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Abstract

This thesis investigates associations between chronic stress (CS) and the physiological parameters heart rate variability (HRV) and transepidermal water loss (TEWL) and the psychological parameter relaxed positive affect (RPA) to deepen the understanding of CS. The negative associations of acute psychological stress and HRV, skin barrier integrity and RPA were displayed in several studies. Yet, it is unclear whether CS is associated with those three parameters similarly. This thesis explores the nature of the associations of HRV, TEWL and RPA with CS. Within the ramifications of an overarching project with experimental design that investigated associations between stress, music listening and wound healing, baseline data of 96 participants with a regular menstrual cycle were assessed to investigate this thesis' hypotheses. Operationalization was done by combining subjective measures, assessing self-report CS and RPA, and physiological measures in form of HRV and TEWL. There were no significant associations found between CS and TEWL or HRV respectively; however, there was a significant small negative association of CS and RPA ($r = -0.238$; $p = 0.02$). This association aligns with previous findings regarding CS, although it is rather small. An exploratory finding regarding a large negative correlation of TEWL and RPA ($r = -0.507$; $p < 0.001$) might potentially be due to acute stress correlates. The results of this analysis indicate that CS is a far more complex construct than previously assumed. Future research should emphasize differentiating characteristics of the stressors and personal factors that accompany CS to gain a clearer insight into how they differently relate to physiological phenomena.

Key words: chronic stress, psychological stress, heart rate variability, root mean square of successive differences, transepidermal water loss, skin barrier homeostasis, HPA axis, ANS, physiology of stress

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Introduction

Stress is an essential part of human experience as a reaction to the environment. Especially in the last years the environment on earth and its potential threats changed dramatically. For example, during the start of the Covid-19 pandemic a meta-analysis found a relatively high global prevalence of stress of 25.18% between the 30th of December 2019 and 30th of August in 2020. While people were under threat of the virus, the authors found that stress prevalence started to rise globally (Mahmud, Mohsin, Dewan, & Muyeed, 2022). In a meta review of other meta-analyses ranging from 2019 to March 2021 a prevalence regarding psychophysiological stress of 31.99% was found (De Sousa et al., 2021). Especially in the last years many possible new stressors arose for the general population that made stressful situations more common. But stress can have serious effects on mental health and physical health. High work stress for example is associated with a higher likeliness of mental disorders (Wang, Lesage, Schmitz, A Drapeau, 2008). Likewise, stress is also linked to risk of chronic diseases and heart disease risk (Cohen, Janicki-Deverts, & Miller, 2007; Gianaros, & Wagner, 2015). Especially chronic stress (CS) can lead to physiological dysregulation like impaired cardiovascular, endocrine and immune functioning and in turn pose a threat to health (Schetter, & Dolbier, 2011). Exploring how stress specifically works and how it exactly affects the health and lives of our species seems crucial to cope with an ever-changing environment and its new threats and challenges.

The concept of stress

Stress is elicited by anything severely challenging homeostasis, a state of balance among all body systems needed for the body to survive and function correctly (Selye, 1956). A stressor, any stimulus inducing stress, triggers psychological, physiological and behavioural responses aimed at reinstating homeostasis (de Kloet et al., 2005). This may happen through any stressor that is perceived as such. According to the transactional model of stress a stress response happens after the subjective appraisal of a possible stressor leads to the assumption of harm/loss, threat or challenge. This process is called primary appraisal. During secondary appraisal it is determined if and what can be done to cope with the situation, as well as what is at

stake in this particular situation. In this complex process possible coping options and their respective consequences are evaluated. This is crucial for secondary appraisal. After the situation is resolved new information about the given experience is evaluated again, which is called reappraisal. So stress arises when a situation is appraised as stressful and coping resources are not deemed enough to deal with the situation (Lazarus & Folkman, 1984). Different phases in the model are associated with different bodily correlates. For example, the anticipatory evaluation of the stressor as threatening or challenging during primary appraisal has been found to be associated with the suppression of the immune system, whereas the anticipatory evaluation of the available resources during secondary appraisal is not (Kuebler et al., 2015)

When exposed to stress, an organism's intent is to return to homeostasis. That means stress promotes adaptation to a new situation. The process of activating the body's neural, neuroendocrine and neuroendocrine-immune mechanisms to maintain stability and to adapt to challenges in daily life or with major life stressors is called allostasis (McEwen, 1998). Generally, the changes during this process are beneficial for the individual, but if the regulation of cortisol and adrenaline in this process is not initiated adequately or in general extensively overused, then this can lead to strain, also called "allostatic load" or "allostatic overload" (McEwen, 2004). Prolonged secretion of the hormones epinephrine, norepinephrine and cortisol through overactivation of the sympatho-adrenomedullary system (SAM) and the hypothalamic-pituitary-adrenal axis (HPA axis) can damage brain and body instead of helping to regulate the distressed individual (McEwen, 2006). Acute stress promotes immune function by enhancing movement of immune cells to body parts that could need defence against pathogens, CS on the other hand can suppress immune function using the same hormonal mediators (Dhabhar, & McEwen, 1999). Inadequate activation of regulatory processes like chronic activation or inactivity in the cardiovascular, metabolic, immune and central nervous system are associated with respective problems such as hypertension, potential for stroke, obesity, diabetes, atherosclerosis, inflammatory or autoimmune disorders, immunosuppression, neuronal atrophy and death of nerve cells (Seemann et al., 1997). Even though in extreme cases the risks of allostatic load seem quite severe it is very important to note that allostasis in itself is a crucial process for dealing with stressors and for an organism to return to a healthy balance (McEwen, 2004).

Physiology of stress

On the one hand a stress response involves the activation of the SAM, which is part of the autonomous nervous system (ANS) and on the other hand the activation of the HPA axis (de Kloet et al., 2005; Charmandari et al., 2005). The HPA and the SAM are the core neuroendocrine components of the stress response and help prepare an individual to cope with metabolic, physical or psychological stressors (Negrão et al., 2000). Though both systems operate in a highly interconnected and coordinated way, they can still function differently in terms of speed and bodily changes. In a situation that is perceived as stressful a significant corticotropin-releasing hormone (CRH) release occurs and with it the activation of both the HPA axis and SAM ensues (de Kloet et al., 2005).

The HPA-axis

CRH in the hypothalamus is regulated by two brain structures, the amygdala, which is critical for fear, and the hippocampus, taking up a role in the downregulation of the HPA. When the amygdala's nucleus becomes active, information is sent to the hypothalamus and a stress response ensues (Bear et al., 2020). During HPA axis activation hypothalamic output of CRH and arginine vasopressin (AVP) leads to the release of glucocorticoids like cortisol. To go into detail, CRH stimulates the secretion of adrenocorticotropin hormone (ACTH) from the anterior pituitary. AVP potentiates the effect of CRH and plays a role as a mediator of the HPA response to chronic stress. ACTH in return affects the adrenal cortex to regulate glucocorticoid and adrenal androgen secretion. (Charmandari et al., 2005; de Kloet et al., 2005; Lolait et al., 2007) Peak levels of cortisol after acute stress are usually shown fifteen to twenty minutes after stress onset because of the time it takes for the whole process to take place (Lightman, 2008). During non-stressful situations CRH and AVP, both associated with the stress response, are secreted in a circadian pulsatile fashion. In the absence of stressors this process helps to maintain the time-of-day dependent regulations of physiological systems in the body (Russell & Lightman, 2019). The pulsatile secretion is also affected by food intake, changes in lighting, activity or following stress (Charmandari et al., 2005).

Glucocorticoids have a far-reaching influence on the body and an excess can also lead to harm. They have an anti-inflammatory function, regulate cytokine encoding, play a role in metabolic regulation through glucose utilization and modulate emotion and cognition (Belanoff et al., 2001; Busillo & Cidlowski, 2012; Plaschke et al., 1996; Sorrells, & Sapolsky, 2007). Circulating glucocorticoids can even potentiate sympathetically mediated effects and advance activation of stored energy or peripheral vasoconstriction (Steckler et al., 2005). Through low affinity glucocorticoid receptors in the hippocampus, high concentrations of glucocorticoids like following a stress response, cause a negative feedback loop inhibiting the HPA axis which in turn then downregulates glucocorticoid secretion (Ulrich-Lai & Herman, 2009). Being exposed to high levels of glucocorticoids regularly, like exposure to chronic stress, can cause hippocampal neurons to diminish. In some cases, this may lead to lacking inhibition of the HPA axis followed by stronger stress responses with more cortisol release and more damage to the hippocampus (Bear et al., 2020).

The ANS

The ANS is separated into two branches, the sympathetic and the parasympathetic branch. Their physiological influence generally oppose each other. The two branches appear to be reciprocal, when one is less activated the other tends to be more activated. The ANS is involved in adapting quickly to external stimuli in an automatic way without conscious or voluntary control. The sympathetic division of the ANS deals with physical activation and triggers physiological changes like dilated pupils, accelerated heartbeat, constricted blood vessels and stimulated glucose production and release, while the parasympathetic division deals with resting or vegetative states and emphasises activation of digestive functions, sexual arousal, a slower heartbeat and stimulation of the urinary bladder (Bear et al., 2020). As part of the sympathetic branch of the ANS, the SAM responds fast to stressful stimuli and involves the activation of the behavioural fight or flight response. By exciting the cardiovascular system, blood pressure and heart rate can be increased rapidly. Activation of SAM also results in increased circulating levels of adrenaline and noradrenaline, peripheral vasoconstriction, energy mobilization and cardiac activity. Exceptions for vasoconstrictions include vessels that supply skeletal muscles and external genitalia for which a dilation occurs. This effect can also diminish again

quickly through parasympathetic activation, making the reaction rather short lived (Charmandari et al., 2005; Karemaker, 2017; Ulrich-Lai & Herman, 2009).

Heart rate variability

The heart and heart rate are influenced greatly by the ANS and its sympathetic or parasympathetic activity, an interaction vital for our survival. The muscular heart consists of two atria and two ventricles. Deoxygenated blood enters the right atrium and is pumped to the lungs to clean up wastes and replace oxygen. Then through the left ventricle the oxygenated blood is pumped back to the arterial system. Two nodes, the sinoatrial and the atrioventricular, are the internal pacemakers to initiate a heartbeat. Usually, the sinoatrial node initiates each cardiac cycle, but if it is injured or diseased it can be replaced by the atrioventricular node. They receive input from autorhythmic cells within the heart, generating the pacemaker potentials spontaneously that then lead to the heartbeat. With the electrocardiogram one is able to measure the heart's electrical conduction and contraction resulting in a potential visual representation of the heart rate (Marieb, 2003; Shaffer, McCraty & Zerr, 2014).

In a healthy individual there is a relative balance between sympathetic and parasympathetic nervous system (SNS/PNS) activity that regulates the heart. At rest parasympathetic activity leads to an average heart rate (HR) of 75 beats per minute (Opthof, 2000). Sensory information from proprioceptors (recording limb position), chemoreceptors (recording blood chemistry) and baroreceptors (recording pressure) from the heart and information from the cerebral cortex and limbic system are gathered and integrated in the medulla of the brainstem to direct the heart's activity. Through shifts in the relative balance of sympathetic and parasympathetic activity the heart rate is adjusted as deemed necessary for a situation (Shaffer & Venner, 2013). In a healthy organism the HR depicts the effect of the neural output of the parasympathetic nerve, slowing it down, or the sympathetic nerves, accelerating it. This means that the relative activity of sympathetic and parasympathetic systems is reflected by the HR (Shaffer, McCraty, & Zerr, 2014). While parasympathetic nerves, for example the vagus nerve, exert their influence on the heart rapidly in under one second, sympathetic nerves need up to five seconds (Nunan et al., 2010). Sympathetic activity increases the HR after a delay of up to five seconds, resulting in a growing increase in HR until a

continuous stimulation of twenty to thirty seconds leads to a steady HR level. Fast changes in HR are attributed to parasympathetic activity as increases and decreases in HR can also be achieved by parasympathetic vagal activation or block (Hainsworth, 1995). The variability of the distance between R peaks of the heartbeat signal reflects the hearts' ability to react to physiological and environmental stimuli. Because of the specific autonomous nervous innervations of the heart through sympathetic activity and vagal parasympathetic activity, heart rate variability (HRV) is considered a quantitative marker of the ANS (Malik et al., 1996).

HRV describes the variability of the heart rate according to bodily needs. The HRV is calculated by observing the time between R peaks in an individual's heart rate (Figure 1). The adaptability of the heart is assessed by investigating the shifts in time peaks, that allow the computing of the general variability of the heart in a certain pre-defined time frame (Shaffer, McCraty, & Zerr, 2014).

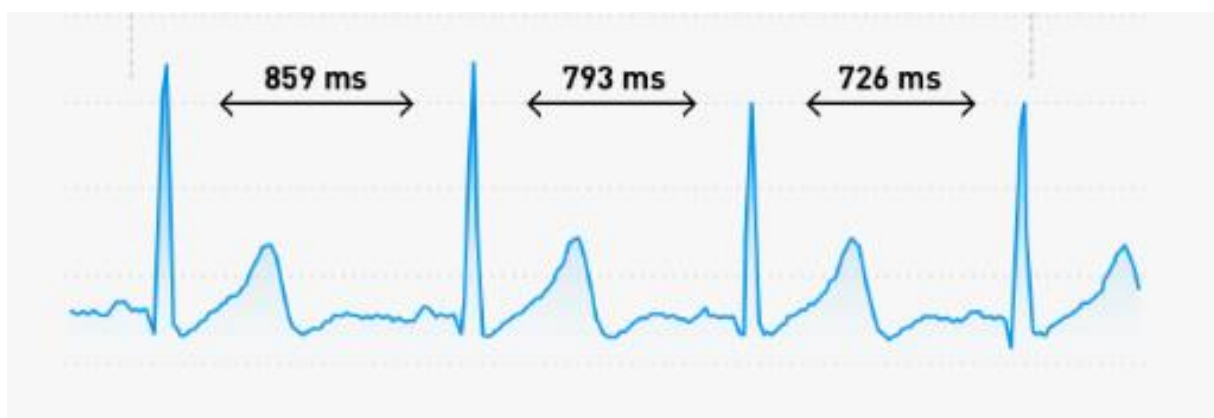


Figure 1: Heart beat with time between R-peaks (WHOOP, 2021)

Highly irregular fluctuations in the normal resting sinus rhythm during steady-state conditions are very usual and happen due to complex non-linear interactions of different physiological systems (Reyes Del Paso et al., 2013). These influences allow for a dynamic physiological control system in healthy individuals, which is always adapting and responsive to necessary changes when needed. Observing these changes in HR allows the identification of an individual's HRV. HRV is considered a measure for neurocardiac function that reflects heart-brain interactions and ANS dynamics. While too much instability in HRV may lead to inefficient functioning and energy utilization, not enough change in HR can suggest pathology and/or depletion. A crucial and necessary flexibility, adaptability and resilience within the hearts

regulatory systems point towards healthy function and well-being and is only possible with an appropriate amount of variability (Shaffer, McCraty, & Zerr, 2014). Low HRV especially seems to be a strong predictor for future health problems and a correlate for disease and even all-cause mortality (Berntson et al., 2008; Dekker et al., 1997).

After elaborating the impact of the ANS on the heart and the stress response it seems only logical that stress and HRV are deeply connected. In fact, a meta-analysis found reason to suggest a link between HRV and reduced threat perception, a vital aspect for an individual's perception of a stressor and the following stress response (Kim et al., 2018). Another meta-analysis highlights the importance of HRV being a potential marker for stress, due to HRV being an indicator for the brain's context dependent regulation to a stressor (Thayer et al., 2012). It was even suggested that the root mean square of successive differences (rMSSD), a measurement for HRV, could also be used as a measurement for the PNS. And as CS seems to affect the PNS strongly a possible link between CS and HRV might be plausible (Michels et al., 2013)

So, what happens to the body when stressful situations happen frequently, and many situations of acute stress become CS?

Chronic Stress

CS is described as enduring, with multiple stressors and with ongoing demands that threaten to exceed the resources of an individual (Schetter & Dolbier, 2011). Usually this is coupled with the individual's inability to efficiently deal with the presenting stressors and achieve homeostasis. Persistent exposure to chronic stress may lead to allostatic load and a wear and tear of bodily functions (McEwen, 2004).

Through CS glucocorticoid receptor mRNA is downregulated, which leads to impairments in terminating the stress response (Furay, Bruestle, & Herman, 2008; Ulrich-Lai & Herman, 2009). Prolonged exposure to stressors can lead to the overstimulation of the HPA-axis and fluctuating cortisol levels which lead to a disruption of the natural 24-hour cortisol cycle found in healthy individuals (Jones & Gwenin, 2020). Cortisol is essential for many processes like learning, memory, emotion, regulation of glucose storage and utilization, and regulation of the duration

of inflammatory responses (Sapolsky, Romero, & Munck, 2000). So, a dysregulation in cortisol levels can have far reaching consequences across the human body. Multiple studies report a direct impact of chronic stress on immune function, namely, suppression of the immune system, higher susceptibility to pathogens and deficits in responses to vaccination (Dhabar & McEwen, 1997; Glaser et al., 2000; Glaser et al., 2001). Furthermore, chronic stress was found to impair prefrontal cortex dependent response inhibition and working memory (Mika et al., 2012).

According to a meta study by Miller, Chen and Zhou (2007) chronic stress may increase or decrease HPA activation and following also cortisol secretion. The deciding factor for an increase or decrease seem to be the features of the stressors and the features of the person. According to the authors the impact of chronic stress on health manifests in varying and complex ways.

Not only the HPA axis but also the ANS is affected when stress becomes chronic. Imbalances that develop under conditions of stress are associated with decreased parasympathetic and increased sympathetic activity. Low HRV, increased HPA axis activity and reduced gamma amino butyric acid activity in the CNS can point to parasympathetic underactivity (Kim & Yosipovitch, 2013). CS is associated with decreased cardiac autonomic function as measured by HRV (Lampert et al., 2016). Also, when exposed to acute stress cardiovascular and endocrine responses seemed to be suppressed when individuals were highly chronically stressed (Matthews, Gump, & Owens, 2001). CS appears to promote deregulation of the ANS by inducing an autonomic imbalance towards an increased sympathetic activation that can last for several weeks after end of stress, even in stress free intervals (Bhatnagar et al., 1998; Cacioppo et al., 2000; Grippo et al., 2002). Furthermore, a study found that a hyperactivation of the HPA in chronically stressed males led to an inhibited reactivity of the ANS in acute stress situations which affected cognitive performance negatively (Teixeira et al., 2015). During chronically stressful conditions it is suggested that hypersensitivity of the SNS may occur, more specifically in context with habitual stressors, but not with novel stressors. Hyperactivity of the SNS on a chronic basis can harm the cardiovascular system by for example interfering with vasodilatory processes. Direct consequences of chronic stress and SNS hyperactivity can include endothelial dysfunction, cardiomyopathy, cardiac ischemia and arrhythmias, and disturbances in haemostasis (Golbidi, Frisbee, & Laher, 2015). Furthermore, it seems like CS also induces structural remodelling in the prefrontal cortex and hippocampus

resulting in dysfunctional PNS activity and vagal brake (Kim & Yosipovitch, 2013). Maladjusted PNS activity appears to be connected with high mortality, morbidity and poor health in various stress related disorders. Anxiety, depression, posttraumatic stress disorder and schizophrenia are also associated with dysfunctional PNS activity through prefrontal cortex hypoactivity (De Couck, Mravec & Girdon, 2012; Streeter et al., 2012). At the same time, the ANS has been linked to resilience to stress and chronic stress as well. Resilience to stress and faster stress recovery are associated with an increased basal vagal tone and PNS activity (Kogan & Weihs, 2012; Walker et al., 2017). Nonetheless it is still unclear whether a high vagal tone is cause or consequence of resilience.

When PNS regulation of the heartbeat via the sinus node is attenuated, the sinus node should tend to fire at its intrinsic rate. In this case the variability of the heart rate is expected to be lower than usual. To conclude, if chronic stress leads to PNS hypoactivity, low HRV could also be an indicator for chronic stress. In their findings Chandola, Heraclides and Kumari (2010) did indeed find this proposed connection between chronic and work stress and HRV. Another study (Michels et al., 2013) found a connection between chronic stress, measured by questionnaire data on negative emotions and peer problems, and HRV, especially low PNS activity, in children. It was also pointed out that still further research was needed to illuminate the complexity of CS to be able to prove that HRV can be a viable indicator for CS.

Transepidermal water loss / Skin barrier integrity

The skin is an essential organ for the human being. It is innervated by sensory nerves expressing receptors that can sense pain, itch, temperature and touch (Zimmermann, Bai, & Ginty, 2014). Furthermore, its functions entail preventing fluid loss, stabilizing body temperature and immune function (Bear, Connors, & Paradiso, 2020; Nguyen & Soulika, 2019). The skin can also work in establishing and maintaining tissue homeostasis, defending and repairing parts of the body.

Our skin is generally structured into three layers: the epidermis, the dermis and subcutaneous fat tissue. The epidermis, being the outmost layer of the skin, is categorized into the stratum corneum, the stratum lucidum, the stratum granulosum, and the stratum basale. The layers contain keratinocytes in different forms that

structure them. The stratum basale additionally contains immune cell such as Langerhans cells and T cells, and melanocytes that provide pigmentation for the skin (Hsu & Fuchs, 2014, Ovaere et al., 2009). The dermis, just underneath the epidermis, is organized into the papillary and reticular sub-layers. The papillary dermis has extensions up into the epidermis allowing for a better transportation of nutrients there. The reticular dermis contains on the one hand hair follicles, sebaceous glands, sweat glands and on the other hand collagenous and reticular fibres that are interwoven and make the reticular dermis thicker than the papillary dermis. The dermal layers also include, beside other cells, immune cells like macrophages, lymphocytes and mast cells (Woodley, 2017). Beneath the dermis the subcutaneous fat is located. In this layer energy is stored. The subcutaneous fat is important for glucose homeostasis and lipid metabolism and contains cytokines and various immune cells. Additionally due to the insulating capabilities of fat tissue this layer helps in regulating body temperature (Driskell et al., 2014; Tran et al., 2008).

By employing physical barriers like biomolecules, forming an intricate network of resident immune and non-immune cells and skin structures, the skin protects from harm when the host is being exposed to environmental challenges. Additionally, the skin plays a role in tissue homeostasis (Nguyen & Soulika, 2019).

The stratum corneum is composed of corneocytes (a differentiated form of keratinocyte) that form three layers of barriers to prevent entry of alien substances and microorganisms into the body and the loss of water through the skin (Kubo et al., 2013).

When something damages the skin, the acute wound healing process commences in four phases: hemostasis, inflammation, proliferation, remodelling. During hemostasis the injured area is isolated and further bleeding is stopped by forming a clot. In the inflammation phase immune cells infiltrate the wound. Pathogens are warded off and necrotic debris is cleaned off. Now the proliferation phase commences and skin resident cells like keratinocytes and others become active. Keratinocytes migrate and expand to restore the barrier function of the epidermis. The clot is replaced by newer cells and newly generated blood vessels. The residuum blood forms a scab. In the last phase, the remodeling phase, the injured tissue attempts to restore its original form and structure. Many cells involved in the previous phases vacate the injured tissue leaving the newly formed extracellular matrix and

collagen fibres behind (Nguyen & Soulika, 2019; Willenborg et al., 2012). The acute wound healing process differs from the healing process of a chronic wound. It is also important to note that tape stripping, a process where the stratum corneum is damaged by applying and removing adhesive tape, and the ensuing skin barrier recovery differs from a classical wound healing process, as there is no bleeding involved.

A meta-analysis found an association between impaired healing or dysregulation of a biomarker associated with stress in most of the analysed studies. This was consistent across many different clinical, experimental, acute and chronic wound types including tape-stripped skin (Walburn et al., 2009). To evaluate the time that the body needs to heal, an indicator for wound healing is necessary. Recovery of the skin barrier integrity can be measured and therefore instrumentalized to solve this problem.

Transepidermal water loss (TEWL) is an objective measurement for the amount of water evaporating passively through the epidermis of the skin. More specifically it measures the water lost through the stratum corneum, due to the water vapour pressure gradient on the inside and outside of the skin. It can be used as a measure for the skin barrier integrity and barrier water function in healthy individuals (Honari & Maibach, 2014). Generally high levels of TEWL are associated with impairments in skin barrier whereas lower TEWL levels with a healthy and intact or recovered skin barrier (Akdeniz et al., 2018)

Psychological stress can significantly inhibit permeability recovery (Garg et al., 2001). Additionally, it is also possible that stress inhibits functioning of skin barrier integrity without wound related impairment. Stress compromises the integrity of the stratum corneum, responsible for the loss of water through the skin (Choi et al., 2005; Kubo et al., 2013). Furthermore, not just the innate but also the adaptive immunity of the epidermis seem to be compromised through psychological stress (Aberg et al., 2007; Kleyn et al., 2008). It was found that psychological stress affects the skin barrier integrity negatively, not only through the activation of the HPA axis and release of cortisol, but also through the activation of 11 β -hydroxysteroid dehydrogenase type I. As 11 β -hydroxysteroid dehydrogenase type I seems to convert the inactive cortisone to active cortisol, it appears to play a role in inhibited skin barrier integrity under stress. After administering selective serotonin reuptake inhibitors (SSRI) on patients with

anxiety, barrier function improved again when psychological stress was relieved and 11 β -hydroxysteroid dehydrogenase type I levels decreased (Choe et al., 2018; Kao et al., 2003; Terao et al., 2011). These findings suggest a strong link between psychological stress and skin barrier integrity, which should be assessable through TEWL measurements. This points out the question whether chronic stress has a similar association with skin barrier integrity compared to acute psychological stress. Because chronic stress affects the immune balance and susceptibility to external pathogens (Dhabar & McEwen, 1997; Glaser et al., 2000; Glaser et al., 2001) it could be assumed that chronic stress has a negative influence on skin barrier integrity.

Relaxed positive affect

When discussing stress and its influence on the body one should also converse about positive affect (PA). It not only seems to build resilience but also trigger an upward spiral toward emotional well-being (Fredrickson & Joiner, 2002). Indeed, this kind of affect is talked about quite a bit in the context of positive psychology. With the work and introduction of positive psychology by Seligman and Csikszentmihalyi (2000) positive affect shifted much more into focus. This shift brought a focus on resilience, psychological well-being and flourishing along with them, in which positive affect plays a big role (Fredrickson, 2001; Seligman, 2011).

The broaden-and-build theory by Fredrickson (2001) states that positive emotions result in broadened thought- action repertoires and lead to enduring personal resources. Positive emotions are declared to positively influence attention, cognition, action as well as physical, intellectual and social resources. The theory suggests that multiple discrete positive emotions are essential elements for an individual to function optimally.

Furthermore, the stress buffering model specifies the relationship of PA and (chronic) stress and the association it has with health. It proposes that PA reduces stress and its effects on the body, by reducing stress reactivity and accelerating stress recovery (Pressman & Cohen 2005).

In general, greater PA has been associated with healthier immune function outcomes, lower cortisol levels and healthier cardiovascular function (Bhattacharyya

et al. 2008; Blanchflower & Oswald 2008; Brummett et al. 2009; Marsland et al. 2007). Moreover, PA interventions have been tied to an elevated vagal tone, pointing towards more physiological relaxation and heart health (Kok & Fredrickson 2010). A paper of Hoyt et al. (2015) states a positive correlation between high arousal PA and elevated but healthy cortisol secretion levels, pointing towards HPA axis activity. Another finding declares an association between PA and a higher relaxation related parasympathetic nervous system function assessed by HRV (Bhattacharyya et al. 2008). These findings could seem contradicting at first glance, but upon further inspection they make more sense.

PA can be differentiated into distinct but also interacting regulation systems. On the one hand there is PA linked to activation, drive and seeking, which seems to be linked to the dopamine system. This kind of PA regulation system deals with doing, achieving, and anticipating rewards or successes. On the other hand, there seems to be a kind of positive affect that is mediated by opiates and oxytocin and has soothing, contentment and relaxing characteristics. It seems to be associated with reward consummation and turning off seeking (Depue & Morrone-Strupinsky, 2005; Panksepp, 1998).

There is also evidence pointing towards a link of oxytocin as a stress buffer (Heinrichs et al., 2003). Specifically, the oxytocin-opiate system seems to be connected with soothing, calming, and feelings of social connectedness and safeness. (Depue & Morrone-Strupinsky, 2005; Gilbert, 2016) This seems to be a very important mechanism especially when dealing with stress, as social stimuli and clues in form of voice tones facial expressions, touching and holding were found to be regulators of arousal, emotion and physiological processes such as stress hormones, immune functioning and brain maturation (Cacioppo et al., 2000; Schore, 2015; Trevarthen & Aitken, 2001).

Gilbert et al. (2007) examined the different aspects of PA and found not only two but three underlying aspects of PA, developing a self-report questionnaire based on them. Namely these are activated positive affect (energetic, lively, adventurous, active, enthusiastic, dynamic, excited, eager), relaxed positive affect (RPA; relaxed, peaceful, calm, tranquil, laid back, serene) and safeness and contentment positive affect (safe, content, secure, warm). In this context activated PA is associated with higher arousal, and RPA is associated with low arousal. Interestingly, safeness and

contentment PA is not defined by a level of arousal. In contrast to the other two positive affects, safeness and contentment PA was distinguishable by a different aspect that might be seeking versus contentment according to Gilbert et al. (2007).

After accounting for high arousal PA, low arousal PA was found to significantly predict outcomes for life satisfaction, depression, feeling good, mindfulness, anxiety and stress. Furthermore, for stress and anxiety, low arousal PA seemed to predict the outcome significantly more strongly than high arousal PA (McManus, Siegel, & Nakamura, 2018). Also, between RPA and stress a significant moderate to large negative correlation was found (Gilbert et al., 2007). In the context of PA, low arousal might be qualitatively different compared to high arousal PA, particularly in the context of stress. Especially so as feelings such as calm and relaxed emphasize a soothing quality associated with parasympathetic activity (Gilbert 2009; Richardson et al., 2016). According to Depue and Morrone-Strupinsky (2005) this quality and the system of emotion regulation associated with consummatory pleasure, deactivation, soothing and affiliation is connected to naturally occurring opioids and oxytocin.

In the context of stress, chronic stress and the prevention of it, RPA is an extremely important mechanism to explore. Not only might RPA and the soothing qualities of the PNS provide an individual with coping capacities in or after acute stressful situations but might also result in increased resilience to chronic stress. The emphasis on the qualities of the parasympathetic system and states of relaxed positive affect might not be regarded enough when looking at chronic stress.

The research gap

To summarize, chronic stress has a detrimental influence on our mental and physical health (Dhabar & McEwen, 1997; Glaser et al., 2000; Glaser et al., 2001; McEwen, 2004; Mika et al., 2012; Schetter, & Dolbier, 2011). Especially in times where many individuals have to deal with the current effects and aftermaths of the Covid-19 pandemic, war, the climate crisis and the struggle to afford basic needs, chronic stress is an issue of overwhelming urgency. To further the understanding of chronic stress there are still many research gaps to be closed. While it was shown that stress can have a detrimental effect on the heart rate and the PNS there does not seem to be enough evidence in literature regarding the associations of chronic stress with HRV as a health indicator for the coronary system and healthy PNS function (Chandola,

Heraclides & Kumari, 2010; Michels et al., 2013; Schetter, & Dolbier, 2011). Although it seems to be generally accepted that psychological stress can lead to adverse cardiovascular consequences, the mechanisms that may underpin this are still not well understood (Golbidi, Frisbee, & Laher, 2015). A meta study even found that HRV might be a potential marker for stress, due to HRV being an indicator for the brain's context dependent regulation to a stressor (Thayer et al., 2012). However, this still leaves the question whether CS is connected to HRV in a similar way. Furthermore, especially a low HRV seems to be a strong predictor for future health problems and a correlate for disease and even all-cause mortality (Berntson et al., 2008; Dekker et al., 1997). In the light of the just presented literature it seems only logical to expect that a connection between CS and HRV exists, but it also shows that this association still needs more elaboration.

The association between CS and RPA appears to fit just in with the research gap regarding CS and HRV. RPA represents a subjective measure of a state of relaxation (Gilbert et al., 2008). Usually, the activation of the PNS accompanies a feeling of calmness and serenity in the body (Bear et al., 2020). It is also important that the subjective state of relaxed affect seems to be inversely related to stress (Gilbert et al., 2007; McManus, Siegel, & Nakamura, 2018). Generally, PA appears to play a role when talking about resilience to stress (Fredrickson, 2001; Pressman & Cohen 2005). Considering this, a negative relationship between CS and RPA would be expected, but there is little literature concerning this. This master's thesis tries to elaborate further how RPA and CS are connected to also help close this gap in the literature.

It is already established in literature that skin barrier integrity and wound healing are impacted by acute stress (Choi et al., 2005; Garg et al., 2001; Kubo et al., 2013; Walburn et al., 2009). Higher levels of TEWL are associated with impairments in skin barrier whereas lower TEWL levels with a healthy and intact or recovered skin barrier (Akdeniz et al., 2018). Especially the activation of the HPA axis and the expulsion of cortisol impacts skin barrier integrity negatively (Choe et al., 2017; Kao et al., 2003; Terao et al., 2011). This is especially important as CS seems to play a role in dysregulating the HPA axis and output of cortisol (Furay, Bruestle, & Herman, 2008; Jones & Gwenin, 2020; Ulrich-Lai & Herman, 2009). As CS seems to affect the susceptibility to external pathogens and the immune balance it appears to be important to investigate the associations of CS and skin barrier integrity further (Dhabar &

McEwen, 1997; Glaser et al., 2000; Glaser et al., 2001). All in all, it would be expected that according to the just presented literature CS could have a negative association with skin barrier integrity.

Research question and hypotheses

The topic that is of interest in this master's thesis explores the associations of chronic stress with heart rate variability, skin barrier permeability homeostasis and relaxed positive affect in a sample of healthy female identifying individuals (assessed by the German word "Geschlecht", which doesn't differentiate between gender and sex), who reported having a regular menstrual cycle. This thesis deals with the research question *"Does chronic stress negatively correlate with skin barrier permeability homeostasis, heart rate variability and relaxed positive affect?"*.

Resulting from the presented research gaps and the underlying findings of previous studies, following hypotheses will be investigated:

H1: Transepidermal water loss is positively correlated with chronic stress

H2: Heart rate variability is negatively correlated with chronic stress

H3: Relaxed positive affect is negatively correlated with chronic stress

Methods

The data used for this master's thesis was gathered within a two-study project called "Effects of music on stress and skin barrier recovery" conducted by Dr. Jasminka Majdandžić and Univ.-Prof. Dr. Urs Nater from the Music and Health Lab within the department of Clinical and Health Psychology at the University of Vienna. The project's main focus lies on the associations between music listening and skin barrier recovery and how this association is mediated by stress. The studies assessed various self-report state and trait variables like positive affect, subjective stress and chronic stress while also measuring manifest variables like heart rate or salivary flow in the laboratory during the testing. Study one and study two of the project differed mainly in that the Trier Social Stress Test (TSST; Kirschbaum et al., 1993) was included in study two to induce and measure acute stress.

Sample

The recruitment of participants was done with the help of social media, a mailing list of the university of Vienna and distribution of flyers. Communicated information consisted of basic inclusion and exclusion criteria, a contact email address and information about the expense allowance of 35€ in the flyer for study one and 45€ in the flyer for study two. Upon expressing their interest via email, possible participants were asked for a cell phone number and possible timeslots for a twenty-minute telephone screening to assess their compatibility with the studies inclusion and exclusion criteria. Following a standardized manual, specifically instructed members of the study team conducted the interview.

Participants in both studies had to fit with a number of specific exclusion and inclusion criteria. Not all of these criteria were central to the hypotheses proposed here, nonetheless they will be detailed to thoroughly describe the sample.

As measurements for salivary cortisol and alpha amylase were involved in both studies the sample had to fit specific exclusion criteria to control for potential confounders of biomarkers. The sample was selected following a set of recommendations for measurements of cortisol and alpha amylase (Strahler, Skoluda, Kappert &, Nater, 2017). Participants had to be between 18 and 35 years of age,

healthy, assigned the gender female at birth and not define their identity otherwise, not be pregnant or breastfeeding, not use hormonal contraceptives or general medication affecting hormonal levels, not be in menopause or climacteric, have a regular menstrual cycle and be in the follicular phase during testing. Furthermore participants had to be free from chronic somatic illnesses including cardiovascular diseases like coronary heart disease angina pectoris, myocardial infarction, cardiac arrhythmia, heart failure or arterial occlusive diseases, pulmonary and respiratory diseases for example pneumonia, asthma, chronic bronchitis or tuberculosis, Liver diseases like hepatitis, jaundice or fatty liver, hypertension or extremely low blood pressure, chronic pain, kidney and urinary tract diseases like kidney or bladder stones, diabetes mellitus or other metabolic diseases like hypercholesterolemia or hyperuricemia, diseases of the digestive tract like stomach diseases or chronic intestinal diseases, neurological diseases, infectious diseases like HIV, Hepatitis or TBC, thyroid abnormality, autoimmune diseases, diseases of the skeletal system, muscle disease and blood disorders like anaemia, allergies, hay fever or hypersensitivity reactions to medicines, patches, latex gloves, hay fever, grasses or pollen. Additionally, only participants were included that had no visual impairment except if it was correctable with glasses or contact lenses, no current mental disorder or psychiatric illness accounting for depression, psychosis, anxiety disorders or eating disorders within the last five years, did not have a tropical stay in the last six months, no vaccinations in the last two weeks, a BMI between 18 and 25 and not use alcohol excessively meaning no substance abuse within the last two years and a regular consumption of less than eight small alcoholic beverages the size of 0.33liters of beer or 0.125 liters of wine. Moreover, only participants who did not consume substances like amphetamines, MDMA, barbiturates, benzodiazepines, cocaine, opiates in the last year or cannabinoids in the last fourteen days, had no (dental) surgery in the last eight weeks, no other health anomalies like tumours, meningitis or an accident, did not use psychopharmaca in the past fourteen days and did not take cardiovascular medication.

Specific criteria to enable tape-stripping were also important to account for. Participants were only included if they did not have any chronic or acute inflammatory skin diseases, no allergies to adhesive tape, no eczema, rashes, burn marks or similar on the volar forearm and did not take any immunosuppressive drugs.

Additionally, both studies had to be controlled for confounders through unusual experience of music. The sample consisted of participants with no hearing impairment,

chronic tinnitus, music-related profession, music related studies and no absolute hearing.

Lastly for study two, individuals were only allowed to participate if they had no previous experience with the Trier Social Stress Test (TSST) and no personal relationship with the members of the study team. Participants in sample two had to meet these criteria in order to ensure similar efficacy of the TSST for everyone. This was the only prerequisite that was different for the samples in both studies regarding exclusion and inclusion criteria, as study one did not entail a TSST.

Eligible individuals were given basic information about the studies ramifications and were asked for consent regarding needed procedures like administration of equipment during the study. Towards the end of the screening suitable individuals were asked for the start of their last menstrual cycle and the average time of their menstruation and full menstrual cycle to be able to compute a possible date for testing. All participants were tested in their respective follicular phase, optimally in the second half, four to seven days after the beginning of their menstruation.

Participants were asked to complete a battery of questionnaires that was available to them through a link in the email confirming their date of testing, until 24 hours before testing. Two days before the testing date an additional email was sent as a reminder.

Power analysis

With G-Power (Faul et al., 2007) a power analysis was conducted a priori. To be able to reliably find a correlation with a small effect size of 0.3, an $\alpha = 0.05$ and a power of 0.8 a sample size of at least 64 participants would be required. As the data of this thesis is derived from a superordinate study, it was not possible to ensure this requirement was met for every single hypothesis. A-posteriori power analyses are included in the results for every hypothesis.

Trier Social Stress Test

The TSST (Kirschbaum, Pirke, & Hellhammer, 1993) is a tool to induce moderate psychological stress in a laboratory setting. In MuSkiBa II it consisted of an anticipatory period of three minutes and a test period, where the test subject had to speak freely about their personal abilities and characteristics qualifying them for their dream job for five minutes and then perform mental arithmetic in front of an audience. The participant was told that the audience, which consisted of the active stressor that was perceived as male and the passive stressor that was perceived as female, are professional analysts of behaviour. While the active stressor gave instructions to the participant the passive stressor stayed silent and assisted in handling the equipment and stopping the time. Both stressors did not show emotion towards the participant and kept a serious outlook and took fake notes of the participant's behaviour. If the participant seemed very calm the active stressor asked the test subject to focus more on the stressors themselves or on cameras pointed at them to elicit the stress response that is wanted in the TSST. Although the cameras were not running, the participant was led to believe that they were being filmed. During the arithmetic task the participant had to count down from 2043 in steps of 17 and was asked by the active stressor to begin from the start if they would make a mistake. Participants that had no problem doing this task were asked to try to be a bit faster or concentrate on the camera or on the stressors more.

The TSST has been found to lead to a noticeable change in cortisol and heart rate levels and does not seem to change in effectiveness with different personality traits.

Operationalization

Chronic stress

A part of the self-report "*Trier Inventar zum chronischem Stress: TICS*" Questionnaire (Schulz & Schlotz, 1999) was used to measure chronic stress. It was filled out at home before the experiment as part of a general battery of questionnaires that participants had to complete latest one day before participating in the study. Specifically, the scale called "*Screening Skala zum chronischen Stress: SSCS*"

concerning chronic stress was used, which delivered a score of general chronic stress and consisted of 12 items. The questionnaire involved a 5-point Likert scale and items like *“Zeiten, in denen mir die Sorgen über den Kopf wachsen”*, (in English: *“Times when my worries get the better of me”*) or *“Zeiten in denen ich mir viele Sorgen mache und nicht damit aufhören kann”* (in English: *“Times when I worry a lot and can’t stop”*). Participants were asked to rate how often they experienced the content of the item in the last three months. The items are reported to have a discriminatory power between 0.72 and 0.54. Furthermore, the scale is reported to have a very good Cronbach's α of 0.91, a good Rasch-model reliability of 0.89 and a good content-related validity.

Trans-epidermal water loss

Baseline TEWL was assessed via TEWAMETER TM300 to measure skin barrier integrity. The TEWAMETER TM300 (Medelink) provides an electrical measurement of the hydration state of the skin surface. In other words, the humidity lost through a specific part of the skin on the inner arm of the not dominant hand was measured. Because the first measurement of TEWL in MuSkiBa II was after the TSST, only measurements of participants in MuSkiBa I were included in the analysis. In MuSkiBa I the measurement took place after the acclimatisation phase and some questionnaires, shortly after Marker 1 (see figure 2).

For every participant a small area of the skin located approximately two centimetres from the elbow crease on the lower non-dominant inner arm was marked. The area was separated into three distinct areas right below each other, which were all measured every time a measurement was taken. A fourth area was located just below the other three and functioned as a control site. Each area was measured until 20 consecutive measurements with a standard deviation of less than 0.5 were recorded by the device. Measurements took place with a room temperature between 22.5 and 23.5 °C and a probe temperature of 34°C. During a measurement participants and experimenters were told to refrain from speaking or breathing around the probe and hold as still as possible. Air conditioning was switched off and all doors were closed during the procedure to not disturb the sensitive measurement procedure. The water evaporation rate was recorded with the unit g/h/m². A mean value of the three areas was computed, when the different measurements did not differ more than

10 g/h/m² from each other. This mean measurement of the baseline was used to explore hypothesis regarding skin barrier integrity.

Relaxed positive affect

To quantify RPA “*The Types of Positive Affect Scale: TTPAS*” (Gilbert et al., 2008) was used. As testing was done in German, the original version was translated and then back translated by a native speaker to check for possible errors. The used German version was not further validated. It was measured right after the acclimatisation phase and after the marker I was set. This questionnaire measures three types of positive affect: activated positive affect, relaxed positive affect and safeness/contentment positive affect. In this thesis measurements of RPA will be of main interest. Items are assessed with the statement “at the moment I feel....” with the item filling the dots and a five-point Likert scale from “not at all” to “very much”. The emotion words used for the items of relaxed positive affect were relaxed, peaceful, calm, tranquil, laid back and serene. The scale showed good psychometric properties with a Cronbach's α of 0.83. The retest reliability however was low with $r = 0.34$, which could imply that the relaxed positive affect scale is more of a state variable, related to low activity in the threat system.

Heart rate variability

HRV was operationalized by computing ECG data. The Root Mean Square of Successive Differences between successive R-R intervals (rMSSD) was calculated with four-minutes segments compared to a one-minute segment as reference using the Data Analyzer software (Movisens GmbH, Karlsruhe, Germany). RMSSD is a time domain measure and can be used to assess parasympathetic influence on the ANS as it is an index of vagal cardiac modulation. It is thought to be the most appropriate method for quantifying short term HRV (Ciccone et al., 2017; Sammito et al., 2015). Low rMSSD values are interpreted as higher physiological arousal whereas high rMSSD values indicate lower physiological arousal (Kothgassner et al., 2016).

The ECG data were collected by a movisens sensor strapped to the chest of the participants during the experiment. Via double tapping the EDA sensor the participant was instructed to set markers, that were then later visible in the data. The

five-minute period before marker 1 (see figure 2 and 3) was used to calculate HRV. For that the Movisens Data Analyzer software (Movisens GmbH, Karlsruhe, Germany) used the last minute of the five-minute interval as reference to compute the HRV for the remaining four minutes.

Procedure

Overarching project and study design

The main project is divided into two studies, namely MuSkiBa I and MuSkiBa II. In the study MuSkiBa I associations between music and skin barrier recovery are being investigated, whereas in study MuSkiBa II mediating effects of acute psychosocial stress on the association between music and skin barrier recovery are examined. The project was devised as a randomized control trial. Participants were randomly assigned to a music listening group, functioning as the experimental condition or to either an audiobook listening or a silence group, both being used as the control condition.

The focus of this investigation lies upon chronic stress as independent variable and trans-epidermal water loss, heart rate variability and relaxed positive affect as dependent variables.

Since not the whole project is directly relevant to the research questions at hand only crucial parts of the studies will be discussed in detail, while a general overview will assist in placing given focus points in the timeline.

First MuSkiBa I (figure 2) will be detailed as MuSkiBa II just additionally incorporates other procedures like the TSST.

MuSkiBa I

Every participant filled out a battery of questionnaires latest one day before testing. Participants were given specific instructions to not drink twenty-four hours prior to testing and not eat or brush teeth in the hours before because of the saliva measurements.

Every test session was conducted by a team of two individuals, one study leader who gave the instructions and one study assistant who would carry out the TEWL measures. The study leader could be male read or female read, whereas the study assistant always had to be female read. This was implemented because the study assistant would need to touch or be in close physical proximity to the participant to be able to measure TEWL. A read-male study assistant could have induced stress through a feeling of uncomfortability in some participants, so it was decided that the study assistant always had to be female-read to control for bias.

Participants arrived at 12.50 o'clock and were picked up by the study lead at the front of the faculty of psychology in the Liebiggasse 5, 1010 Vienna. They were led to the testing rooms on the second floor of the building. During the following thirty-minute acclimatisation phase their temperature was taken, and their COVID-19 vaccination status or test status was checked, while they filled out a COVID-19 interview. The individuals were given enough time to thoroughly read through their declaration of consent for the study and sign it. Afterwards the area that would be measured during the TEWL procedure was marked and the sensors for electrocardiogram data (ECG) and electrodermal activity (EDA) were put on, one on the not dominant hand the other at the chest on the height of the solar plexus. The participant had time to select the playlist they were about to hear (music condition) or the topic for the audio book (audio book condition). Then instructions on how to take saliva samples were given. Participants had to collect their saliva for two minutes and then transfer it through a tube into a polypropylene tube (SaliCap, IBL International, Hamburg, Germany). Shortly after the first saliva sample was taken, a marker was set for the EDA and ECG data and a set of state questionnaires were filled out. Once this was finished TEWL measurements began, a base line measure was taken, and then the tape stripping procedure followed just before another TEWL measure. Afterwards another saliva sample was taken, and the same state questionnaires were filled out again. Then the participant proceeded to either listen to music, an audio book or sit in silence according to their condition for thirty minutes. They were asked to not fall asleep or look at their phones during this time. Afterwards four more measurements of saliva and filling out the set of state questionnaires followed, intermediated by thirty minutes of reading geo magazines. Lastly a briefing about the purposes of the study and the remuneration completed the study trial.

Ablauf Muskiba I

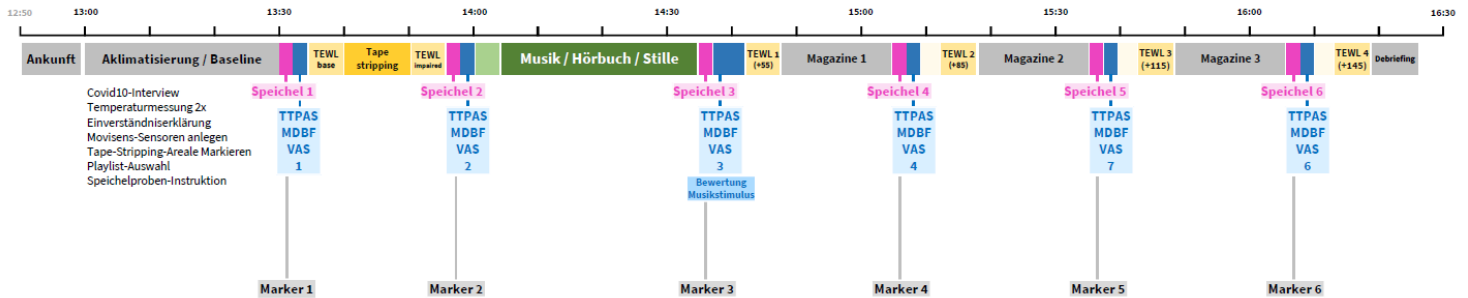


Figure 2: timeline of study one/MuSkiBa I

Muskiba II

MuSkiBa II also incorporated the TSST (figure 3). The TSST was done by two additional study assistants, one perceived male as the active stressor and the other perceived female as the passive stressor. Outside of the TSST they did not have contact with the individual that was tested. After the first saliva sample was taken and the set of state questionnaires was filled out, participants were introduced to the TSST task in the room where the active and passive stressor were already waiting in. After a short preparation time another saliva sample was taken, and a set of state questionnaires was filled out. Following that the individual that was tested started their presentation and subsequently the maths part as well. Directly thereafter the participant proceeded to take another saliva sample and fill out another set of questionnaires, just before they were led back to the testing room to start the TEWL measurements. After this point the study proceeded just like MuSkiBa I.

Ablauf Muskiba II

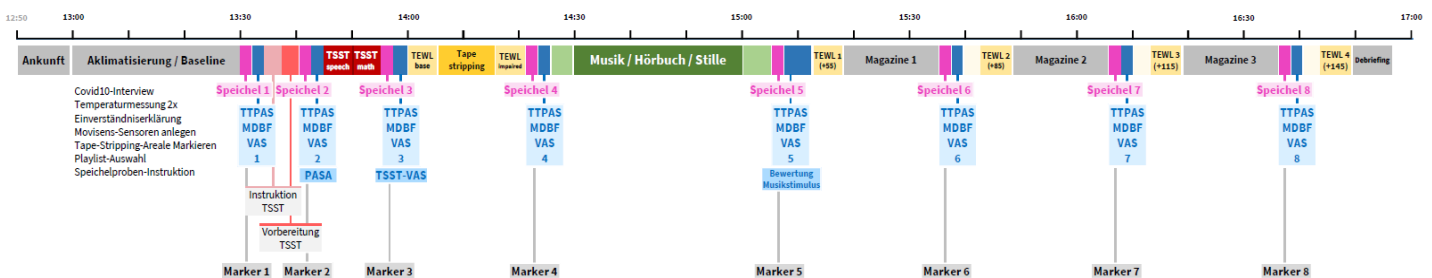


Figure 3: timeline study two/MuSkiBa II

Results

Statistical analysis

For the analysis the statistical program SPSS (version 27) was used, and every test was conducted with a significance level of $p < .05$ (two-tailed). Three two sample t-tests were conducted to check whether an analysis encompassing both studies would lead to possible biases. Afterwards descriptive data was analysed. H1 was analysed using only data from MuSkiBa I. H2 and H3 used data from both MuSkiBa I and II. To control for outliers, a boxplot analysis was performed for every parameter that is part of the analysis. All hypotheses were analysed by performing Spearman's correlation analyses, as metricity of the data could not be assumed, and therefore a Pearson correlation would not have been suitable. According with the requirements of a Spearman's correlation all used parameters were paired observations and at least scaled ordinally.

Sample description

For this thesis, data of a total of $N=96$ participants was gathered and analysed. Only participants who finished the experiment and reported meeting all given requirements could be included. To test H1 it was necessary to exclude all participants from MuSkiBa II for this specific analysis, as their first TEWL measurement was right after the TSST which is likely a confounding factor. This is due to the stress participants experience while doing the TSST and the association stress has been shown to have with TEWL (Choi et al., 2005; Kubo et al., 2013). Additionally, one data point was excluded, as their value was far above the usual range of 10-18 g/h/m² units. The exceptionally high value (22.8 g/h/m²) was probably due to a measurement mistake with the very sensitive instruments used to measure TEWL. For the other hypotheses participants of both studies could be included. For H2 two data points had to be excluded (see boxplot HRV) and 9 participants could not be included in the analysis due to problems regarding the data measurement with the ECG sensor. Reasons for this were issues during testing, malfunctions or incorrect usage of the sensor or artifacts that made interpretation of the data impossible. All in all, for H1 data

of N= 46 participants, for H2 data of N=85 and for H3 data of N= 96 participants could be investigated.

As required for this study all participants identified female (assessed with the German word “Geschlecht” which doesn’t differentiate between sex and gender) and had a regular menstrual cycle. Participants were between the age of eighteen and thirty-five with a mean age of 24.06 (SD= 3.71). The BMI of participants ranged from 17.58 to 25.39 with a mean of 20.95 (SD= 1.74). Most participants reported an Austrian nationality (56.3%) or German nationality (24%). Other individuals reported an Albanian, Chilean, French, Chinese (Hong Kong), Iraqi, Italian, Columbian, Croatian, Luxembourgish, Russian, Swiss, Ukrainian and Hungarian nationality (in total 19.7%). Of the participants 90.6% reported finishing at least Abitur/Matura, while the rest reported different qualifications. In terms of occupation, 36.5% reported not to be working but studying, 34.4% working less than half-time, 12.5% working more than half-time, 8.3% working full-time and 8.3% being unemployed. In total 50% identified as single, 44.8% as partnered, 1% as married, another 1% as separated/divorced and 3,1% as something different.

To check for outliers boxplot analyses were performed. For all parameters except for HRV all data points could be included. As shown (Figure 3) there were two extreme outliers in the HRV measure that were excluded from the analysis, as they could impose a bias on the results. The other variables showed no significant outliers that had to be excluded, as shown in the boxplots regarding CS, RPA and TEWL (Figure 2, Figure 4, Figure 5).

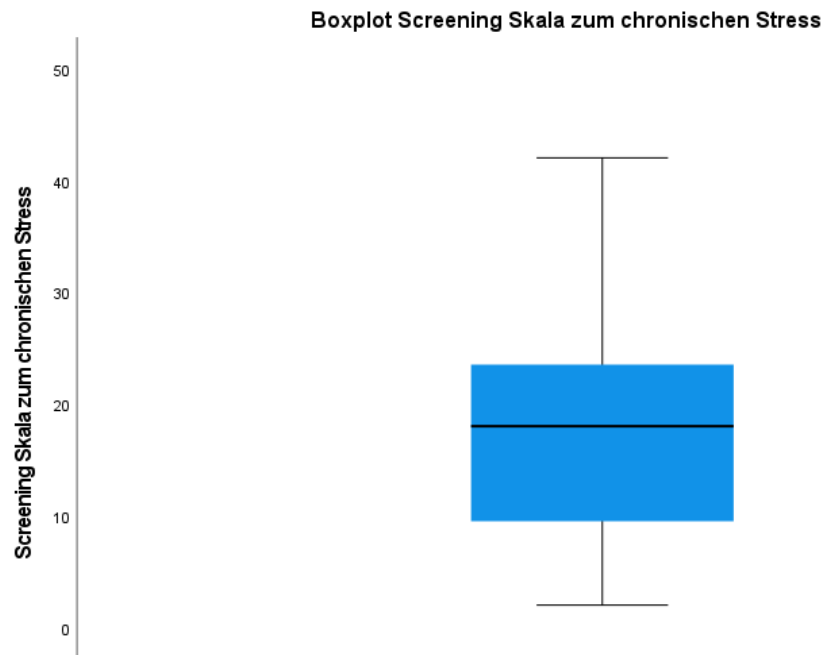


Figure 4: Boxplot picturing the distribution of scores on the "Screening Skala zum chronischen Stress"

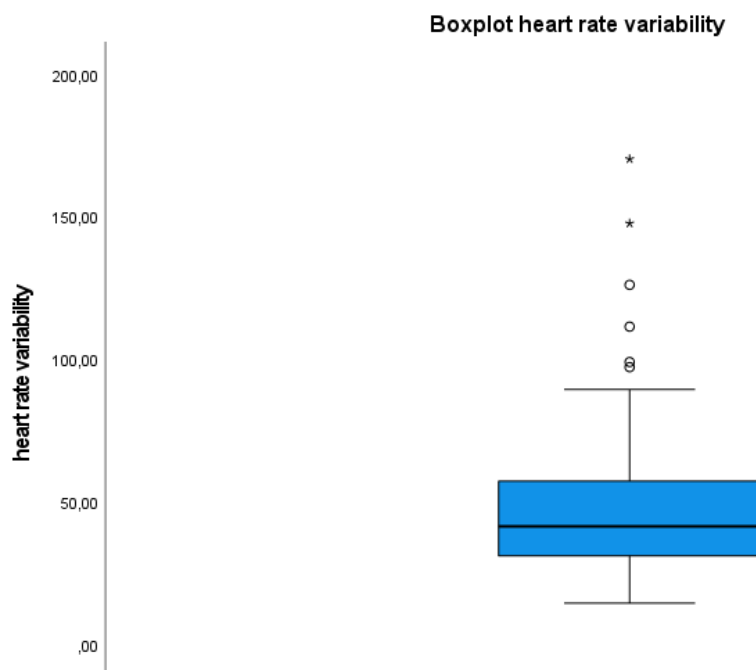


Figure 5: Boxplot picturing the distribution of heart rate variability are baseline; extreme outliers are marked as stars

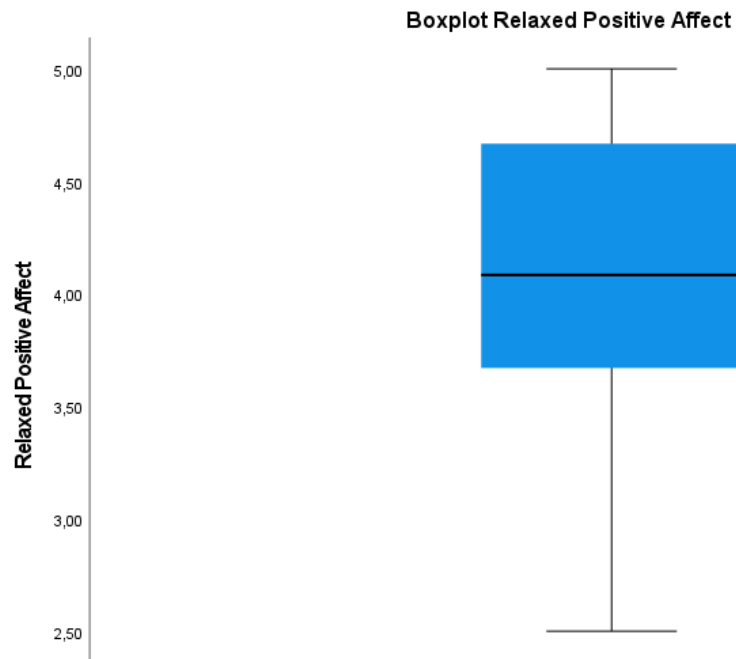


Figure 6: Boxplot picturing the distribution of relaxed positive affect at baseline

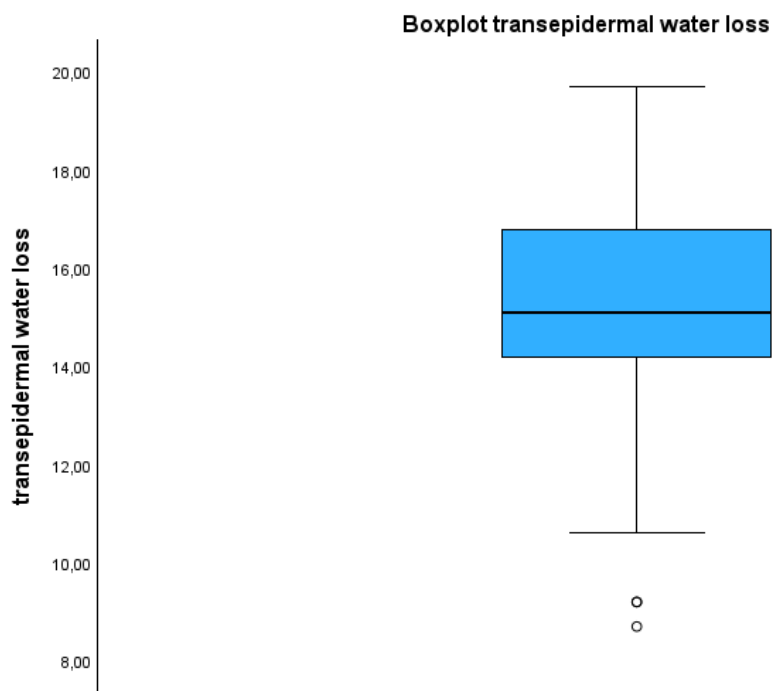


Figure 7: Boxplot picturing the distribution of transepidermal water loss at baseline

Descriptive statistics of the parameters are shown in Table 1. The average score of chronic stress, measured by the “Screening Skala zum chronischen Stress”, was 17.86 (SD= 9.23), ranging widely from two to forty-two points. The mean score of HRV using rMSSD was 45.8 milliseconds (ms; SD=22.56), varying from 14.32ms to 125.91ms. In the measurements for RPA a mean value of 18.34 (SD=3.66) with a minimum of nine and a maximum of twenty-four points was found. TEWL baseline scores showed a mean of 15.01 g/h/m² (SD=2.66).

Descriptive statistics of used parameters

	Heart rate variability	Chronic stress	Relaxed positive affect	Transepidermal water loss
N	85	96	96	46
minimum	14,3200	2	9,00	8,7000
maximum	125,9093	42	24,00	19,7000
mean	45,795239	17,86	18,3438	15,012319
standard deviation	22,5603774	9,232	3,65579	2,6635849

Table 1: Descriptive statistics of the parameters heart rate variability, chronic stress, relaxed positive affect, and transepidermal water loss

To make sure that the groups of Muskiba I and Muskiba II did not differ from each other regarding the variance in the data a two-sample t-test to compare the means of both groups was performed. This was necessary to exclude a potential bias, as the name of the studies (“music and well-being” and “stress and music listening”) and therefore potentially the applicants might have varied. There was no significant difference found between the groups of the different studies for HRV ($p = 0.597$), CS ($p = 0.782$) nor RPA ($p = 0.574$). For TEWL this analysis was not necessary as there were only data of participants included that participated in MuSkiBa I. As a result, it was assumed that the data of the two groups of participants did not differ significantly in their expression of the parameter between each other. Furthermore, it was assumed that using data of both studies to investigate this thesis` research question would not lead to bias due to a difference of the groups in the measured parameters.

Transepidermal water loss and chronic stress

In the first hypothesis a possible connection between TEWL and CS was investigated. For this data only of MuSkiBa I was used. After conducting the Spearman analysis no significant association between CS and TEWL was found ($r= 0.077$; $p=0.609$). This indicated that in this sample reported CS and the amount of TEWL measured during baseline did not predict each other at all. As for the low not significant result, not even a mild trend can be reported.

In figure 8 a scatterplot can be seen, demonstrating that there was no visible shape of data points recognizable. The regression line, that is shown merely explains 0.5% of variance in the data. As there was no significant connection between the two parameters found this variance is not representative and probably random.

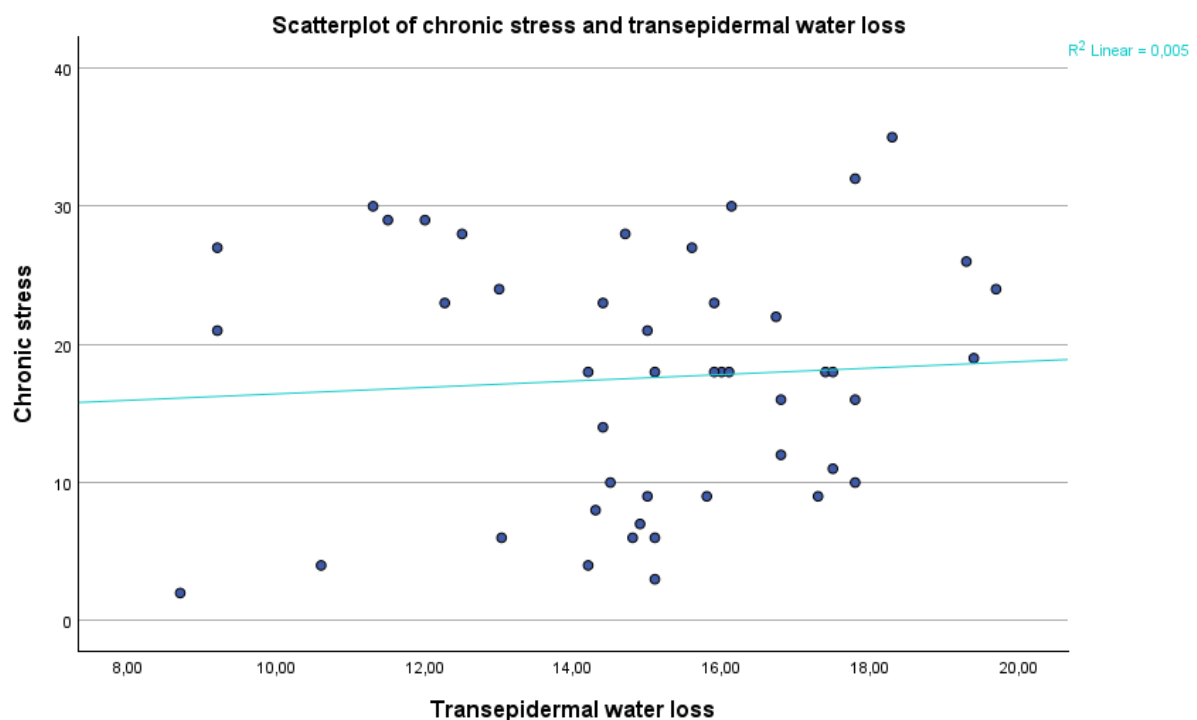


Figure 8: Scatterplot of chronic stress and transepidermal water loss; regression lone explaining 0.5% of variance

Heart rate variability and chronic stress

The second hypothesis examined a possible link between HRV and CS. There was no spearman correlation found between HRV and CS ($r=-0.008$; $p=0.94$). This

means that for this sample reported CS and the values of HRV that were measured during baseline were not connected.

In figure 9 the scatterplot of HRV and CS is shown. There appears to be no visible form of data points, which leads to the assumption that the two variables might not be correlated. The regression line in the scatterplot explains 0.7% of variance, which due to the lacking significance in the correlation between HRV and CS might just be coincidentally in the data.

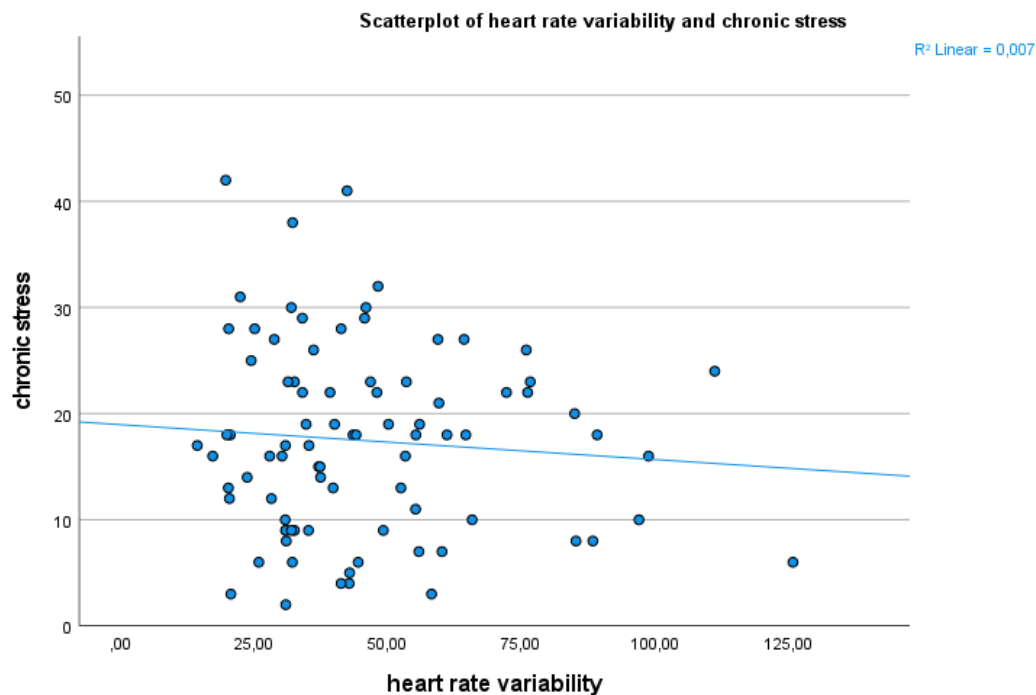


Figure 9: Scatterplot of heart rate variability and chronic stress; regression line explaining 0.7% of variance

Relaxed positive affect and chronic stress

The third hypothesis analysed a possible connection in the data between RPA and CS. The analysis showed that a significant association between RPA and CS with a weak negative correlation ($r = -0.238$; $p = 0.02$) could be found. In this sample participants who reported a higher chronic stress level also reported a slightly lower state of relaxed positive affect during baseline and vice versa.

Figure 10 demonstrates the distribution of data for RPA and CS. With the help of the regression line a slight oval form in the data points is visible. When considering

the significant connection of the variables, this can be interpreted as a correlation. The regression line explains a variance of 4.7% in the data, which can be interpreted as a small to medium effect size.

A post-hoc power analysis revealed that the analysis that led to this finding was done with a power of 0.66. This was computed by using the size of the correlation, an $\alpha = 0.05$ and the sample size of 96 participants, while considering the two tailed approach of the analysis. To achieve a power of at least 0.8 with this effect size it would be necessary to have a sample of at least 133 participants. This means that this result should be interpreted with caution, even though a significant finding resulted.

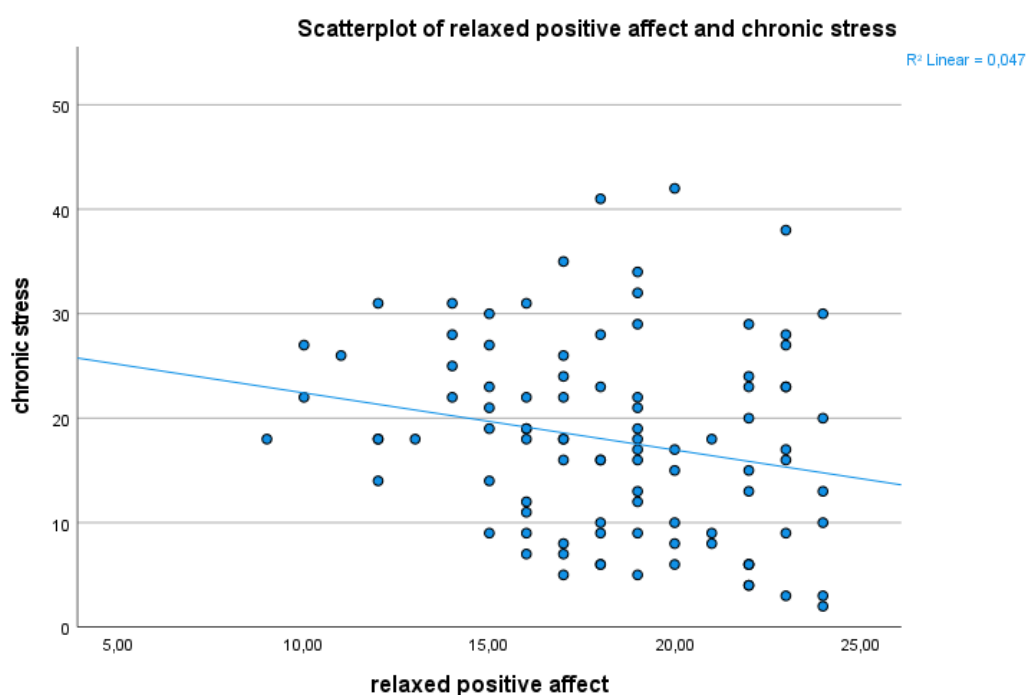


Figure 10: Scatterplot of relaxed positive affect and chronic stress; regression line explaining 4.7% of variance

Additional exploratory analyses

During the investigation of the hypotheses other analyses were also carried out. A significant correlation between TEWL and RPA ($r=-0.507$; $p<0.001$) stood out. A significant negative association of large size was found between water loss through the skin and self-reported RPA. This means that less water was lost through the skin in participants that reported feeling more relaxed, peaceful, calm, tranquil, laid back and/or serene.

In figure 11 a scatterplot of TEWL and RPA is shown. The form of the data points can be interpreted as a longer drawn-out shape. The regression line shows a definitive negative slope and as the correlation analysis found a significant large association, a connection between TEWL and RPA is indicated. The regression line even shows an explained variance of $R^2=26.5\%$, which can be interpreted as a large effect size.

To interpret the reliability of this finding a post-hoc power analysis was conducted here, as well. With the given size of effect, $\alpha = 0.05$, a two-sided analysis and the small sample size of $N=46$ for this connection a power of 0.78 was calculated. For a power of at least 0.80 a necessary minimum sample size of 49 would have been needed. Although this finding seems a little more robust than the significant association of RPA and CS, it should still also be interpreted with caution as no direct assumption for the population can be done.

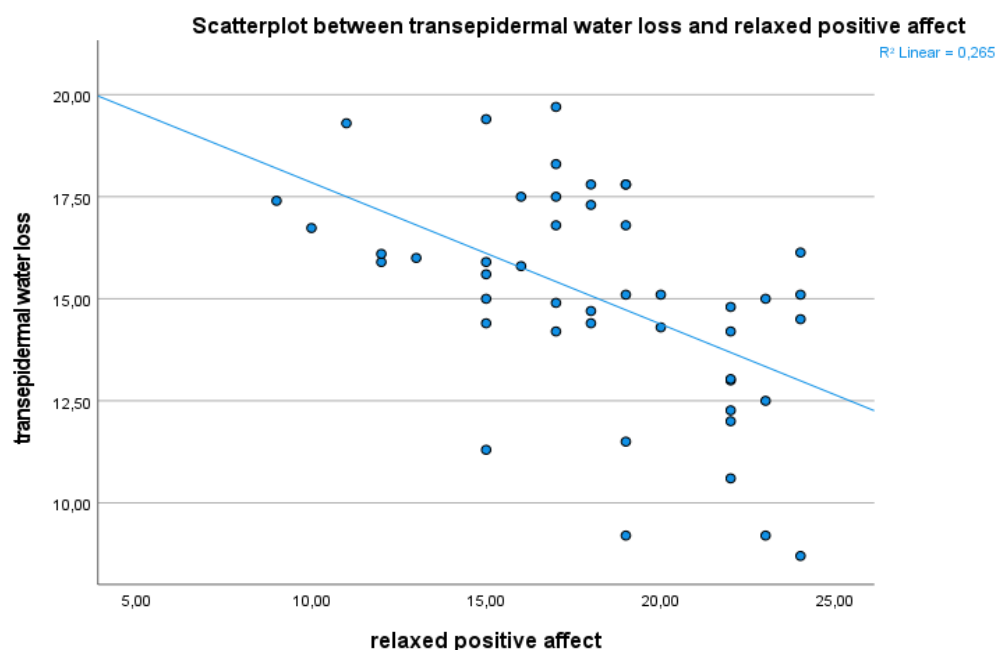


Figure 11: Scatterplot of transepidermal water loss and relaxed positive affect; regression line explaining 26.5% of variance

Discussion

Goal of this thesis was to further elaborate the associations between chronic stress in the human body and the feeling of being relaxed. To be able to include data from MuSkiBa I and MuSkiBa II both studies were analysed for differences in the data. As there was no significant variation in the expression of data between the studies, it was assumed that it would be plausible to use all data available for the analysis of the hypotheses. After the appropriate tests were conducted, reported CS levels were not found to be significantly correlated with either HRV or TEWL. Therefore hypotheses 1 and 2 have to be rejected. Between CS and RPA, a significant association could be identified, suggesting a negative correlation between the amount of chronic stress reported and the amount of relaxation in the moment. Even though only a small correlation could be demonstrated, and the sample was limited, hypothesis 3 can be accepted. Furthermore, a significant negative association was found regarding TEWL and RPA following exploratory analysis. This may provide interesting implications for further research on the topic.

Chronic stress and transepidermal water loss

The data of this thesis showed no association between CS and TEWL. This suggests no connection between the skin barrier integrity and the amount of reported chronic stress. However, the low amount of data that could be used may limit this finding. Considering the literature, it seems counterintuitive that water loss through the skin barrier was not predicted by the amount of CS. As susceptibility to external pathogens was connected to CS in the past this finding seems puzzling (Glaser et al., 2001). A possible explanation might be the negative effect of cortisol on the skin barrier (Choe et al., 2018). CS interacts with the HPA axis, which is responsible for release of cortisol, in complex and varying ways. CS is able to either increase or decrease HPA activity. The more time has passed after CS onset, the less HPA activity is shown. The closer to CS onset, the stronger HPA activity still is (Miller, Chen & Zhou, 2007). This means that the outcome of the association of CS and TEWL in this analysis might be influenced by external factors, as there was no measurement of the beginning of CS. If for some individuals who were chronically stressed the outbreak of CS was

recent, these individuals might experience a contrary effect regarding their cortisol output and skin barrier integrity compared to individuals who have been chronically stressed for a while.

An interesting approach regarding this hypothesis might be the investigation of CS and TEWL with cortisol as a mediator. If the assumption of fluctuating cortisol levels as reason for the highly not significant finding is true, then testing the proposed hypothesis with cortisol as mediator might be very relevant to understand the effects of CS better. This theory would also fit with the findings of acute stress impacting skin barrier integrity negatively as cortisol as mediator is also plausible for this effect (Choi et al., 2005; Kubo et al., 2013; Walburn et al., 2009).

Chronic stress and heart rate variability

In the analysis of the sample used for this thesis no significant connection between CS and HRV was found. It came to a surprise that previous findings on this association could not be replicated. Lampert et al. (2016) were able to find an association between CS and what they labelled decreased cardiac autonomic functioning and measured by using HRV. They found that CS and adverse life events were associated with ultra-low frequency, a measure of HR and standard deviation of NN intervals, a measure of HRV. Possible reasons for that are different measurements of the same concepts. Compared to SDNN, rMSSD seems to be more of a short term HRV measure (Wang, & Huang, 2012). The measure of CS was focused also on adverse life events in addition to the subjective experience of being overwhelmed and challenged by ongoing stressors. This contrasts with the TICS by Schulz & Schlotz (1999), that was used here, which mainly focusses on the accumulation of feelings of constant distress and inordinate worries, without specifying life events. There might be a fine but decisive difference between the present thesis and the study by Lampert et al. (2016) in that two slightly separate things were measured. On the one hand this analysis showed no significant association between the frequency of feeling stressed constantly and having an immense amount of worries and a rather short term HRV measure. On the other hand, Lampert et al. (2016) found a connection between adverse life events with associated overwhelmedness and a HRV measure that is used for a longer time frame (Wang, & Huang, 2012).

The other study was a meta study investigating CS and found a connection between chronic work stress and HRV (Chandola, Heraclides & Kumari, 2010). However, the longitudinal measures of stress, that were then defined as chronic stress were done in a very specific context and show little comparability with the assessment of chronic stress in this thesis. And again, in this study the chronic stressor was event related and the HRV measure was SDNN. Possibly the measure of chronic stress in an event related way leads to a different outcome in CS values. Perhaps CS only interacts significantly with the measure SDNN, as it is a measurement designed for longer time frames and incorporates an effect related to chronic stress that is still unknown. It may be that effects of chronic stress on the automatic cardiovascular regulatory mechanisms like the vagal brake manifest in changes over a time frame that rMSSD fails to measure.

Another factor that might have an effect is the relative importance of limbic glucocorticoid signalling in HPA axis inhibition. It regulates the HPA axis responses to psychogenic but not to systemic stress and as a result provides context specific feedback signalling that modifies HPA axis inhibition (Ulrich-Lai & Herman, 2009). Chronic stress might be interpreted as a systemic stressor because it manifests in a way that harms the body, poses a threat to the organism's homeostasis and can't be dealt with usual allostatic means (McEwen, 2017). This context specific HPA axis regulation might explain the lack of associations between HPA and chronic stress in this study. CS might be way more complicated than initially thought. The measurement of CS in this study might not fully encompass the variety in different types of CS and its underlying factors and therefore lead to no association between HPA and CS. A meta-analysis showed that the variability in HPA axis response can be attributed to personal and stressor features. Therefore, CS might elicit a wide variety of HPA axis responses, that are not measured with the methodological approach used in this thesis (Miller, Chen, & Zhou, 2007).

Chronic stress and relaxed positive affect

For hypothesis 3 a significant but small negative association between CS and RPA was found. This means that the more chronically stressed participants were the higher the tendency for them to report lower levels of RPA. One could argue that a

bigger association could have been expected, as the perception of being chronically stressed would seem to go hand in hand with self-report relaxed affect. From a logical standpoint, a person that scores highly on a questionnaire for CS would probably tend to not report that high levels of feeling relaxed overall, maybe especially in a setting that may be generally stressful as participant of a study. On the other hand, a person that has been chronically stressed for a long time might not even feel that stressed by this study, as its more relaxing compared to their everyday possibly even higher stress levels. This might be a reason for this association to be relatively small, because the comparison of highly chronically stressed individuals dampens makes them feel relatively more relaxed in a clinical study environment, where they just have to follow instructions and not actively do something proactively. Being in a situation where individuals are not so prone to think about other highly stressful things in their life, because they receive specific instructions about what to do, might also feel relaxing to some. Especially as the groups female identified and young tend to score higher on CS questionnaires, a comparative approach regarding the everyday stress to the situational possibly relaxing moment in a study with clear instructions and without the necessity to control might explain the small association found (Hoffmann & Sallen, 2015; Schulz, Schlotz, & Becker, 2004).

Furthermore, RPA has been connected to parasympathetic activity, while CS was connected to the hypoactivation of parasympathetic and hyperactivation of the sympathetic branch of the ANS (Bhatnagar et al., 1998; Cacioppo et al., 2000; Gilbert 2009; Grippo et al., 2002; Richardson et al., 2016). As the PNS is generally connected to bodily relaxation a negative association between CS and RPA could be assumed (Bear et al., 2020). But the detected correlation appears to be rather small in light of these findings. A reason for the small effect size could be the expression of data in the sample regarding CS or the proposed comparative approach of individuals dampening the association.

Still, all in all the significant negative association of CS and RPA seems to be in line with previous findings regarding the inhibiting effects of CS on the PNS (Bhatnagar et al., 1998; Cacioppo et al., 2000).

Exploratory findings

TEWL and RPA

The exploratory analysis of the significant large negative association between TEWL and RPA revealed a very interesting possible connection. With the given power of .78 and a sample of just $N=46$ a substantial significant effect can be expected with a higher sample size. A possible connection between the two might be explained through acute stress. Both parameters were found to have a direct association with acute stress in other studies. On the one hand it is already established in literature that skin barrier integrity is impacted by acute stress (Choi et al., 2005; Garg et al., 2001; Kubo et al., 2013; Walburn et al., 2009). On the other hand, the subjective state of relaxed affect seems to be inversely related to stress (Gilbert et al., 2007; McManus, Siegel, & Nakamura, 2018). Possibly acute stress influences the association between TEWL and RPA, leading to this correlation. Investigating this, might prove useful in understanding this strong association.

Another possible explanation could lie with the PNS. If the PNS does not function appropriately regeneration of the skin barrier or preservation of the skin barrier integrity might be inhibited, which could lead to greater water loss. Interesting to note here is that a finding regarding PNS activity being associated with cutaneous barrier function has been found in healthy subjects even though parasympathetic nerves are not innervated in the forearm skin (Roosterman et al., 2006). Furthermore, a delaying effect of psychological stress, which also leads to a reduction in parasympathetic tone, on skin barrier recovery after barrier disruption was found (Altemus et al., 2001; Garg et al., 2001). To summarize, an effect of acute stress and reduced parasympathetic activity seems like a plausible explanation for the negative association between TEWL and RPA.

Beside that, it is also possible that participants that were not as relaxed started to sweat more during the testing, which due to the humidity lead to higher TEWL values for not as relaxed individuals.

Limitations

Study design

The first and probably most important limitation to bring up is the very specific sample. The studies, from which the data was used, were designed to fit very specific criteria regarding music listening, acute stress responses and stress recovery. The project “Effects of music on stress and skin barrier recovery” was intentionally created as a means to do basic research to better understand the acute stress response and the recovery period afterwards. Therefore, the sample was very specifically adjusted to this aim. To control for deviations in alpha amylase or cortisol the sample was supposed to be very homogenous in regards to sex and gender identification, time in the menstruation cycle, physical health and specifically psychological health. Many participants were excluded on the basis of having a diagnosis for a mental disorder or doing psychotherapy. As fitting as this may be for the research of the acute stress response and acute stress recovery as detrimental it appeared to be after conducting research on chronic stress with this sample. Many mental disorders, if not all involve the inability to cope with the stress at hand adequately. Especially chronic stress is a part of many mental disorders and tightly connected to their prevalence (Wang et al., 2008; Woo et al., 2021). Furthermore, the exclusion of individuals with chronic somatic diseases or hypersensitivities might also be connected to the indirect exclusion of individuals with higher chronic stress levels. Chronic stress has been connected to various chronic somatic diseases or hypersensitivities (Glaser et al., 2001; Glaser, & Kiecolt-Glaser, 2005; Rohleder, 2019). The sample for the MuSkiBa studies probably didn't include many individuals with higher levels of chronic stress, as many potential factors connected to chronic stress were part of the exclusion criteria. This may have led to an artificially reduced variance in chronic stress. Coupled with the limited sample size, this may have had a big effect on the possible outcomes of the analysis. With the sample at hand, possibly only very strong correlations that would have been noticeable in a moderately chronic stressed sample as well could have been detected. A solution for this problem might be testing the same hypothesis with a bigger sample, that includes a representative variance of chronic stress data.

Another limitation is the limited number of participants itself. As the Muskiba studies are still running it might be interesting whether the same results would be replicated at a later point with more data or if different outcomes might be found.

Unfortunately, acquiring the data of participants necessary for a power of 0.8, would have probably taken more time than was available for the completion of this thesis. With the sample and effect sizes at hand, it was not possible to reach an adequate power. Hence there might be correlations of the analysed parameters that were not found in the sample due to limited power. Specifically for hypothesis I this limitation is strong, as only data from 46 participants could be used to explore a possible association between CS and TEWL.

Additionally, the measurement of CS might not display the CS of the population, maybe not even of a female identified group. Comparing the mean of the sample (adjusted to the raw values of the original) to the all gender norm tables of the TICS, one finds that a score of 18 is equivalent of 55 percentpoints. This means that in the norm sample of 16 to 30 year old individuals 55% percent reached a score that was either at or below 18 (Schulz & Schlotz, 1999). But especially in the last years a rise in chronic stress would be expected, as also acute stress levels rose globally due to stressors like the Covid-19 pandemic or the climate crisis (Mahmud, Mohsin, Dewan, & Muyeed, 2022). A relatively recent study using the TICS found a mean of 20.73 points in chronic stress for women participating in competitive sports. Compared to that for men in competitive sports a mean of 16.65 was reported (Hoffmann & Sallen, 2015). The gap between the groups with different gender identification seems quite big and points out the question whether a general all gender norm table is an appropriate comparison for a group consisting of only female identified individuals, like the sample of this analysis. It is possible that the expression of chronic stress in the sample of the MuSkiBa studies might not be interpreted correctly, when it is compared to the norm tables of an all-gender group almost 20 years ago. Regarding the norm tables of the TICS that were created 2004 the used sample would have a mean above average. But actually, it would be likely to have an even higher CS score for this part of the population, as many individuals that would supposedly have higher CS scores were excluded. Furthermore, especially female identified individuals and younger individuals are both categories who seem to score exceptionally high in the TICS (Hoffmann & Sallen, 2015; Schulz, Schlotz, & Becker, 2004). This would mean that the current associations probably lack validity as the data might not be as representative.

Generalizability

Additionally, the very specific sample used for the exploration of the hypotheses of this thesis might lead to a lack in generalizability. As only a selected group of participants were eligible to test, the result of the analysis is probably not representative for the general population. This did not seem to be the goal for the general research project but still it's important to note considering the studies ramifications. The sample of female identifying, assigned female at birth with a regular menstrual cycle, no hormonal contraception and completely healthy participants is simply not the status quo of our population. One could furthermore assume that a specific group either interested in the scientific process or in need of the monetary recompensation would even apply for the study. The biggest part of the sample, about 90% consisted of participants who at least finished Abitur/Matura resulting in a quite homogenous education level within the sample. Finally, it must also be noted that data collection happened during the COVID-19 pandemic and is therefore probably biased in terms of chronic and acute stress levels (De Sousa et al., 2021; Mahmud, et al., 2022). This means that results of this analysis should be interpreted with care and would definitely need further investigation in a bigger and more representative sample at a different time. Greater heterogeneity and generalizability would definitely improve validity of the study's results substantially.

Implications

Possible implications of this thesis seem to be on a mostly theoretical level. Nonetheless they may provide insights to further understand the concepts that were investigated.

In this thesis it was shown that a simple straightforward approach to chronic stress will probably not yield satisfying results. In fact, contrasting the results of this analysis with the literature showed that the way chronic stress seems to affect the body is far more complicated than assumed previously. A simple assessment of chronic stress with a self-report questionnaire might not be enough to operationalize the personal and stressor-related aspects to CS that lead to the variation of different effects it has on the human body (Miller, Chen, & Zhou, 2007). For future research on CS the duration, type of stressors, resources, subjective burden and strain, affected

areas of life and personal characteristics should be assessed with CS as well. CS itself could be differentiated into aspects, that affect the human body distinctly.

The relationship between CS and RPA suggests that even though no association between CS and physiology was found, the self-report measures seem accurate. It would make sense that individuals that feel constantly stressed and under pressure also have more difficulties relaxing. Still, it should be noted that no self-report measures correlated with physiological measures. This leaves the question in which ways the concepts that are investigated by the self-report measures coincide with bodily reactions to stress or relaxation. Further investigation of RPA would be necessary to understand in which way it is connected to physiological processes, if at all.

The exploratory analysis may provide deeper insights on the relationship of skin barrier permeability with RPA. A connection between TEWL and RPA might be explainable with acute stress or PNS activity. Now it would be interesting to investigate further which mechanisms underlie this connection, perhaps by additionally investigating the role of acute stress or parasympathetic activity. The examination of the role of psychological stress or parasympathetic activity as a possible influence for the association between TEWL and RPA could further the understanding of the biological mechanisms underlying the feeling of relaxedness and its consequences in the body.

Conclusion

This thesis provides insight on the concept of chronic stress. With a direct approach no association with physiological measures was found. Contrasting this with findings in the literature it appears as if a simple self-report measure of chronic stress might not be enough to capture the complexity of it. Chronic stress has varying and complex interactions with, and effects on, the human body, depending on personal factors and nature of the stressors (Miller, Chen, & Zhou, 2007). Not incorporating this into the measurements of CS, seems to lead to an oversimplification, that fails to represent the effects of CS on the ANS and skin barrier integrity found in other studies (Glaser et al., 2000; Glaser et al., 2001; Kim & Yosipovitch, 2013; Lampert et al., 2016). Especially under the constant and global rise of CS in the population, it is critical to further investigate and understand the effects of it (Mahmud, Mohsin, Dewan, & Muyeed, 2022). A differentiated approach towards the complex concept of CS might allow understanding of its varying effects. As HRV is an important indicator of PNS activity, adequate adaptability to stressors through the ANS and resilience, it is important to find a reliable association between CS and HRV (Pereira, Campos, & Sousa, 2017; Schetter & Dolbier, 2011).

It should be of great interest to illuminate varying influences of (chronic) stress on the body, to be able to find ways to better help individuals suffering from it. As most, though not all psychological diseases are based on failure to deal with stress, stress research is fundamental to understand psychological ill-being. Comprehending the facets of (chronic) stress may be highly influential in regard to treatment. Especially in an ever-changing environment the ability to cope with stressors adequately and without taking harm should be promoted and enhanced on a societal level. And how is that supposed to happen without furthering our understanding of (chronic) stress?

References

- Aberg, K. M., Radek, K. A., Choi, E. H., Kim, D., Demerjian, M., Hupe, M., Kerbleski, J., Gallo, R. L., Ganz, T., Mauro, T. M., Feingold, K. R., & Elias, P. M. (2007). Psychological stress downregulates epidermal antimicrobial peptide expression and increases severity of cutaneous infections in mice. *Journal of Clinical Investigation*, 117(11), 3339–3349. <https://doi.org/10.1172/jci31726>
- Akdeniz, M., Gabriel, S., Lichterfeld, A., Blume-Peytavi, U., & Kottner, J. (2018). Transepidermal water loss in healthy adults: a systematic review and meta-analysis update. *British Journal of Dermatology*, 179(5), 1049–1055. <https://doi.org/10.1111/bjd.17025>
- Altemus, M., Rao, B. K., Dhabhar, F. S., Ding, W., & Granstein, R. D. (2001). Stress-induced changes in skin barrier function in healthy women. *Journal of Investigative Dermatology*, 117(2), 309–317. <https://doi.org/10.1046/j.1523-1747.2001.01373.x>
- Bear, M., Connors, B., & Paradiso, M. A. (2020). *Neuroscience: Exploring the Brain, Enhanced Edition: Exploring the Brain, Enhanced Edition*. Jones & Bartlett Learning.
- Belanoff, J. K., Gross, K., Yager, A. R., & Schatzberg, A. F. (2001). Corticosteroids and cognition. *Journal of Psychiatric Research*, 35(3), 127–145. [https://doi.org/10.1016/s0022-3956\(01\)00018-8](https://doi.org/10.1016/s0022-3956(01)00018-8)
- Bhatnagar, S., Dallman, M. F., Roderick, R. E., Basbaum, A. I., & Taylor, B. K. (1998). The effects of prior chronic stress on cardiovascular responses to acute restraint and formalin injection. *Brain Research*, 797(2), 313–320. [https://doi.org/10.1016/s0006-8993\(98\)00382-5](https://doi.org/10.1016/s0006-8993(98)00382-5)
- Bhattacharyya, M. R., Whitehead, D. L., Rakhit, R., & Steptoe, A. (2008). Depressed mood, positive affect, and heart rate variability in patients with suspected coronary artery disease. *Psychosomatic Medicine*, 70(9), 1020–1027. <https://doi.org/10.1097/psy.0b013e318189afcc>
- Blanchflower, D. G., & Oswald, A. J. (2008). Hypertension and happiness across nations. *Journal of Health Economics*, 27(2), 218–233. <https://doi.org/10.1016/j.jhealeco.2007.06.002>

- Brummett, B. H., Boyle, S. H., Kuhn, C. C., Siegler, I. C., & Williams, R. (2009). Positive affect is associated with cardiovascular reactivity, norepinephrine level, and morning rise in salivary cortisol. *Psychophysiology*, 46(4), 862–869. <https://doi.org/10.1111/j.1469-8986.2009.00829.x>
- Busillo, J. M., & Cidlowski, J. A. (2013). The five Rs of glucocorticoid action during inflammation: ready, reinforce, repress, resolve, and restore. *Trends in Endocrinology and Metabolism*, 24(3), 109–119. <https://doi.org/10.1016/j.tem.2012.11.005>
- Cacioppo, J. T., Berntson, G. G., Sheridan, J. T., & McClintock, M. K. (2000). Multilevel integrative analyses of human behavior: Social neuroscience and the complementing nature of social and biological approaches. *Psychological Bulletin*, 126(6), 829–843. <https://doi.org/10.1037/0033-2909.126.6.829>
- Cacioppo, J. T., Burleson, M. H., Poehlmann, K. M., Malarkey, W. B., Kiecolt-Glaser, J. K., Berntson, G. G., Uchino, B. N., & Glaser, R. (2000). Autonomic and neuroendocrine responses to mild psychological stressors: Effects of chronic stress on older women. *Annals of Behavioral Medicine*, 22(2), 140–148. <https://doi.org/10.1007/bf02895778>
- Chandola, T., Heraclides, A., & Kumari, M. (2010). Psychophysiological biomarkers of workplace stressors. *Neuroscience & Biobehavioral Reviews*, 35(1), 51–57. <https://doi.org/10.1016/j.neubiorev.2009.11.005>
- Choe, S., Kim, D., Kim, E. K., Lee, J., Choi, E. H., Son, E. D., Lee, T. H., & Choi, E. H. (2018). Psychological stress deteriorates skin barrier function by activating 11 β -hydroxysteroid dehydrogenase 1 and the HPA axis. *Scientific Reports*, 8(1). <https://doi.org/10.1038/s41598-018-24653-z>
- Choi, E. H., Brown, B. B., Crumrine, D., Chang, S., Man, M., Elias, P. M., & Feingold, K. R. (2005). Mechanisms by which psychologic stress alters cutaneous permeability barrier homeostasis and stratum corneum integrity. *Journal of Investigative Dermatology*, 124(3), 587–595. <https://doi.org/10.1111/j.0022-202x.2005.23589.x>
- Chrousos, G. P. (2009). Stress and disorders of the stress system. *Nature Reviews Endocrinology*, 5(7), 374–381. <https://doi.org/10.1038/nrendo.2009.106>

- Ciccone, A. B., Siedlik, J. A., Wecht, J. M., Deckert, J. A., Nguyen, N. D., & Weir, J. P. (2017). Reminder: RMSSD and SD1 are identical heart rate variability metrics. *Muscle & Nerve*, 56(4), 674–678. <https://doi.org/10.1002/mus.25573>
- Cohen, S., Janicki-Deverts, D., & Miller, G. E. (2007). Psychological stress and disease. *JAMA*, 298(14), 1685. <https://doi.org/10.1001/jama.298.14.1685>
- De Couck, M., Mravec, B., & Gidron, Y. (2011). You may need the vagus nerve to understand pathophysiology and to treat diseases. *Clinical Science*, 122(7), 323–328. <https://doi.org/10.1042/cs20110299>
- De Kloet, E., Joëls, M., & Holsboer, F. (2005). Stress and the brain: from adaptation to disease. *Nature Reviews Neuroscience*, 6(6), 463–475. <https://doi.org/10.1038/nrn1683>
- De Sousa, G. M., De Oliveira Tavares, V. D., De Meiroz Grilo, M. L. P., Coelho, M. T., De Lima-Araújo, G. L., Schuch, F. B., & Galvão-Coelho, N. L. (2021). Mental Health in COVID-19 Pandemic: A Meta-review of Prevalence Meta-analyses. *Frontiers in Psychology*, 12. <https://doi.org/10.3389/fpsyg.2021.703838>
- Depue, R. A., & Morrone-Strupinsky, J. V. (2005). A neurobehavioral model of affiliative bonding: Implications for conceptualizing a human trait of affiliation. *Behavioral and Brain Sciences*, 28(03). <https://doi.org/10.1017/s0140525x05000063>
- Dhabhar, F. S., & McEwen, B. S. (1999). Enhancing versus suppressive effects of stress hormones on skin immune function. *Proceedings of the National Academy of Sciences of the United States of America*, 96(3), 1059–1064. <https://doi.org/10.1073/pnas.96.3.1059>
- Driskell, R. R., Jahoda, C. A., Chuong, C., Watt, F. M., & Horsley, V. (2014). Defining dermal adipose tissue. *Experimental Dermatology*, 23(9), 629–631. <https://doi.org/10.1111/exd.12450>
- Faul, F., Erdfelder, E., Lang, A., & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*, 39(2), 175–191. <https://doi.org/10.3758/bf03193146>

- Fredrickson, B. L. (2001). The role of positive emotions in positive psychology: The broaden-and-build theory of positive emotions. *American Psychologist*, 56(3), 218–226. <https://doi.org/10.1037/0003-066x.56.3.218>
- Fredrickson, B. L., & Joiner, T. E. (2002). Positive emotions trigger upward spirals toward emotional well-being. *Psychological Science*, 13(2), 172–175. <https://doi.org/10.1111/1467-9280.00431>
- Furay, A. R., Bruestle, A. E., & Herman, J. G. (2008). The role of the forebrain glucocorticoid receptor in acute and chronic stress. *Endocrinology*, 149(11), 5482–5490. <https://doi.org/10.1210/en.2008-0642>
- Garg, A. X., Chren, M., Sands, L. P., Matsui, M. S., Marenus, K. D., Feingold, K. R., & Elias, P. M. (2001). Psychological stress perturbs epidermal permeability barrier homeostasis. *Archives of Dermatology*, 137(1). <https://doi.org/10.1001/archderm.137.1.53>
- Gianaros, P. J., & Wager, T. D. (2015). Brain-body pathways linking psychological stress and physical health. *Current Directions in Psychological Science*, 24(4), 313–321. <https://doi.org/10.1177/0963721415581476>
- Gilbert, P. (2009). *The Compassionate Mind: a new approach to life's challenges*. <https://lib.ugent.be/en/catalog/rug01:002040613>
- Gilbert, P. (2016). Human nature and suffering. In *Routledge eBooks*. <https://doi.org/10.4324/9781315564258>
- Gilbert, P., McEwan, K., Mitra, R., Franks, L., Richter, A., & Rockliff, H. (2008). Feeling safe and content: A specific affect regulation system? Relationship to depression, anxiety, stress, and self-criticism. *The Journal of Positive Psychology*, 3(3), 182–191. <https://doi.org/10.1080/17439760801999461>
- Glaser, R., & Kiecolt-Glaser, J. K. (2005). Stress-induced immune dysfunction: implications for health. *Nature Reviews Immunology*, 5(3), 243–251. <https://doi.org/10.1038/nri1571>
- Glaser, R., MacCallum, R. C., Laskowski, B., Malarkey, W. B., Sheridan, J. T., & Kiecolt-Glaser, J. K. (2001). Evidence for a shift in the TH-1 to TH-2 cytokine response associated with chronic stress and aging. *The Journals of Gerontology*, 56(8), M477–M482. <https://doi.org/10.1093/gerona/56.8.m477>

- Grippe, A. J., Moffitt, J. A., & Johnson, A. K. (2002). Cardiovascular alterations and autonomic imbalance in an experimental model of depression. *American Journal of Physiology-regulatory Integrative and Comparative Physiology*, 282(5), R1333–R1341. <https://doi.org/10.1152/ajpregu.00614.2001>
- Hainsworth, R. (1995). The control and physiological importance of heart rate. *Armonk: NY Futura*, 3–9. <https://ci.nii.ac.jp/naid/10011596184/>
- WHOOP (2021). Heart rate variability [online image]. WHOOP. <https://www.whoop.com/us/en/thelocker/heart-rate-variability-hrv/>
- Heinrichs, M., Baumgartner, T., Kirschbaum, C., & Ehlert, U. (2003). Social support and oxytocin interact to suppress cortisol and subjective responses to psychosocial stress. *Biological Psychiatry*, 54(12), 1389–1398. [https://doi.org/10.1016/s0006-3223\(03\)00465-7](https://doi.org/10.1016/s0006-3223(03)00465-7)
- Hoffmann, K. K., & Sallen, J. (2012). Spezifische Normierung des Trierer Inventars zum chronischen Stress (TICS) zur diagnostischen Anwendung im Spitzensport. *Zeitschrift Fur Sportpsychologie*, 19(3), 95–109. <https://doi.org/10.1026/1612-5010/a000074>
- Honari, G., & Maibach, H. I. (2014). Skin structure and function. In *Elsevier eBooks* (pp. 1–10). <https://doi.org/10.1016/b978-0-12-420130-9.00001-3>
- Hoyt, L. T., Craske, M. G., Mineka, S., & Adam, E. K. (2015). Positive and negative affect and arousal. *Psychosomatic Medicine*, 77(4), 392–401. <https://doi.org/10.1097/psy.0000000000000178>
- Hsu, Y., Li, L., & Fuchs, E. (2014). Emerging interactions between skin stem cells and their niches. *Nature Medicine*, 20(8), 847–856. <https://doi.org/10.1038/nm.3643>
- Jones, C. A., & Gwenin, C. (2020). Cortisol level dysregulation and its prevalence—Is it nature’s alarm clock? *Physiological Reports*, 8(24). <https://doi.org/10.14814/phy2.14644>
- Kao, J., Fluhr, J. W., Man, M., Fowler, A. M., Hachem, J., Crumrine, D., Ahn, S. S., Brown, B. B., Elias, P. M., & Feingold, K. R. (2003). Short-Term Glucocorticoid Treatment Compromises Both Permeability Barrier Homeostasis and Stratum Corneum Integrity: Inhibition of Epidermal Lipid

Synthesis Accounts for Functional Abnormalities. *Journal of Investigative Dermatology*, 120(3), 456–464. <https://doi.org/10.1046/j.1523-1747.2003.12053.x>

Karemaker, J. M. (2017). An introduction into autonomic nervous function. *Physiological Measurement*, 38(5), R89–R118. <https://doi.org/10.1088/1361-6579/aa6782>

Kim, H., Cheon, E., Bai, D., Lee, Y. H., & Koo, B. (2018). Stress and Heart Rate Variability: A Meta-analysis and Review of the literature. *Psychiatry Investigation*, 15(3), 235–245. <https://doi.org/10.30773/pi.2017.08.17>

Kim, H., & Yosipovitch, G. (2013). An aberrant parasympathetic response: a new perspective linking chronic stress and itch. *Experimental Dermatology*, 22(4), 239–244. <https://doi.org/10.1111/exd.12070>

Kirschbaum, C., Pirke, K., & Hellhammer, D. H. (1993). The 'Trier Social Stress Test' – A Tool for Investigating Psychobiological Stress Responses in a Laboratory Setting. *Neuropsychobiology*, 28(1–2), 76–81. <https://doi.org/10.1159/000119004>

Kleyn, C., Schneider, L., Saraceno, R., Mantovani, C., Richards, H. L., Fortune, D. G., Cumberbatch, M., Dearman, R. J., Terenghi, G., Kimber, I., & Griffiths, C. E. (2008). The effects of acute social stress on epidermal langerhans' cell frequency and expression of cutaneous neuropeptides. *Journal of Investigative Dermatology*, 128(5), 1273–1279. <https://doi.org/10.1038/sj.jid.5701144>

Kogan, A. V., Allen, J. F., & Weihs, K. L. (2012). Cardiac vagal control as a prospective predictor of anxiety in women diagnosed with breast cancer. *Biological Psychology*, 90(1), 105–111. <https://doi.org/10.1016/j.biopsycho.2012.02.019>

Kok, B. E., & Fredrickson, B. L. (2010). Upward spirals of the heart: Autonomic flexibility, as indexed by vagal tone, reciprocally and prospectively predicts positive emotions and social connectedness. *Biological Psychology*, 85(3), 432–436. <https://doi.org/10.1016/j.biopsycho.2010.09.005>

- Kothgassner, O. D., Felnhöfer, A., Hlavacs, H., Beutl, L., Palme, R., Kryspin-Exner, I., & Glenk, L. M. (2016). Salivary cortisol and cardiovascular reactivity to a public speaking task in a virtual and real-life environment. *Computers in Human Behavior*, 62, 124–135. <https://doi.org/10.1016/j.chb.2016.03.081>
- Kubo, A., Ishizaki, I., Kawasaki, H., Nagao, K., Ohashi, Y., & Amagai, M. (2013). The stratum corneum comprises three layers with distinct metal-ion barrier properties. *Scientific Reports*, 3(1). <https://doi.org/10.1038/srep01731>
- Lampert, R., Tuit, K., Hong, K., Donovan, T., Lee, F. A., & Sinha, R. (2016). Cumulative stress and autonomic dysregulation in a community sample. *Stress*, 19(3), 269–279. <https://doi.org/10.1080/10253890.2016.1174847>
- Lazarus, R. S., & Folkman, S. (1984). *Stress, appraisal, and coping*. New York : Springer Publishing Company.
- Lightman, S. L. (2008). The Neuroendocrinology of Stress: a Never ending story. *Journal of Neuroendocrinology*, 20(6), 880–884. <https://doi.org/10.1111/j.1365-2826.2008.01711.x>
- Lolait, S. J., Stewart, L. A., Jessop, D. S., Young, R. W. S., & O'Carroll, A. (2007). The hypothalamic-pituitary-adrenal axis response to stress in mice lacking functional vasopressin V1B receptors. *Endocrinology*, 148(2), 849–856. <https://doi.org/10.1210/en.2006-1309>
- Mahmud, M., Mohsin, M., Dewan, M. N., & Muyeed, A. (2022). The Global Prevalence of depression, anxiety, stress, and insomnia among general population during COVID-19 Pandemic: A Systematic review and Meta-analysis. *Trends in Psychology*, 31(1), 143–170. <https://doi.org/10.1007/s43076-021-00116-9>
- Malik, M., Bigger, J. T., Camm, A. J., Kleiger, R. E., Malliani, A., Moss, A. J., & Schwartz, P. J. (1996). Heart rate variability: Standards of measurement, physiological interpretation, and clinical use. *European Heart Journal*, 17(3), 354–381. <https://doi.org/10.1093/oxfordjournals.eurheartj.a014868>
- Marieb, E. N. (2003). *Human anatomy and physiology*. Benjamin-Cummings Publishing Company.

- Marsland, A. L., Pressman, S. D., & Cohen, S. (2007). Positive affect and immune function. In *Elsevier eBooks* (pp. 761–779). <https://doi.org/10.1016/b978-012088576-3/50042-3>
- Matthews, K. A., Gump, B. B., & Owens, J. F. (2001). Chronic stress influences cardiovascular and neuroendocrine responses during acute stress and recovery, especially in men. *Health Psychology*, 20(6), 403–410. <https://doi.org/10.1037/0278-6133.20.6.403>
- McEwen, B. S. (1998). Stress, adaptation, and disease: allostasis and allostatic load. *Annals of the New York Academy of Sciences*, 840(1), 33–44. <https://doi.org/10.1111/j.1749-6632.1998.tb09546.x>
- McEwen, B. S. (2004). Protection and Damage from Acute and Chronic Stress: Allostasis and Allostatic Overload and Relevance to the Pathophysiology of Psychiatric Disorders. *Annals of the New York Academy of Sciences*, 1032(1), 1–7. <https://doi.org/10.1196/annals.1314.001>
- McEwen, B. S. (2006). Protective and damaging effects of stress mediators: central role of the brain. *Dialogues in Clinical Neuroscience*, 8(4), 367–381. <https://doi.org/10.31887/dcns.2006.8.4/bmcewen>
- McEwen, B. S. (2017). Neurobiological and Systemic Effects of Chronic Stress. *Thousand Oaks*, 1, 247054701769232. <https://doi.org/10.1177/2470547017692328>
- Michels, N., Sioen, I., Clays, E., De Buyzere, M., Ahrens, W., Huybrechts, I., Vanaelst, B., & De Henauw, S. (2013). Children's heart rate variability as stress indicator: Association with reported stress and cortisol. *Biological Psychology*, 94(2), 433–440. <https://doi.org/10.1016/j.biopsycho.2013.08.005>
- Mika, A., Mazur, G. J., Hoffman, A. N., Talboom, J. S., Bimonte-Nelson, H. A., Sanabria, F., & Conrad, C. D. (2012). Chronic stress impairs prefrontal cortex-dependent response inhibition and spatial working memory. *Behavioral Neuroscience*, 126(5), 605–619. <https://doi.org/10.1037/a0029642>
- Miller, G. E., Chen, E., & Zhou, E. S. (2007). If it goes up, must it come down? Chronic stress and the hypothalamic-pituitary-adrenocortical axis in humans.

Psychological Bulletin, 133(1), 25–45. <https://doi.org/10.1037/0033-2909.133.1.25>

Nakagawa, M., Iwao, T., Ishida, S., Yonemochi, H., Fujino, T., Saikawa, T., & Ito, M. (1998). Circadian rhythm of the signal averaged electrocardiogram and its relation to heart rate variability in healthy subjects. *Heart*, 79(5), 493–496. <https://doi.org/10.1136/hrt.79.5.493>

Negrão, A. B., Deuster, P. A., Gold, P. W., Singh, A. K., & Chrousos, G. P. (2000). Individual reactivity and physiology of the stress response. *Biomedicine & Pharmacotherapy*, 54(3), 122–128. [https://doi.org/10.1016/s0753-3322\(00\)89044-7](https://doi.org/10.1016/s0753-3322(00)89044-7)

Nunan, D., Sandercock, G., & Brodie, D. A. (2010). A quantitative systematic review of normal values for short-term heart rate variability in healthy adults. *Pacing and Clinical Electrophysiology*, 33(11), 1407–1417. <https://doi.org/10.1111/j.1540-8159.2010.02841.x>

Opthof, T. (2000). The normal range and determinants of the intrinsic heart rate in man. *Cardiovascular Research*, 45(1), 177–184. [https://doi.org/10.1016/s0008-6363\(99\)00322-3](https://doi.org/10.1016/s0008-6363(99)00322-3)

Ovaere, P., Lippens, S., Vandenabeele, P., & Declercq, W. (2009). The emerging roles of serine protease cascades in the epidermis. *Trends in Biochemical Sciences*, 34(9), 453–463. <https://doi.org/10.1016/j.tibs.2009.08.001>

Panksepp, J. (1998). *Affective neuroscience: The Foundations of Human and Animal Emotions*. Oxford University Press.

Pereira, V. M., Campos, I., & Sousa, N. (2017). The role of autonomic nervous system in susceptibility and resilience to stress. *Current Opinion in Behavioral Sciences*, 14, 102–107. <https://doi.org/10.1016/j.cobeha.2017.01.003>

Plaschke, K., Muller, D. R., & Hoyer, S. (1996). Effect of adrenalectomy and corticosterone substitution on glucose and glycogen metabolism in rat brain. *Journal of Neural Transmission*, 103(1–2), 89–100. <https://doi.org/10.1007/bf01292619>

- Pressman, S. D., & Cohen, S. (2005). Does positive affect influence health? *Psychological Bulletin*, 131(6), 925–971. <https://doi.org/10.1037/0033-2909.131.6.925>
- Reyes Del Paso, G. a. R., Langewitz, W., Mulder, L. J., Van Roon, A. M., & Duschek, S. (2013). The utility of low frequency heart rate variability as an index of sympathetic cardiac tone: A review with emphasis on a reanalysis of previous studies. *Psychophysiology*, 50(5), 477–487. <https://doi.org/10.1111/psyp.12027>
- Richardson, M., McEwan, K., Maratos, F. A., & Sheffield, D. (2016). Joy and Calm: How an Evolutionary Functional Model of Affect Regulation Informs Positive Emotions in Nature. *Evolutionary Psychological Science*, 2(4), 308–320. <https://doi.org/10.1007/s40806-016-0065-5>
- Rohleder, N. (2019). Stress and inflammation – The need to address the gap in the transition between acute and chronic stress effects. *Psychoneuroendocrinology*, 105, 164–171. <https://doi.org/10.1016/j.psyneuen.2019.02.021>
- Roosterman, D., Goerge, T., Schneider, S., Bunnett, N. W., & Steinhoff, M. (2006). Neuronal control of skin function: the skin as a neuroimmunoendocrine organ. *Physiological Reviews*, 86(4), 1309–1379. <https://doi.org/10.1152/physrev.00026.2005>
- Russell, G. M., & Lightman, S. L. (2019). The human stress response. *Nature Reviews Endocrinology*, 15(9), 525–534. <https://doi.org/10.1038/s41574-019-0228-0>
- Sammito, S., Thielmann, B., Zimmermann, P., & Böckelmann, I. (2015). Einfluss einer posttraumatischen Belastungsstörung auf die Herzfrequenzvariabilität als Marker des autonomen Nervensystems – eine systematische Literaturübersicht. *Fortschritte Der Neurologie Psychiatrie*, 83(01), 30–37. <https://doi.org/10.1055/s-0034-1398779>
- Sapolsky, R. M., Romero, L., & Munck, A. (2000). How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions*. *Endocrine Reviews*, 21(1), 55–89. <https://doi.org/10.1210/edrv.21.1.0389>

- Schetter, C. D., & Dolbier, C. L. (2011). Resilience in the context of chronic stress and health in adults. *Social and Personality Psychology Compass*, 5(9), 634–652. <https://doi.org/10.1111/j.1751-9004.2011.00379.x>
- Schore, A. N. (2015). *Affect regulation and the origin of the self: The Neurobiology of Emotional Development*. Routledge.
- Schulz, P. J., Schlotz, W., & Becker, P. B. (2004). Trierer Inventar zum chronischen Stress. In *Hogrefe eBooks*. <https://katalog.ub.uni-heidelberg.de/titel/67781025>
- Seeman, T. E. (1997). Price of adaptation--allostatic load and its health consequences. MacArthur studies of successful aging. *Archives of Internal Medicine*, 157(19), 2259–2268. <https://doi.org/10.1001/archinte.157.19.2259>
- Seligman, M. E. P. (2011). Flourish: a visionary new understanding of happiness and well-being. *Choice Reviews Online*, 48(12), 48–7217. <https://doi.org/10.5860/choice.48-7217>
- Seligman, M. E. P., & Csikszentmihalyi, M. (2000). Positive psychology: An introduction. *American Psychologist*, 55(1), 5–14. <https://doi.org/10.1037/0003-066x.55.1.5>
- Shaffer, F., McCraty, R., & Zerr, C. L. (2014). A healthy heart is not a metronome: an integrative review of the heart's anatomy and heart rate variability. *Frontiers in Psychology*, 5. <https://doi.org/10.3389/fpsyg.2014.01040>
- Shaffer, F., & Venner, J. (2013). Heart rate variability anatomy and physiology. *Biofeedback*, 41(1), 13–25. <https://doi.org/10.5298/1081-5937-41.1.05>
- Sorrells, S. F., & Sapolsky, R. M. (2007). An inflammatory review of glucocorticoid actions in the CNS. *Brain Behavior and Immunity*, 21(3), 259–272. <https://doi.org/10.1016/j.bbi.2006.11.006>
- Steckler, T., Kalin, N., & Reul, J. (2005). *Handbook of Stress and the Brain Part 1: The Neurobiology of Stress*. Elsevier.
- Strahler, J., Skoluda, N., Kappert, M., & Nater, U. M. (2017). Simultaneous measurement of salivary cortisol and alpha-amylase: Application and recommendations. *Neuroscience & Biobehavioral Reviews*, 83, 657–677. <https://doi.org/10.1016/j.neubiorev.2017.08.015>

- Streeter, C. C., Gerbarg, P. L., Saper, R. B., Ciraulo, D. A., & Brown, R. M. (2012). Effects of yoga on the autonomic nervous system, gamma-aminobutyric-acid, and allostasis in epilepsy, depression, and post-traumatic stress disorder. *Medical Hypotheses*, 78(5), 571–579.
<https://doi.org/10.1016/j.mehy.2012.01.021>
- Teixeira, R. R., Díaz, M. M., Da Silva Santos, T. V., Bernardes, J. T. M., Peixoto, L. G., Bocanegra, O. L., Neto, M. B., & Espindola, F. S. (2015). Chronic stress induces a hyporeactivity of the autonomic nervous system in response to acute mental stressor and impairs cognitive performance in business executives. *PLOS ONE*, 10(3), e0119025.
<https://doi.org/10.1371/journal.pone.0119025>
- Terao, M., Murota, H., Kimura, A., Kato, A., Ishikawa, A., Igawa, K., Miyoshi, E., & Katayama, I. (2011). 11B-hydroxysteroid dehydrogenase-1 is a novel regulator of skin homeostasis and a candidate target for promoting tissue repair. *PLOS ONE*, 6(9), e25039.
<https://doi.org/10.1371/journal.pone.0025039>
- Thayer, J. F., Åhs, F., Fredrikson, M., Sollers, J. J., & Wager, T. D. (2012). A meta-analysis of heart rate variability and neuroimaging studies: Implications for heart rate variability as a marker of stress and health. *Neuroscience & Biobehavioral Reviews*, 36(2), 747–756.
<https://doi.org/10.1016/j.neubiorev.2011.11.009>
- Tran, T. H., Yamamoto, Y., Gesta, S., & Kahn, C. R. (2008). Beneficial effects of subcutaneous fat transplantation on metabolism. *Cell Metabolism*, 7(5), 410–420. <https://doi.org/10.1016/j.cmet.2008.04.004>
- Trevarthen, C., & Aitken, K. J. (2001). Infant Intersubjectivity: research, theory, and clinical applications. *Journal of Child Psychology and Psychiatry*, 42(1), 3–48.
<https://doi.org/10.1111/1469-7610.00701>
- Ulrich-Lai, Y. M., & Herman, J. G. (2009). Neural regulation of endocrine and autonomic stress responses. *Nature Reviews Neuroscience*, 10(6), 397–409.
<https://doi.org/10.1038/nrn2647>
- Walburn, J., Vedhara, K., Hankins, M., Rixon, L., & Weinman, J. (2009). Psychological stress and wound healing in humans: A systematic review and

meta-analysis. *Journal of Psychosomatic Research*, 67(3), 253–271.

<https://doi.org/10.1016/j.jpsychores.2009.04.002>

Walker, F. R., Pfingst, K., Carnevali, L., Sgoifo, A., & Nalivaiko, E. (2017). In the search for integrative biomarker of resilience to psychological stress.

Neuroscience & Biobehavioral Reviews, 74, 310–320.

<https://doi.org/10.1016/j.neubiorev.2016.05.003>

Wang, H., & Huang, S. (2012). SDNN/RMSSD as a surrogate for LF/HF: A revised investigation. *Modelling and Simulation in Engineering*, 2012, 1–8.

<https://doi.org/10.1155/2012/931943>

Wang, J., Lesage, A., Schmitz, N., & Drapeau, A. (2008). The relationship between work stress and mental disorders in men and women: findings from a population-based study. *Journal of Epidemiology and Community Health*,

62(1), 42–47. <https://doi.org/10.1136/jech.2006.050591>

Willenborg, S., Lucas, T., Van Loo, G., Knipper, J. A., Krieg, T., Haase, I., Brachvogel, B., Hammerschmidt, M., Nagy, A., Ferrara, N., Pasparakis, M., & Eming, S. A. (2012). CCR2 recruits an inflammatory macrophage subpopulation critical for angiogenesis in tissue repair. *Blood*, 120(3), 613–

625. <https://doi.org/10.1182/blood-2012-01-403386>

Woodley, D. T. (2017). Distinct fibroblasts in the papillary and reticular dermis.

Dermatologic Clinics, 35(1), 95–100. <https://doi.org/10.1016/j.det.2016.07.004>

Yosipovitch, G., Xiong, G. L., Haus, E., Sackett-Lundeen, L., Ashkenazi, I. E., & Maibach, H. I. (1998). Time-dependent variations of the skin barrier function in humans: transepidermal water loss, stratum corneum hydration, skin surface PH, and skin temperature. *Journal of Investigative Dermatology*, 110(1), 20–

23. <https://doi.org/10.1046/j.1523-1747.1998.00069.x>

Zimmerman, A., Bai, L., & Ginty, D. D. (2014). The gentle touch receptors of mammalian skin. *Science*, 346(6212), 950–954.

<https://doi.org/10.1126/science.1254229>

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Appendix

Abstract German

Ziel dieser Arbeit ist es, Zusammenhänge zwischen chronischem Stress (CS) und den physiologischen Maßen Herzfrequenzvariabilität (HRV) und transepidermaler Wasserverlust (TEWL) sowie dem subjektiven Maß des entspannten positiven Affekts (RPA) zu untersuchen, um das Verständnis von CS zu vertiefen. Der negative Zusammenhang zwischen akutem psychischem Stress und HRV, Integrität der Hautbarriere und RPA konnte in verschiedenen Studien gezeigt werden. Es ist jedoch unklar, ob CS in ähnlicher Weise mit diesen drei Parametern verbunden ist. In dieser Arbeit wird versucht, die Art der Assoziationen von HRV, TEWL und RPA mit CS zu untersuchen. Im Rahmen eines größeren Projekts mit experimentellem Design, das Zusammenhänge zwischen Stress, Musikhören und Wundheilung untersuchte, wurden die Ausgangsdaten von 96 Teilnehmerinnen mit regelmäßigem Menstruationszyklus ausgewertet, um die Hypothesen dieser Arbeit zu untersuchen. Die Operationalisierung erfolgte durch die Messung von CS und RPA anhand von Selbstberichten sowie von HRV und TEWL anhand physiologischer Messungen. Es wurden keine signifikanten Zusammenhänge zwischen CS und TEWL oder HRV festgestellt. Allerdings gab es einen signifikanten Zusammenhang zwischen CS und RPA ($r = -0,238$; $p = 0,02$). In Anbetracht früherer Befunde zu CS scheint dieser Zusammenhang passend, auch wenn er eher klein ist. Ein exploratives Ergebnis hinsichtlich einer starken Korrelation zwischen TEWL und RPA ($r = -0,507$; $p < 0,001$) könnte möglicherweise auf akute Stresskorrelate zurückzuführen sein. Die Ergebnisse dieser Analyse deuten auf die Annahme hin, dass CS ein weitaus komplexeres Konstrukt ist als angenommen. In der zukünftigen Forschung sollte der Schwerpunkt auf die Differenzierung der Merkmale der Stressoren und der persönlichen Faktoren gelegt werden, die mit CS einhergehen, um die unterschiedlichen Assoziationen mit physiologischen Phänomenen besser zu ergründen.

Schlüsselwörter: chronischer Stress, psychologischer Stress, Herzratenvariabilität, root mean square of successive R-R peak differences, transepidermaler Wasserverlust, Homöostase der Hautbarriere, HPA-Achse, ANS, Physiologie des Stresses

English Abstract

This thesis investigates associations between chronic stress (CS) and the physiological measurements heart rate variability (HRV) and transepidermal water loss (TEWL) and the subjective measure of relaxed positive affect (RPA) to deepen the understanding of CS. The negative associations of acute psychological stress and HRV, skin barrier integrity and RPA were displayed in several studies. Yet, it is unclear whether CS is associated with those three parameters similarly. This thesis explores the nature of the associations of HRV, TEWL and RPA with CS. Within the ramifications of an overarching project with experimental design that investigated associations between stress, music listening and wound healing, baseline data of 96 participants with a regular menstrual cycle were assessed to investigate this thesis' hypotheses. Operationalization was done by assessing CS and RPA with self-report measures, and HRV and TEWL with physiological measures. There were no significant associations found between CS and TEWL or HRV respectively; however, there was a significant small negative association of CS and RPA ($r = -0.238$; $p = 0.02$). This association aligns with previous findings regarding CS, although it is rather small. An exploratory finding regarding a large negative correlation of TEWL and RPA ($r = -0.507$; $p < 0.001$) might potentially be due to acute stress correlates. The results of this analysis indicate that CS is a far more complex construct than previously assumed. Future research should emphasize differentiating the characteristics of the stressors and personal factors that accompany CS to gain a clearer insight into how they differently relate to physiological phenomena.

Key words: *chronic stress, psychological stress, heart rate variability, root mean square of successive differences, transepidermal water loss, skin barrier homeostasis, HPA axis, ANS, physiology of stress*