these three interactions (genetic disposition, early life environment and later life environment) contribute to an individual’s resilience capacity to cope with a stressor (Daskalakis, Bagot, Parker, Vinkers, & de Kloet, 2013). The genetics and the early environment can either make an individual more vulnerable or resilient to later life stressors (Daskalakis et al., 2013). Some researchers explain resilience as similar to the immune system. Some small exposure to a virus is good for the immune system because then the body makes anti-body cells to the virus and the body is thereby resistant to the virus. This is similar to resilience, the exposure to negative life experience can make the individual cope with it and develop effective coping strategies (Hornor, 2016).

Factors that promote resilience are many, such as self-confidence, planning skills, academic achievement, good connection to family and friends, a perception of control and coping ability (Hornor, 2016). What makes an individual resilient? If the stressor is greater than the protective factors it is more likely that an individual develops psychopathology, this even if the person has been resilient in the past. But if the individual experiences hardship and has a sufficient amount of resources such as
social support and control over the perceived situation, the person can be resilient (Tusaie & Dyer, 2004).

The body’s way to cope with a stressor and to be resilient relates to allostasis. When the stressor is greater than the resources to cope with the stressor the body’s system goes from allostasis to allostatic load, which can lead to psychopathology and sickness (McEwen, 2002).

The early theories about resilience were trying to find out what kind of genetics and environment that leads to resilient individuals, while the more recent theories are trying to find out how and why any specific environment or genetics lead to a positive outcome, and thereby focus more on how protective factors can be built (Seligman & Csikszentmihalyi, 2000).

3.1 Genetic influences

One way to study the relationship between coping, resilience and stress and how it interacts with individuals is to measure the genetics with the environment. There is a theory that is called the stress coping mismatch (SCM) hypothesis by Homberg (2012). This theory states that an individual will cope well with a stressful experience if it matches something similar in the past. Then it is a match between genetics and the environment and the individual will adapt to the stressor. If the stressor is greater than the past stressors and mismatch with earlier experiences, the individual is likely to develop psychopathology because it will affect the serotonin transporter polymorphism (5-HTTLPR; Puglisi-Allegra & Andolina, 2015). If an individual has one or two short alleles of the serotonin transporter, they are more vulnerable to developing stress-related disorders compared to individuals with two long alleles of the 5-HTTLPR transporter (Puglisi-Allegra & Andolina, 2015).

To measure resilience, researchers use genes and combine them with the environment. For example, Individuals that have two long alleles and have been exposed to child maltreatment are considered to be more resilient than individuals that have two short alleles and have experienced the same environment (Hornor, 2016).

It is important to note that resilience affected by how both the genetics and the environment interact. Studies have found that exposure to some stressors in childhood can make an individual resilient to later life stressors, but it depends on what kind of
stressor. For example, parental divorce with a healthy environment with supportive parents can lead to later resilient adults. On the other hand, a parental divorce with unhealthy communication and conflict can lead the child to be more vulnerable to later adult life stress disorders (Rutter, 2013).

3.2 The neurobiology of resilience

To explore the biology of resilience research needs to investigate studies with individuals that have a genetic vulnerability to stress-related disorders and a stressful environment (Hornor, 2016).

Resilient individuals have in some way been exposed to life-stressors, but they have developed ways to deal with it (Hornor, 2016). One way to measure the neurobiology of resilience is to look at the mesolimbic dopaminergic reward system. The brain structures that are involved in the circuitry are the amygdala, nucleus accumbens, ventral tegmental area, medial prefrontal cortex, lateral habenula, hippocampus and lateral hypothalamus among other parts (Pfau & Russo, 2015). Studies have found that in mood disorders such as depression and anxiety, the PFC and hippocampus have reduced volumes. Also, the amygdala and nucleus accumbens are over-activated (Russo, Murrough, Han, Charney, & Nestler, 2012).

The human brain is capable of resilience in the form of neuronal plasticity. Neuronal plasticity means the generation of new neurons and either shrinkage or growth of dendrites in PFC, amygdala, and Hippocampus. This is in form of top-down interventions, which include pharmaceutical agents such as selective serotonin reuptake inhibition (SSRI), food restriction and physical activity (Karatsoreos & McEwen, 2013).

3.2.1 Neuropeptide y

The neuropeptide y (NPY) is especially important when it comes to research about resilience to stress (Reichmann & Holzer, 2016). NPY has a stress protective function because it counteracts the stress hormone CRH. Overexpression of CRH makes an individual to perceive anxiety whereas NPY diminishes the anxious feeling (Reichmann & Holzer, 2016).
The NPY involves 36 amino acids. This peptide is involved in functions such as regulating the wake and sleep cycle, mood, feeding behavior, learning, memory and blood pressure (Sabban, Alaluf, & Serova, 2016). NPY is active both in the central nervous system and in the periphery. In the central nervous system the NPY is active in the amygdala, neocortex, hypothalamus, basal ganglia, hippocampus, dorsal raphe nucleus, periaqueductal gray, nucleus accumbens, thalamus and in the brainstem (Reichmann & Holzer, 2016; Sabban et al., 2016). In the periphery, the NPY is most active in the adrenal medulla, plateles and in the sympathetic ganglia (Sabban et al., 2016). A major source of NPY is responding to the paraventricular nucleus of the hypothalamus that is releasing CRH. This collaboration between these two systems has a major role in the stress response that either can lead to resilience or psychopathology (Reichmann & Holzer, 2016). When individuals perceive acute danger, the HPA axis is activated and CRH is released from the hypothalamus (McEwen & Gianaros, 2010). Then the NPY has a stress-protective function because it’s counteracted by the action of the CRH. The NPY expression can also change in comparison to the duration of stress, like in chronic restraint stress in mice where the genetic expression of the NPY in the hippocampus was decreased (Reichmann & Holzer, 2016)

### 3.3 The difference between resilience and coping

There are individual differences when it comes to handling everyday stressors. Some people are able to see stressors constructively (Gazzaniga et al., 2013). According to Kobasa (1979) this personality trait is called hardiness, which means that an individual is seeing a stressor as a challenge rather than a threat, they are committed to the daily activities and see themselves as having control of their lives. These individuals use active coping styles, which means that they take action to solve a problem (Gazzaniga et al., 2013). People that are considered to be low in hardiness are more likely to use passive coping style, which means that they avoid the problem (Gazzaniga et al., 2013). According to Leipold and Greve (2009) it is easy to make the mistake to believe resilience is a personality trait. Because individuals that are considered to have the hardiness mindset are also considered to be high in resiliency. However, other factors contribute to a persons resilience capacities, like the external
factors such as the early environment that shapes an individuals brain structure and external factors such as resources to cope with a stressor (Leipold & Greve, 2009).

Individuals who can be flexible and use the right coping strategies at the right time are considered to be resilient (Puglisi-Allegra & Andolina, 2015). A resilient individual is a person that can cope with the perceived stressor (Hornor, 2016). Depending on which coping strategies that are used in relation to stressful situation, it can either make the individual more vulnerable to psychopathology or be more likely to develop resilience (Puglisi-Allegra & Andolina, 2015).

This chapter included background information about how resilience is defined and what factors that can lead to stress-related disorders or resilience. To summarize the chapter, some exposure to stressors in childhood can be an advantage for an individual if the individual could cope with it in the correct way. If the stressors are greater than the perceived resources available, it is more likely that the individual develops stress-related disorders. The genetics play a crucial role when it comes to being resilient. If individuals have two long alleles of the 5-HTTLPR polymorphism, they are more protected compared to people that have one or two short alleles from developing stress-related sickness (Hornor, 2016). Since the environment plays a crucial role in the face of resilience, the next chapter will focus on what factors that can contribute to building resilient individuals.

4. Emotion regulation and resilience

To understand emotion regulation techniques, it is important to know how emotions are generated. So, what is emotion generation? One model to explain emotion generation is the modal model of emotion by Gross and Thompson (2007). This model explains how emotions can be generated. The model states that emotions increase for every step in the emotion generation phase and the model involves four steps. The first step is the situation that can be a stimulus from either the external or internal environment (Gross & Thompson, 2007). The second step is when the individual either draws attention to the stimulus or just ignores the stimulus. If the stimulus is in the center of attention the stimulus is going through the next step of the emotion-generative stages (Ochsner, Silvers, & Buhle, 2012). Otherwise, if the stimulus is unattended it will be excluded from the emotion-generative stages.
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(Ochsner et al., 2012). The third step is how the individual appraises the perceived stimulus. This focuses on how the stimulus is relevant to one’s needs, goals and wants. The fourth step is, dependent on how the individual appraises the situation; an emotional response will be elicited (Gross & Thompson, 2007). This model goes in circles and when the emotional response interacts with a new stimulus, a new emotion-generation phase is elicited.

According to Gross (1998) emotion regulation is “the processes by which individuals influence which emotions they have, when they have them, and how they experience and express these emotions” (p. 275). People differentiate in the process (Gross, 2002).

To understand emotion regulation, one model for explaining this is the process model of emotion regulation by Gross and Thompson (2007). This model states that depending on which emotion regulation strategy is used, the emotion can change because of the change in the emotion-generation process as mentioned earlier. This model includes five stages which are, first, the selection of a specific situation; second, modification of the situation; third, deployment of attention; fourth, cognitive change of the situation; fifth and last, response modulation (Gross & John, 2003). These five stages are included in the five families of emotion regulation (ER) and relate to the steps in the modal model of emotion (Gross & Thompson, 2007).

To understand this model, researchers differentiate between two strategies (Ochsner et al., 2012). The first strategy is antecedent-focused which refers to the fact that emotions are regulated before an emotion has elicited fully. The other strategy is response-focused which refers to emotion regulation which takes place during or after an emotion has been expressed (Gross & John, 2003). The three first stages of the process model of emotion regulation are considered to be antecedent-focused strategies, whereas the stages four and five are considered to be response-focused strategies (Gross & Thompson, 2007). There are different emotion regulation techniques and this thesis will focus on cognitive reappraisal, which is an antecedent-focused strategy.

Studies have found that ventral medial PFC has an especially important role in regulating emotions and to guide appropriate behavior (Phillips, Drevets, Rauch, & Lane, 2003). Orbitofrontal cortex (OFC) and ventral medial PFC take in and integrate
emotional stimuli and sensory information (Bechara, Damasio, Damasio, & Anderson, 1994). The Orbitofrontal cortex is located on the lateral and medial part of the PFC and ventral medial PFC is located more rostral to the OFC (Bouret & Richmond, 2010). The ventral medial PFC has a connection to the autonomic nervous system in relation to emotional stimuli such as blood pressure, heart rate variability and changes in skin conductance (Damasio & Sutherland, 1994). Lesions in the ventral medial PFC have shown to results in disability to make decisions, inappropriate affect, psychosocial dysfunction, irritability and poor frustration tolerance (Damasio et al., 2000).

4.1 Cognitive reappraisal

Cognitive reappraisal is considered to be an antecedent-focus strategy (Gross, 2002). There are different subtypes of reappraisal from which one is self-focused reappraisal and the other one is situation-focused reappraisal (Willroth & Hilimire, 2016).

Self-focused reappraisal considers that the individual reinterprets their own inner emotions about specific stimuli, while and situation-focused means that the individual reappraises the situational context about a specific stimulus. Self-focused reappraisal seems to be associated with medial PFC and situation-focused reappraisal seems to be associated with lateral PFC regions. Both these techniques are associated with diminished amygdala activation (Willroth & Hilimire, 2016).

Cognitive reappraisal seems to be an emotion-focused coping strategy and it is useful when a stressor is uncontrollable. However, when a stressor is under control, problem-focused coping is more adaptive according to Troy, Shallcross, and Mauss (2013).

In what conditions can cognitive reappraisals be used? One example is: if an individual is doing a presentation in front of a group of people and believes that the audience will make fun of the individual, the persons stress response will turn on and the individual will probably feel a lot of anxiety. On the other hand, if the individual believes that the audience will be curious about what the person wants to say and show compassion, this will result in that the individual will probably experience joy and excitement. The situation is important because how individuals perceive a
situation will also lead to an emotional response (Folkman et al., 1986). The emotional response is important for either building resilience or to be vulnerable to psychopathology. All stressful events are mostly emotional; therefore to build resilience research is needed about how to handle emotions and thoughts.

When an individual is engaged in self-regulated tasks the dorsal lateral PFC, Orbitofrontal cortex, ventral lateral PFC and anterior cingulate cortex are activated (Buhle et al., 2014). These brain parts are also responsible for the inhibition of the amygdala. Since the amygdala is responsible for affective stimuli, the self-talk about how an individual perceives a situation is of big importance for the behavioral response. Because if an individual perceives a situation as threatening, the amygdala will be activated and following the SAM and HPA axis (LeDoux, 2007). PFC is used to set the threat in context and diminish amygdala activity (Arnsten, 2009). In the face of chronic stress the PFC will not work appropriately and the amygdala response can therefore not anymore be inhibited. If the individual can perceive a situation as less threatening from the beginning, the HPA axis will not be activated. In this case, the individual can be more resilient (Folkman et al., 1986; John, & Gross, 2004).

Gross (1998) did an experiment where participants watched emotional film clips. In this, the participant was instructed to either use reappraisals or just watch the film clips. His finding was that the individuals that used reappraisal techniques reported less negative emotions compared to the other groups that used other emotional regulation techniques or just watch conditions. This finding was important in the research of how emotions can be regulated to prevent stress illness and enhance resilience (Troy et al., 2010).

Studies have found that individuals who use more reappraisal strategies can reappraise a stressful experience to a less stressful experience and in that way experience more positive emotions and enhanced well-being (John & Gross, 2004). People who use suppression experiences more stress and less positive emotions (John & Gross, 2004). With effective cognitive reappraisal employment, individuals can diminish their sympathetic nervous system activity and perceive a better control of their emotions (Picó-Pérez, Radua, Steward, Menchón, & Soriano-Mas, 2017).

A study by Troy et al. (2013) measured cognitive reappraisal ability, which is the ability to use cognitive reappraisal. The results showed that cognitive reappraisal
ability is associated with higher psychological health when the participants were confronted with uncontrollable stress, on the other hand, the participants that were confronted with controllable stress and used cognitive reappraisal the psychological health was decreased. This study shows that cognitive reappraisal ability must be used in the right context to have the best effect (Troy et al., 2013).

4.2 Neural correlates of reappraisal

When individuals are involved in cognitive reappraisal tasks, working memory, selective attention, response inhibition and monitoring control processes are used (Ochsner & Gross, 2008). Dorsal PFC is associated with working memory and selective attention. Ventral PFC is associated with response inhibition. Dorsal portions of the anterior cingulate cortex are associated with monitoring control. In studies where participants reflect upon their own or others emotional states, researchers have seen that especially the dorsal medial PFC is activated during cognitive reappraisal tasks (Ochsner & Gross, 2008).

The amygdala and insula are also related to cognitive reappraisal tasks (Ochsner & Gross, 2008). This is understandable since previous studies have shown that amygdala is especially involved with the emotional states (LeDoux, 2007). A study by Ochsner and Gross (2008) shows that in reappraisal tasks the PFC diminishes the activity in the amygdala and the insula during viewing emotionally evocative film clips. The study also shows that the opposite, the suppression of feelings, makes the activation of the PFC more slowly and it results in an increase in the amygdala and insula response over time.

On the other hand, it is important to note that there are individual differences according to the capacity to use effective reappraisals. A study by Perchtold et al. (2017) used electroencephalogram (EEG) to measure prefrontal asymmetry during the use of cognitive reappraisal. More activation of the left PFC is associated with positive affect and the right prefrontal cortex is associated with negative affect (Davidson, 2004). Therefore, the use of EEG in prefrontal asymmetry is used during studies of cognitive reappraisal to see if there are differences between moods and how these cognitive abilities are used. Furthermore, it has to be noted that it is too simplistic to state that the left prefrontal cortex is associated with positive emotions,
but only because of more brain parts are integrated, also even studies of anger have found activations in the left PFC (Davidson, 2004).

However, the study by Perchtold et al. (2017) found that women who perceived high chronic stress experience show less left-lateralized brain activity in the ventral lateral PFC during the task of cognitive reappraisal. This finding is in line with other studies with depressed people or with elderly people where they have less activation in the left ventral lateral PFC during cognitive reappraisal efforts (Johnstone, Van Reekum, Urry, Kalin, & Davidson, 2007; Opitz, Rauch, Terry, & Urry, 2012). Cognitive reappraisal is said to be an effective method to diminish stress that can be learned by using cognitive behavioral therapy (Beck, 2005). These findings suggest that if people are depressed or are of higher age it can be more difficult to use reappraisal techniques (Johnstone et al., 2007; Perchtold et al., 2017). Also, the study by Perchtold et al. (2017) notes that the less activation the women had in the left ventral lateral PFC, the more stress they felt during everyday life.

One study by Troy et al. (2010) showed that people that had higher cognitive reappraisal ability experienced less stress during a stressful period, compared to people that had low cognitive reappraisal ability. These results also indicate that there are individual differences in the capacity to use cognitive reappraisal techniques (Troy et al., 2010).

A study by Morawetz, Bode, Baudewig, and Heekeren (2016) found that effective amygdala and prefrontal cortex connectivity had individual differences. The results of the experimental tasks were that reappraisal was associated with increases in superior temporal gyrus, superior frontal cortex, middle frontal cortex, medial frontal cortex and inferior frontal gyrus. This fMRI study confirms earlier findings that PFC is especially involved with reappraisal activation (Ochsner & Gross, 2008).

Existing models of cognitive reappraisals according to a review by Buhle et al. (2014) shows that parietal and frontal parts of the brain are activated to inhibit the amygdala response in reappraisal tasks. This is important because the goal with reappraisal is to diminish the negative emotion that comes with traumatic experience or perceived acute stress.

More specifically, some researchers have found that dorsal medial PFC, dorsolateral PFC ventrolateral PFC and posterior parietal lobe are activated in
reappraisal task. These brain regions are also activated in front of cognitive control tasks (Buhle et al., 2014).

4.3 How can cognitive reappraisal enhance resilience?

Since earlier research has found associations with prolonged negative affect and a dysregulated HPA-Axis, cognitive reappraisal can be used to down-regulate negative emotions and up-regulate positive emotions (Buhle et al., 2014; Olff, 1999).

The goal with reappraisal is to reappraise a situation to a more positive view than the situation was from the beginning or change ones individual feelings about the situation. Studies about affect labeling, which means to express emotions and to speak about them have been shown to diminish negative affect (Hariri, Bookheimer, & Mazziotta, 2000). Studies have found that amygdala activity is diminished when individuals can reevaluate emotional pictures to a more positive view than only watching an emotional picture without changing ones thoughts to the picture (Lieberman et al., 2007). Furthermore, this study showed more activation in the right ventrolateral prefrontal cortex during emotional labeling of a picture compared to no labeling. This area is associated with top-down inhibition processes. This study shows that putting feelings into words can both diminish the amygdala activity and enhance the right Ventrolateral PFC. Therefore, reappraisal techniques may help when it comes to reevaluating a specific situation to diminish emotional distress (Lieberman et al., 2007).

5. Discussion

The aim of this thesis has been to investigate some of the factors that contribute to stress resilience, by focusing on the following three questions:

- What are some of the more important factors that contribute to an individual’s stress resilience capacity?
- Can emotion regulation techniques such as cognitive reappraisal be used to strengthen an individual’s stress resilience?
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- What are the neural correlates of cognitive reappraisal, related to stress and resilience?

To answer the first question, the first factor to start with is how individuals perceive a stressful situation. Because, according to the cognitive appraisal theory of stress, depending on how an individual perceives a stressor, an emotional response will be elicited (Morrison & Bennett, 2012). Therefore, in relation to stress, it seems important to be conscious of our thoughts and emotions to be able to regulate them to our benefit. If individuals perceive a stressor as a challenge, research shows that this mindset can lead to better performance and confidence (Morrison & Bennett, 2012). On the other hand, if stressors are perceived as a threat, individuals are more likely to experience fear or anxiety.

So if individuals could just change the mindset and see the stressors as challenges, would resilience be the outcome for everyone? According to McEwen (2016), it is not only about having the right mindset. To be able to experience good stress and see a stressor as a challenge, it is also important that an individual has a well-functioning PFC. In stressful situations, the PFC diminishes the activity in the amygdala. In toxic stress, for example, there is damage to brain architecture damage, such that the PFC does not function in an optimal manner. It is difficult to see a stressor as a challenge if the brain architecture is damaged (McEwen, 2016). Some individuals can be more vulnerable to experience toxic stress and psychopathology as the result of inappropriate brain development (Felitti et al., 1998).

Depending on how an individual perceives their environment; the HPA axis, the autonomic nervous system, the immune system and the metabolic system work together to get the body in a constant inner stability and promote allostasis (McEwen, 2002). Resilient individuals seem to cope well with stressors and maintain allostasis in the body (McEwen, 2002). Factors that can contribute to resilience and prevent individuals from developing allostatic load and chronic stress include exercise, a healthy diet, and sleep (McEwen & Gianaros, 2010). Other factors that contribute to resilience include coping strategies. Since a review by Skinner et al. (2003) found over 400 ways to cope with stressors, the important findings of these reviews were that most of the coping strategies used top-down regulation in relation to stress. These
findings show that the PFC is especially important when it comes to coping with stressors (Skinner et al., 2003).

It seems like serotonin also has a crucial role when it comes to resilience to stress. Since the SCM hypothesis states that individuals will be vulnerable to psychopathology if a stressor is greater than earlier stressors, because the serotonin transporter will be affected (Puglisi-Allegro & Andolina, 2015). Individuals with two long alleles of the serotonin polymorphism seem to cope with environmental risks better than individuals with one or two short alleles (Puglisi-Allegro & Andolina, 2015).

When it comes to taking control of the perceived situation in relation to psychological stress, the body can adapt to the situation and effective allostasis can be developed (McEwen, 2002). In the perception of control, the ventral medial PFC is activated and a direct connection goes to dorsal raphe nucleus. Dorsal raphe nucleus is a serotonin rich-area which contributes to the perception of control (Maier et al., 2006).

Other factors that have been seen to contribute to resilience include planning skills, academic achievement, good social relationships, control of a perceived stressor and to have been exposed to stressors in life and coped with them before (Hornor, 2016; Leipold & Greve, 2009; Puglisi-Allegro & Andolina, 2015). Moreover, if the stressor is greater than earlier experiences and resources available, an individual is more likely to experience psychopathology even if an individual has been resilient in the past (Puglisi-Allegro & Andolina, 2015). The physiology is then affected and the body goes from allostasis to allostatic load (McEwen, 2002).

The answer to the second research question, can emotion regulation techniques such as cognitive reappraisal be used to strengthen an individual’s stress resilience, seems to point in a positive direction. Findings have found that an individual’s thoughts are integrated into their body (Damasio & Sutherland, 1994). Ventral medial PFC is linked with the autonomic nervous system (Damasio & Sutherland, 1994). When individuals have control over a perceived stressor, the ventral medial PFC is activated and can inhibit the dorsal raphe nucleus (a serotonin rich-area) and prevent the autonomic nervous system from activating the fight-or-flight response (Damasio & Sutherland, 1994; Maier et al., 2006). Since Olff (1999)
found that prolonged sympathetic nervous system activation can result in a dysregulated HPA axis, resilience can be enhanced by preventing an individual from falling into psychopathology by an over-activated HPA axis.

Prolonged negative affect can also result in an overactivated HPA axis, which can lead to disorders such as PTSD or MDD (Gaffey et al., 2016; Olff, 1999). Therefore, cognitive reappraisal seems to be able to down-regulate negative affect, and in that way may be a tool to use to be more resilient against stress (John & Gross, 2004).

Since an over-activated amygdala is present in many psychiatric disorders, cognitive reappraisal can be used to diminish the amygdala activity by re-evaluating a negative situation into a more positive one (LeDoux, 2007; Lieberman et al., 2007). Moreover, self-focused reappraisal is associated with medial PFC activity, which is associated with emotion regulation and studies have found that self-focused reappraisal is associated with diminished activity of the amygdala, which in that case might help make an individual more resilient against stress (Willroth & Hilimire, 2016). On the other hand, cognitive reappraisal seems to be most beneficial when a stressor is uncontrollable, since it is an emotion regulation technique (Troy et al., 2013). The study by Troy et al. (2013) found that cognitive reappraisal was beneficial when a stressor was uncontrollable but not when the stressor was under control.

Finally, the third research question asked for the neural correlates of cognitive reappraisal, related to stress and resilience. This thesis has found that stress, resilience, and cognitive reappraisal are especially involved with brain areas such as PFC and the amygdala. The amygdala is responsible for emotional stimuli and the PFC is responsible for putting the environment into context and diminishing the amygdala response in relation to perceived danger (Arnsten, 2009; LeDoux, 2007; Roozendaal et al., 2009).

When it comes to cognitive reappraisal, different parts of the PFC are responsible for different tasks. According to Buhle et al. (2014) cognitive reappraisal is associated with dorsal medial PFC, dorsal lateral PFC, ventral lateral PFC and posterior parietal lobe. In line with this, Perchtold et al. (2017) also found an association in ventral lateral PFC during reappraisal tasks. Furthermore, this study found that the more activation the participants had in the ventral lateral PFC, the less
stressed they felt during everyday life. Therefore, according to these studies, the ventral lateral PFC seems to be especially important in cognitive reappraisal tasks for regulating negative feelings in relation to stress. The study by Ochsner and Gross (2008) found that the ventral PFC was especially involved with response inhibition. On the other hand, Morawetz et al. (2016) found increased activity in other brain areas during reappraisal tasks, such as the superior temporal gyrus and inferior frontal gyrus. It seems that activation in the different brain areas during reappraisal tasks varies depending on the experimental design and what specific task is being measured. However, the studies in the area do not agree exactly which brain areas that are activated in reappraisal tasks, according to the review by Buhle et al. (2014).

The limitation of this thesis is that stress, resilience, and cognitive reappraisals are broad areas and everything could not be included. The focus of the thesis has been what individuals can do to promote resilience from a neuroscientific perspective. Resilience can be measured from a more global perspective, like for example, enhancing resilience in the community or in families or by cultural aspects. Since the area is so broad there are many subjects that are missing in the area of resilience to stress. Areas like self-efficacy, locus of control and social support have also been shown to have importance in the research of stress and resilience. However, since these three areas are broad, more focused research to address these matters would be recommended. Another limitation is the shortage of existing studies that use cognitive reappraisal in relation to stress and resilience. To get a better understanding of the subject, future research needs to investigate studies that directly link cognitive reappraisal to stress.

To conclude, resilience is a broad topic and it seems that many aspects contribute to resilience. An individual’s genetics, the early environment and an individual’s capacity to regulate their emotions seem to affect a human’s resilience capacity. A functioning PFC and amygdala seem to be especially important to have the capacity to use emotion regulation techniques to help cope with a stressful event. However, more research needs to be done to know more about the neural correlates of resilience, stress and cognitive reappraisal, and how resilience can be enhanced.
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