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Physiological and neural mechanisms of negative stimuli processing

Fyziologické a neuronální mechanismy zpracování negativních stimulů

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Declaration:

I hereby declare that I have completed my thesis independently and that I have properly cited and referenced all sources and literature used. I also declare that the thesis has not been used to obtain another or the same degree.

Prague, 30 July 2024 Signature: .....

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Abstract

This thesis investigates the neurophysiological and neuronal mechanisms underlying the processing of different types of stress stimuli, focusing on the brain and body's differential responses to highly affective negative stimuli, processed more automatically versus context-dependent negative stimuli, likely requiring greater cognitive control. Using a multimodal approach that integrates fMRI, heart rate (HR), and respiratory patterns, this study explores the complex interplay between emotional and cognitive processes in response to negative, stress-inducing stimuli. The stimuli were naturalistic visual-text media content, representing daily stressors contributing to chronic ecological stress.

Stress research has evolved from Cannon's foundational "fight or flight" response and Selye's General Adaptation Syndrome to modern perspectives emphasising psychological factors and cognitive appraisal in stress processing. Contemporary studies highlight the importance of brain regions such as the amygdala, prefrontal cortex, anterior cingulate cortex, and insula in emotion regulation, threat detection, and interoceptive awareness, linking psychological factors closely with neurobiological mechanisms in stress responses.

Unexpectedly, the study's neuroimaging results showed significant activation in the posterior cingulate cortex, angular gyrus, fusiform gyrus, and visual association cortices rather than the anticipated amygdala and prefrontal cortex. These results suggest that participants processed the stressors more cognitively than emotionally, underscoring the critical roles of cognitive appraisal and visual processing in stress perception. Physiological measures did not differ significantly across stimulus types, prompting questions about the roles of individual differences, emotion regulation strategies, and the ecological validity of laboratory-based stressors.

These findings challenge traditional views prioritising the amygdala and prefrontal cortex in stress responses. They highlight the importance of cognitive evaluation, sensory processing, and individual differences in stress research. The implications of this work extend to developing a more comprehensive model of the stress process, which could lead to the development of personalized stress management strategies and psychological interventions in the future. The study's limitations, including the controlled laboratory setting and uniform physiological responses, suggest that future research should focus on more ecologically valid methodologies and a deeper exploration of the interactions between brain regions and physiological systems during stress.

Keywords: stress, ecological validity, heart rate, respiratory rate, fMRI, cognitive control, posterior cingulate cortex, visual association cortex

Abstrakt

Tato diplomová práce zkoumá neurofyziologické a neuronální mechanismy zpracování různých typů stresových podnětů, přičemž se zaměřuje na rozdílné reakce mozku a těla na vysoce afektivní negativní podněty, které jsou zpracovávány více automaticky, v porovnání se spíše kontextově závislými negativními podněty, které pravděpodobně podléhají větší kognitivní kontrole. Použitím multimodálního přístupu, který zahrnuje fMRI, měření srdečního tepu (HR) a respiračních vzorců, se studie snažila objasnit komplexní propojení mezi emocionálními a kognitivními procesy při zpracování negativních, možná stres vyvolávajících podnětů. Zejména studie využila naturalistické vizuálně-textové podněty převzaté z médií, které byly diskutovány jako každodenní stresory přispívající k chronickému ekologickému stresu.

Historicky se výzkum stresu vyvíjel od základní práce Cannona o reakci "bojuj nebo uteč" a Selyeho obecného adaptačního syndromu až po moderní pohledy zdůrazňující roli psychologických faktorů a kognitivního zhodnocení při zpracování stresu. Současný výzkum dále zdůrazňuje význam specifických oblastí mozku, jako je amygdala, prefrontální kortex, přední cingulární kortex a insula, které zprostředkovávají tyto procesy. Tyto oblasti jsou klíčové pro regulaci emocí, detekci hrozeb a interoceptivní uvědomění, což zdůrazňuje, jak jsou psychologické faktory a kognitivní zhodnocení úzce propojeny s neurobiologickými mechanismy mozku při stresové reakci.

Výsledky neurozobrazování ve studii odhalily neočekávané vzorce aktivace mozku s významným zapojením zadního cingulárního kortexu, angulárního gyru, fusiformního gyru a vizuálních asociačních kortexů spíše než očekávané amygdaly a prefrontálního kortexu. To naznačuje, že použité stresory mohly být zpracovány spíše kognitivně než emocionálně, což zdůrazňuje roli kognitivního zhodnocení a vizuálního zpracování při vnímání stresu. Fyziologická měření neprokázala významné rozdíly mezi jednotlivými typy podnětů, což vyvolává zásadní otázky týkající se vlivu individuálních rozdílů, strategií regulace emocí a ekologické validity laboratorních stresorů.

Tato zjištění přispívají k pochopení zpracování stresu tím, že zpochybňují tradiční pohledy, které zdůrazňují amygdalu a prefrontální kortex jako hlavní oblasti zapojené do stresových reakcí. Studie zdůrazňuje důležitost zohlednění kognitivního hodnocení, senzorického zpracování a individuálních rozdílů při výzkumu stresu. Implikace této práce se rozšiřují na vývoj komplexnějšího modelu stresového procesu, což by v budoucnu mohlo vést k rozvoji personalizovaných strategií pro zvládání stresu a psychologických intervencí. Omezení této studie, včetně kontrolovaného laboratorního prostředí a jednotných fyziologických reakcí, naznačují, že budoucí výzkum by se měl zaměřit na metodologie s vyšší ekologickou validitou a hlubší zkoumání interakcí mezi mozkovými oblastmi a fyziologickými systémy během stresu.

Klíčová slova: stres, ekologická validita, srdeční frekvence, respirační frekvence, fMRI, kognitivní kontrola, zadní cingulární kůra, zraková asociační kůra

List of abbreviations

Abbreviation (Zkratka)	Full Term (Plný název)
ACC	Anterior Cingulate Cortex
PFC	Prefrontal Cortex
HR	Heart Rate
PTSD	Post-Traumatic Stress Disorder
fMRI	Functional Magnetic Resonance Imaging
mPFC	Medial Prefrontal Cortex
HPA	Hypothalamic-Pituitary-Adrenal (Axis)
HRV	Heart Rate Variability
ANS	Autonomic Nervous System
OFC	Orbitofrontal Cortex
dlPFC	Dorsolateral Prefrontal Cortex
dACC	Dorsal Anterior Cingulate Cortex
vACC	Ventral Anterior Cingulate Cortex
AI	Anterior Insula
TSST	Trier Social Stress Test
CONCERNING	Negative stimuli requiring subject greater cognitive control
DISTURBING	Highly affective negative stimuli
PANAS	Positive and Negative Affect Schedule
TR	Repetition Time
TE	Echo Time
SPACE	Sampling Perfection with Application-optimised Contrasts Evolutions
MP-RAGE	Magnetization-prepared radio-frequency pulses and gradient-echo
MNI	The Montreal Neurological Institute system
RESP	Respiration Measurement
PULS	Heart Rate Measurement
DOWN	Intervention group with downregulation of emotional response
UP	Intervention group with upregulation of emotional response
FOV	The Field of View
VAC	Visual Association Cortex

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1. Introduction

The problem of stress and its impact on the human body and psyche is one of the central topics in modern neuroscience and psychophysiology. Initially, stress reactions were considered solely a physiological response to threats, such as the "fight or flight" response described by Walter Cannon (Cannon, 1915). Later research in this area revealed that stress is a multilevel process involving complex interactions between different brain structures and bodily systems. It is now known that stress involves not only physiological aspects such as heart rate or cortisol levels but also complex cognitive and emotional mechanisms that influence our perception and behaviour (von Dawans et al., 2021).

In addition to understanding the general stress response, it is essential to distinguish between distress and eustress. Distress refers to negative stress that can lead to anxiety, decreased performance, and various health issues (Ridner, 2004). At the same time, eustress is a positive form of stress that can enhance motivation, performance, and overall well-being (Fevre et al., 2003). Recognizing this distinction is crucial as it highlights that not all stress is harmful; instead, the context and perception of the stressor determine its impact.

Current stress research shows that the stress response involves the interaction of different brain regions, such as the amygdala (LeDoux & Pine, 2016), prefrontal cortex (PFC) (Suzuki & Tanaka, 2021), anterior cingulate cortex (ACC) (Jhang et al., 2018) and insular lobe (Greco & Liberzon, 2016). These brain regions play key roles in emotion regulation, cognitive appraisal, and threat perception. For example, activation of the amygdala is associated with processing emotionally intense stimuli such as fear (LeDoux & Pine, 2016), whereas the PFC is involved in cognitive control and emotion regulation (Suzuki & Tanaka, 2021). The anterior cingulate cortex ensures the integration of cognitive and emotional processes (Silvestrini et al., 2020), while the insula is responsible for perceiving bodily sensations and integrating them with emotional experiences (R. Zhang et al., 2024).

At the same time, physiological responses such as heart rate (HR) serve as key indicators of emotional arousal and stress response. Increases in HR are often observed in response to stressful or emotionally intense stimuli and are associated with sympathetic nervous system activity (Mason et al., 2018). Research also shows that different types of stimuli, including high-affective negative stimuli and cognitively controlled stimuli, can differentially affect the body's physiological and neural responses, highlighting the importance of effective emotional regulation (Atilano-Barbosa et al., 2022; Ochsner et al., 2004; Polo et al., 2024).

Most research attention has focused on traditional stressors such as physical pain or restraint (Lívea Dornela Godoy et al., 2018; J. Zhang et al., 2017). However, daily environmental stressors of modern life, such as news media content, remain poorly understood. To remediate this gap, we decided to study naturalistic and ecologically valid stimuli, namely stimuli taken from the Czech media. We opted for stimuli with both visual and textual components because they reflect real-life situations, which often include images and text, making them difficult to process.

Numerous studies and meta-analyses show that negative exposure to media, especially news, can have a significant impact on mental health, causing anxiety, depression, and post-traumatic stress disorder (PTSD) (Dick et al., 2021; DiMaggio & Galea, 2006; Holman et al., 2020; Thompson et al., 2017). The continuous flow of information and the accompanying uncertainty contribute to anxiety and provoke both adaptive and maladaptive stress management strategies (Koolhaas et al., 2011). Individual differences, such as aversion to uncertainty and high levels of anxiety, can make a person more vulnerable to the negative effects of media (Liekefett et al., 2023).

In addition, research shows that different types of stressors, such as real-life events, news coverage, and visual stimuli, can elicit different stress responses (Polo et al., 2024). For example, real-life news coverage that includes images of violence or suffering can evoke powerful moral emotions, such as empathy or outrage, and activate specific neural and physiological responses (Soroka et al., 2019).

Thus, the present study aims to investigate specific neurophysiological and neuronal responses to these ecologically valid stimuli. Several key questions arise:

- What are the key brain regions and physiological mechanisms involved in stress processing, and how do they interact?
- What are the considerations in choosing methods for studying stress processing, and how do different approaches complement each other?
- Is there a difference in neural and physiological responses to different types of stimuli?
- How exactly do the combined visual and textual stimuli from the media affect emotional and physiological responses?
- Are these responses subject to greater cognitive control than responses to other types of stressors?

The present study will address these questions, aiming to fill existing gaps in knowledge about responses to media stressors. We aim to elucidate how such stimuli affect the activation of different brain regions and physiological systems and determine what factors may contribute to better cognitive control and regulation of the stress response.

The study will employ advanced neuroimaging and physiological monitoring techniques to achieve this goal. Specifically, we will use functional magnetic resonance imaging (fMRI) to map the activation of different brain regions in response to media stimuli. This method allows us to identify the specific neural structures involved in processing these stressors and how they interact.

Physiological methods such as heart rate monitoring and a breathing belt will also be employed. These measures will help assess how stress stimuli impact the autonomic nervous system and influence the body's physiological response. These measurements will be recorded simultaneously with fMRI to provide a comprehensive view of the interaction between brain activity and physiological responses under stress induced by media stimuli. This combined approach will offer an integrated understanding of how the brain and body respond to such stressors.

2. Theoretical Part

2.1 Historical Overview of Stress Research

This chapter traces the significant milestones in the evolution of stress research, highlighting fundamental theories and discoveries that have shaped our understanding of stress from a physiological and psychological perspective. Beginning in the early 20th century with foundational concepts and progressing to contemporary approaches, this overview underscores the complexity and multifaceted nature of stress as it is understood today.

Walter Cannon first elaborated on the concept of stress and its biological underpinnings in the early 20th century. Cannon introduced the 'fight or flight' concept, which described the body's instinctive responses to threats, laying the groundwork for future research into the autonomic nervous system and its role in stress (Cannon, 1915). This foundational work emphasised the immediate physiological reactions to perceived threats and established a critical basis for the biological study of stress.

By the mid-century, Hans Selye further expanded the biological perspective by introducing the 'General Adaptation Syndrome,' which outlined three stages of stress response: alarm, resistance, and exhaustion (Fig. 1). Selye's theory provided a broader framework for understanding the dynamic and prolonged stress processes beyond immediate reactions, introducing concepts of chronic stress and its potential health impacts. Selye's theory broadened the perspective on stress, suggesting a more complex and dynamic process encompassing both positive and negative aspects. It marked a pivotal shift from viewing stress as a mere immediate reaction to understanding it as a prolonged, multifaceted process (Selye, 1950).

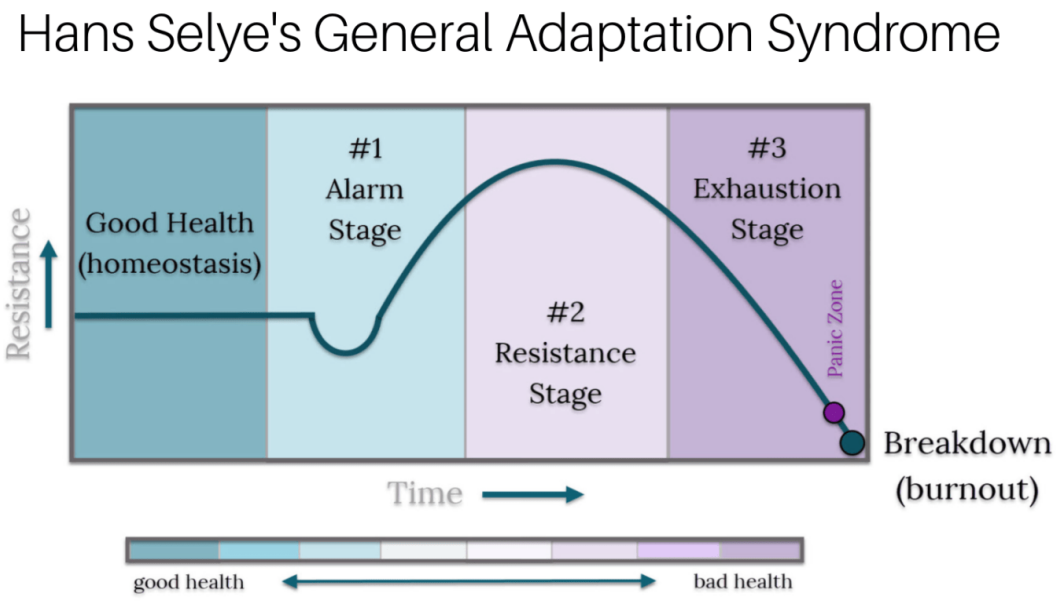

***Figure 1**: General Adaptation Syndrome, reproduced from (Neville, 2023).*

The 1980s marked a significant shift towards understanding the psychological dimensions of stress. Richard Lazarus and Susan Folkman proposed a theory that conceptualised psychological stress as a relationship between the individual and their environment, where stress arises from an appraisal of environmental demands as exceeding personal resources. This theory emphasised the importance of cognitive processes in evaluating and coping with stress, integrating psychological factors into the broader understanding of stress (Lazarus & Folkman, 1984).

Modern research, particularly from the late 20th century onwards, has benefited from advances in neuroscience and psychology, with scholars like Bruce McEwen leading the way. McEwen's "allostatic load" concept described the cumulative burden of chronic stress on the body, highlighting how repeated exposure can lead to significant physiological changes and impact long-term health (McEwen, 2007).

In recent decades, research has increasingly focused on the role of lifestyle, work pressure, and social expectations in stress development, particularly in developed countries. Studies have linked modern life stressors to chronic diseases such as cardiovascular disorders and mental health issues, emphasising the need to consider both psychological and physiological elements of stress (Cohen et al., 2007; Kivimäki & Kawachi, 2015).

The 'Two-hit hypothesis,' initially proposed by Alfred Knudson, provides a nuanced framework for understanding stress responses (Knudson, 1971). It suggests that an initial stressor sensitises the body, heightening reactions to subsequent stressors. In modern life, where individuals frequently encounter stressors like negative news and social media, these can serve as potent 'second hits'. This hypothesis, supported by research from Burks and Martin, underscores the importance of considering ongoing stressors in predicting psychological symptoms (Burks & Martin, 1985). Moreover, Avshalom Caspi's research demonstrates the amplifying effect of chronic ecological stress on daily stressors and underscores the buffering role of social support (Caspi et al., 1987).

Psychologists worldwide develop different types of psychological interventions to improve people's well-being. For example, Situation-level interventions focus on modifying the external environment or context in which stress occurs rather than solely targeting the individual's psychological state. The primary goal is to change the stressors themselves to reduce stress reactivity. Megan Goldring studied 1,323 adults and found the significant role of both individual and situational factors in stress reactivity, particularly situational factors findings. The study identifies three key components of stress reactivity: person-level factors, situation-level factors, and person-by-situation interactions. Each of these components contributes significantly to how individuals react to stress. She found that the situation emerged as the most important factor, accounting for 44% of stress reactivity. In the

discussion, she suggests that stress-reduction interventions may need to be tailored to address the component of stress reactivity most important to each individual (Goldring, 2022).

The evolution of stress research reflects a journey from viewing stress as a physiological response to recognising its complex interactions with psychological factors and environmental stimuli. This progression emphasises the importance of considering cumulative stress exposures in research and therapeutic interventions. Today, we find ourselves at a unique intersection where modern technology, including mass media and digital media, introduces new and complex stressors (Ben-Zur et al., 2012; Bodas et al., 2015; Dick et al., 2021; Garfin et al., 2018). These contemporary environmental factors can amplify stress responses in individuals already sensitised by previous stressors.

2.2 The Neural Mechanisms of Stress Response

Understanding the neural mechanisms underlying stress responses is fundamental to stress physiology. This chapter explores how key structures within the central nervous system the amygdala, prefrontal cortex, anterior cingulate cortex, and insula- manage immediate reactions and long-term adaptations to stress. These brain regions are integral to various aspects of stress processing, including emotion regulation, threat detection, cognitive evaluation, and interoceptive awareness. The chapter delves into each region's specific contributions, examining their interactions within neural circuits underpinning the complex stress response processes. By exploring these mechanisms, we aim to provide a comprehensive understanding of how the brain orchestrates stress responses, offering insights into the biological underpinnings of stress-related disorders and informing potential avenues for psychological interventions.

2.2.1 Amygdala

The amygdala, an essential neural structure in the limbic system, is known for its integral role in processing emotional stimuli and mediating stress responses. Within the scope of this thesis, we examine how the amygdala's interactions with the hypothalamic-pituitary-adrenal axis and its regulatory effects on emotion and behaviour underpin its critical function in stress mechanisms. A deeper understanding of these processes is essential for identifying how stress is regulated and affects neural pathways.

The amygdala's involvement in emotional and stress responses is intricate, functioning as a central hub for processing many emotional stimuli. Research by (Hooker et al., 2006) shows this by featuring the amygdala's acute reactivity to emotional stimuli, such as facial expressions. Fear-related stimuli, such as fearful faces, vocalisations, and emotional music, trigger the amygdala, suggesting a shared neural circuitry dedicated to processing biologically relevant emotional expressions (Jessica McFadyen et al., 2019; William Aubé et al., 2015; William D.S. Killgore et al., 2014).

Interestingly, the amygdala's activation patterns are influenced more by the arousal and intensity of stimuli than by their positive or negative valence. It reacts similarly to high-intensity emotional expressions across different modalities, marking its role in processing emotional intensity rather than the polarity of emotions (Paula Neumeister et al., 2017). Moreover, the structural context surrounding these stimuli, as demonstrated through masking experiments, where a stimulus is presented briefly and then quickly followed by another stimulus that "masks" it, making the first one harder to perceive consciously, can modulate the amygdala's response, indicating its adaptability to contextual nuances in emotional perception (Huiyan Lin et al., 2020).

Beyond its traditional role in emotional processing, the amygdala also processes motivationally relevant stimuli. For instance, it integrates cognitive factors such as fluid intelligence and task performance into activation patterns (Wu et al., 2022). This dual role emphasises the amygdala's involvement in emotional regulation and broader cognitive and motivational processes, suggesting its integral role in behaviour regulation (Kim et al., 2016). Furthermore, direct electrical stimulation of the amygdala, as conducted by (Lanteaume et al., 2007), can induce a broad spectrum of emotions, from fear and sadness to happiness, emphasising its capacity to mediate diverse emotional experiences.

The amygdala also significantly influences memory and decision-making processes, particularly under stress. Stress enhances the memory of events by eliciting increased activation in the amygdala, alongside the hippocampus, which acts as a mnemonic filter that prioritizes emotionally significant memories (Maureen Ritchey et al., 2017). This memory-enhancing effect is crucial for survival, allowing individuals to remember and learn from past emotional experiences. Additionally, the amygdala's connections with brain areas like the locus coeruleus play a crucial role in sensory signal selection, helping to determine which sensory information is prioritised for processing (Cynthia D. Fast & John P. McGann, 2017). This selection is critical for perception and initial reactive responses.

In decision-making contexts, the basolateral amygdala and prelimbic prefrontal cortex circuitry are essential for modulating behavioural responses when faced with conflicting signals of rewards and threats. This illustrates the amygdala's key role in evaluating complex scenarios and making informed decisions under stress (Anthony Burgos-Robles et al., 2017). This decision-making role is further emphasised in Pavlovian fear conditioning, where the amygdala detects imminent threats and conditioned stimuli signalling potential harm, which is essential for survival and forming critical associations (Wen et al., 2022).

Recent investigations using resting-state functional magnetic resonance imaging have explored the amygdala's pivotal role in threat identification and response, revealing its crucial function in maintaining a heightened awareness that prepares the individual for potential dangers (Kirk et al., 2022). These studies underscore the amygdala's comprehensive role in observing and reacting to anxiety-inducing triggers, sustaining an alert state crucial for effective stress management.

Amygdala dysregulation is a critical focus in clinical psychology concerning its role in conditions like post-traumatic stress disorder and anxiety. Enhanced activity within the amygdala emerges as a significant biomarker for PTSD. This hyperactivation is consistently observed in individuals after exposure to traumatic events, correlating strongly with the prevalence of PTSD symptoms. Such findings have catalysed advances in therapeutic approaches, notably real-time fMRI neurofeedback,

which offers new avenues for managing amygdala activity post-trauma and reshaping treatment paradigms (Ressler et al., 2022; Zhiying Zhao et al., 2023)

In PTSD, not only is the amygdala's response to trauma-related cues exaggerated, but there is also an impaired extinction of conditioned fear responses. These maladaptive responses are particularly pronounced when PTSD patients process fearful stimuli unconsciously, indicating a heightened sensitivity of the amygdala under diminished conscious awareness (Slawomira J. Diener et al., 2016).

Sex-specific investigations into amygdalar activity reveal its broader physiological impacts. For instance, studies show that increased amygdalar metabolic activity in women is associated with abnormal cardiac functions, linking emotional stress directly to cardiovascular health issues (Laura Tartari Neves et al., 2019). This connection underscores the systemic influence of amygdala dysregulation beyond the central nervous system.

The significance of amygdala dysregulation extends into developmental psychology. A comprehensive meta-analysis of fMRI studies involving over 2000 children and adolescents presented that heightened amygdala activity from an early age is a strong indicator of anxiety disorders, pointing to its crucial role in early emotional regulation (Ashworth et al., 2021).

Moreover, the dynamic changes in amygdala connectivity with the medial prefrontal cortex (mPFC) across development from positive in early childhood to negative in adolescence illustrate a maturing emotional regulatory mechanism influenced by early-life experiences (Skyberg et al., 2023).

Research into the structural impact of stress on the amygdala provides further insights. For instance, findings from a study involving 272 healthy participants indicate a positive correlation between perceived stress and increased volume of the right amygdala, suggesting that chronic stress can alter brain structure across various life stages (Caetano et al., 2022).

Dysregulation of prefrontal control over amygdala neurons, chiefly those in the basolateral area, is linked to increased anxiety-like behaviour under chronic stress, emphasising the critical role of the amygdala in modulating cognitive and emotional responses (Hugo A. Tejeda & Patricio O'Donnell, 2014; Wei-Zhu Liu et al., 2020). Also, heightened amygdala activity can impair cognitive functions by disrupting hippocampal processes and altering medial prefrontal cortex activity, crucial for effective stress processing and emotional regulation (Eunjoo Kim & Jeansok J. Kim, 2019).

The amygdala's connectivity patterns with regions like the ventromedial prefrontal cortex further elucidate its role in stress management, predicting individual stress responses and regulating cortisol levels (Yuan Zhou et al., 2023; Yuko Hakamata et al., 2017). These interactions spotlight the amygdala's pivotal role in a network that extends beyond simple emotional processing to include

complex cognitive functions and physiological responses, making it a central figure in understanding and managing psychological and neurodevelopmental disorders.

The amygdala's profound influence on the hypothalamic-pituitary-adrenal (HPA) axis demonstrates its pivotal role in stress regulation within the body. Activation of the amygdala significantly enhances the activity of the HPA axis, leading to an increased production of stress-related hormones (Kirsch et al., 2021). This relationship is crucial for initiating appropriate physiological responses to stressors, marking the amygdala as a central player in the body's stress response system.

Likewise, research involving various animal models has supported the critical role of the central amygdala in this regulatory process. Studies demonstrate that impairment or injury to the central amygdala can suppress stress responses, emphasising its indispensable role in controlling physiological reactions to stress (Davern & Head, 2011; Kar et al., 1991; K. Kovács, 2013). The modulation process within the amygdala involves the regulation of crucial neurotransmitters like norepinephrine and serotonin, which are vital for maintaining emotional balance and resilience in stressful situations (Weidenfeld & Ovadia, 2017).

The amygdala's influence extends beyond the HPA axis, impacting the autonomic nervous system (ANS). Notably, increased activation within the amygdala's basolateral and central sectors is linked to elevated anxiety-related behaviours and altered stress management strategies. These changes are observable in physiological markers such as heart rate variability (HRV), a critical indicator of autonomic regulation that reflects the body's ability to adapt to stress (Asim H. Gazi et al., 2021; Yuan Zhou et al., 2023).

Furthermore, variations in respiration patterns might correlate with amygdala activity. For example, a study (Estelle Blons et al., 2019) asked to perform 33 participants' cognitive tasks with or without stressors. They found decreasing variability in breath and heart rate in anxiety responders. This relationship shows the direct impact of amygdala function on respiratory physiology under stress, providing a physiological pathway through which the amygdala influences overall body homeostasis during stressful events.

While often linked to negative emotions, the amygdala's role in processing positive stimuli remains a point of contention. Some sources emphasize its broader role in detecting salience and personal relevance, regardless of valence (Fossati, 2012), while others highlight its heightened activation in response to negative, compared to positive, stimuli (Aldhafeeri et al., 2012). Additionally, the precise roles of different amygdala subregions (lateral, central, basal) in human stress responses are still being investigated (Ho et al., 2014; Phelps & LeDoux, 2005).

2.2.2 Prefrontal Cortex

The prefrontal cortex is the central player in the brain's response to stress, which refines these responses through cognitive evaluation and emotional regulation by integrating cognitive and emotional processes to regulate neuroendocrine functions.

The PFC's interaction with the amygdala and other limbic regions is crucial in appraising the threat value of stressors. The medial prefrontal cortex modulates the HPA axis and the sympathetic nervous system, influencing autonomic and neuroendocrine functions. These interactions are vital for assessing coping resources and determining the emotional and physiological significance of stressful stimuli, highlighting the PFC's role in nuanced stress management (Ironside et al., 2019; Marques et al., 2023; Stefano Delli Pizzi et al., 2017).

The prefrontal cortex, including its orbitofrontal cortex (OFC) subregion, is critical in balancing emotional reactivity and cognitive control. Under stress, the amygdala often drives heightened emotional responses, such as fear or anxiety. However, the PFC, particularly the OFC, helps regulate these responses by exerting cognitive control, which can dampen or modulate the intensity of the emotions generated by the amygdala. This interaction between the amygdala and the PFC is crucial for maintaining emotional stability and cognitive functioning (Girotti et al., 2022; Suzuki & Tanaka, 2021), which was confirmed in a recent meta-analysis (Yang et al., 2020), preventing emotional reactions from overwhelming rational thought.

The dorsolateral prefrontal cortex (dlPFC) is critical in resolving emotional conflicts and regulating stress responses. Its activation during tasks requiring cognitive control and emotional regulation underscores its dual role in managing stress's immediate emotional impact and engaging higher cognitive functions necessary for adapting to stressful situations, as reviewed by (Dixon et al., 2017) and recently supported by (Rieck et al., 2023). It is involved in appraising stressors, decision-making, working memory, and implementing coping strategies like cognitive reappraisal (Koussis et al., 2023).

The medial prefrontal cortex, part of the default-mode network, is typically more active when a person is internally focused, such as during daydreaming or self-referential thoughts (Jobson et al., 2021). The default-mode network is a well-studied network of brain regions that become active during rest or passive tasks that do not require focused attention on the external environment, which was confirmed by a recent meta-analysis (S. Wang et al., 2020). In contrast, the dlPFC is more active when a person is externally focused, such as when performing tasks that require attention and control (Keller et al., 2015). This interaction between the mPFC and dlPFC is crucial for tasks requiring

attention and cognitive control, supporting working memory and decision-making under pressure (Y. Wang et al., 2023).

The mPFC sends inhibitory signals to the paraventricular nucleus of the hypothalamus, reducing the release of corticotropin-releasing hormone and subsequently attenuating the release of glucocorticoids like cortisol (Spencer et al., 2005).

Prolonged exposure can weaken the mPFC's ability to manage these physiological responses, leading to an overproduction of stress hormones and a breakdown in autonomic regulation. This shift heightens the risk of severe health issues, such as cardiovascular disease and mental health disorders (Derek Schaeuble et al., 2019; Larkin et al., 2020).

The PFC's ability to exert inhibitory control over emotional responses is evident in various contexts. Individuals with anxiety disorders often show reduced PFC activation, suggesting a failure to effectively regulate negative emotions (Brehl et al., 2020). Conversely, successful emotional reappraisal is associated with increased activity in the dorsolateral and ventrolateral PFC, illustrating the PFC's capability to dampen emotional responses through cognitive strategies (A. K. Anderson & Phelps, 2001; Ochsner et al., 2002). For instance, individuals with difficulties in emotion regulation, such as those with specific phobias, often display reduced activation in the ventrolateral PFC when confronted with anxiety-provoking stimuli (Schienle et al., 2009).

The mPFC's broad implications for mental health are particularly notable, especially in its response patterns in PTSD and its central role in the autonomic control network. It manages bodily reactions, such as cardiovascular responses during stress, illustrating the mPFC's role in linking mental and physical health (Wei-Zhu Liu et al., 2023; P. Xu et al., 2019). Additionally, the PFC's response to negative stimuli, such as activation in the left inferior frontal gyrus by negative words, highlights the involvement of different PFC regions in processing distinct types of negative stimuli, which is crucial for targeted therapeutic interventions in stress-related disorders (Lea Marie Reisch et al., 2020).

2.2.3 Anterior cingulate cortex

The Anterior Cingulate Cortex is a crucial part of the brain that helps balance cognitive functions and emotional responses. Different parts of the ACC have specific roles, with one area focusing on cognitive control and another on regulating emotions.

Dorsal Anterior Cingulate Cortex

The dorsal anterior cingulate cortex (dACC) is involved in managing tasks that require significant cognitive effort and in resolving conflicts between cognitive demands and emotional disturbances

(Sheth et al., 2012). It plays a crucial role in adaptive behaviour by influencing response speed and accuracy in response to environmental cues and changing situational demands (Heilbronner & Hayden, 2016). The dACC is also linked to maintaining attention and optimizing processing efficiency, particularly in complex problem-solving situations or dynamic environments that require sustained focus and flexible adjustments (Sheth et al., 2012; Veen & Carter, 2002).

Ventral Anterior Cingulate Cortex

Conversely, the ventral anterior cingulate cortex (vACC) is closely integrated with the limbic system. It is involved in managing autonomic and neuroendocrine responses to stress and regulating emotional states (Rigney et al., 2017). It plays a crucial role in top-down emotional regulation by interacting with core emotion-processing areas such as the amygdala and hippocampus (Goldin et al., 2008). The vACC is engaged in processing emotional conflicts, revealing its importance in emotional regulation and social decision-making (Chen et al., 2023; Enneking et al., 2020). Moreover, it detects salient emotional information and contributes to generating emotional states. By modulating amygdala activity, the vACC helps downregulate emotional arousal (Rigney et al., 2017; Šimić et al., 2021).

The connection between the ventral anterior cingulate cortex and the amygdala is crucial for bidirectional communication that influences emotional processing and regulates responses. This functional relationship allows the vACC to modulate amygdala activity, affecting how emotions are processed (Motomura et al., 2013). In addition to this functional connectivity, meaningful structural connections exist between the vACC, amygdala, and hypothalamus (Kleshchova et al., 2019). These structural links mediate visceral and endocrine responses to emotionally significant events (Passamonti et al., 2012; X. Xu et al., 2019).

Furthermore, emerging studies focus on how lifestyle factors, such as sleep deprivation, can influence the functional dynamics between the vACC and the amygdala. Chronic sleep deprivation can impair the vACC's ability to suppress amygdala activity, leading to heightened emotional reactivity, particularly to negative stimuli (Motomura et al., 2014).

In clinical contexts, particularly in populations with emotional dysregulation such as PTSD, the dissociation between vACC and amygdala activities suggests potential defects in communication between these regions. Such insights are pivotal for developing targeted interventions to enhance vACC-amygdala connectivity to improve emotional regulation capabilities (Janet et al., 2023; Kleshchova et al., 2019).

2.2.4 Insula

The anterior insula (AI) primarily involves interoceptive awareness of emotional and bodily states. AI helps organisms become aware of how emotions are felt physically within the body, such as the tightness in the chest associated with anxiety or the warmth of happiness. The AI processes emotionally charged stimuli, like emotional images, and integrates these with bodily sensations, making it crucial for understanding and regulating our emotional experiences (Sheffield et al., 2021; Tsujimoto et al., 2023).

In contrast, the posterior insula focuses more on processing more direct and concrete physical sensations, such as pain, temperature, and touch. This part of the insula is essential for the detailed perception of the body's internal physical condition, contributing to a more precise understanding of how our body feels regarding physical sensations (J. Zhang et al., 2017).

This structural and functional distinction allows the insula to mediate various psychological processes. While the anterior insula integrates emotional and bodily signals to help regulate emotions, the posterior insula is crucial for the precise sensory processing of physical states. Together, these regions enable the insula to play a central role in both interoceptive awareness and emotional regulation, bridging the gap between sensory experiences and complex emotional responses (Namkung et al., 2017; Simmons et al., 2012; Uddin et al., 2017).

The insula is integral to emotional regulation, interacting with the amygdala and the prefrontal cortex (R. Zhang et al., 2024). This triadic network is essential for integrating sensory and emotional information to manage responses to stressors effectively. The AI, in particular, modulates the amygdala's response to highly emotional stimuli, influencing overall emotional regulation and emphasising the insula's pivotal role in this complex neural interplay (Killgore et al., 2013; Suzuki & Tanaka, 2021).

Neuroimaging studies reveal that the insula, especially the left anterior insula, exhibits enhanced neural responses to negatively valenced emotional stimuli. This heightened activity is critical for processing diverse sensory information and regulating emotional responses across various contexts (Malena Mielke et al., 2021). The insula's interaction with the amygdala and prefrontal cortex during evaluating emotionally charged stimuli further cements its central role in managing emotional processing (Linton & Levita, 2021).

The ventromedial prefrontal cortex, crucial for emotion regulation, collaborates closely with the insula and amygdala to process emotional stimuli. This connectivity proves especially important in clinical settings, where altered activation patterns in these regions are observed in conditions such as PTSD (Diener et al., 2016; McLaughlin et al., 2014). The AI's connectivity with the amygdala is

instrumental in processing emotional stimuli, with studies showing increased functional connectivity in conditions such as PTSD, correlating with symptom severity and altered emotional processing (Nicholson et al., 2016).

The AI is a vital component of the salience network, a key brain network that detects and prioritises important or emotionally relevant stimuli (Cloutman et al., 2012). The salience network, which includes the AI and the ACC, functions as a kind of "alert system" in the brain (Cloutman et al., 2012). The insula's broader role in influencing attentional control, particularly the AI, underscores its importance in allocating cognitive resources. The AI helps the brain focus on task-relevant stimuli, enhancing cognitive efficiency, especially during stressful or emotionally charged situations. By efficiently managing these cognitive resources, the AI ensures that we remain focused and effective, even when faced with challenges (Frot et al., 2022; Pedale et al., 2019).

There is ongoing debate about the insula's role in processing different valences of emotion. Some sources suggest it might play a more general role in signalling salience or arousal, showing heightened activity in response to positive and negative stimuli (Phelps et al., 2014). Others highlight its role in anxiety, potentially linked to its involvement in processing threat-related bodily sensations (Stein et al., 2007).

2.3 Integrative Brain and Body Responses

Introduction

After exploring the specific roles of various brain regions in stress processing, it is essential to understand how the complex interplay leads to an effective stress response to keep homeostasis. The amygdala receives information about the stressor. If the stimulus is deemed significant, the amygdala activates a network of brain regions that prepare the body for action. The amygdala's trigger stress reaction is very interconnected with PFC, which evaluates the context of the threat and determines the appropriate level of response. The prefrontal cortex can modulate the intensity of the response, either amplifying or inhibiting the hypothalamus based on the perceived severity of the threat. Concurrently, the anterior cingulate cortex integrates cognitive and emotional demands. The dorsal region monitors conflicts between these demands, ensuring focused attention on relevant tasks. The ventral region modulates the amygdala's activity, adjusting the emotional response to align with cognitive strategies. The anterior insula refines this response by integrating interoceptive signals on how the body experiences stress with emotional processing. The complex interplay of feedback loops of different brain areas allows the CNS to appropriately regulate the Hypothalamic-Pituitary-Adrenal axis and the autonomic nervous system to the threat.

2.3.1 Hypothalamic-Pituitary-Adrenal Axis

This dynamic system, comprising the hypothalamus, pituitary gland, and adrenal glands, coordinates a complex neuroendocrine response that allows the body to adapt to and cope with various environmental, physiological, and psychological challenges (James P. Herman & Jeffrey G. Tasker, 2016). Activation of the HPA axis is a hallmark of the stress response, leading to the release of glucocorticoids that facilitate physiological ranging effects on the cardiovascular system (Fig. 2) (James P. Herman, 2010).

The limbic system, including the hippocampus and amygdala, provides crucial modulatory input to the HPA axis. These structures send excitatory and inhibitory projections to the paraventricular nucleus of the hypothalamus, influencing the release of corticotropin-releasing factor, which is pivotal in mediating stress-induced behavioural responses (Neufeld-Cohen et al., 2010; A. L. Russell et al., 2018). Neurotransmitters such as norepinephrine and serotonin play significant roles in activating the HPA axis in response to stress (Weidenfeld et al., 2012).

During the initial stages of a stress response, there is a shift towards habitual, stimulus-response memory, primarily governed by the dorsal striatum, facilitated by catecholamines and rapid glucocorticoid effects (Quaedflieg & Schwabe, 2018). This shift allows quick, efficient reactions to

stressful situations (Joëls et al., 2018). However, the delayed genomic effects of glucocorticoids might restore and even enhance executive functioning and cognitive control of memory, primarily in the hippocampus and prefrontal cortex, enabling more thorough processing and rationalization of stressful events (Joëls et al., 2018). Research suggests stress can have differential effects on the striatum, with some studies showing enhanced activity in the dorsal striatum during physiological stress, potentially reflecting a shift towards habitual, potentially survival-oriented behaviours (Phelps et al., 2014; Sep et al., 2019). Other studies highlight decreased activity in other subregions - ventral striatum during psychosocial stress, potentially reflecting a downregulation of reward processing and motivation (Kogler et al., 2015). The precise mechanisms by which stress impacts different striatal subregions and their implications for behaviour are still unknown.

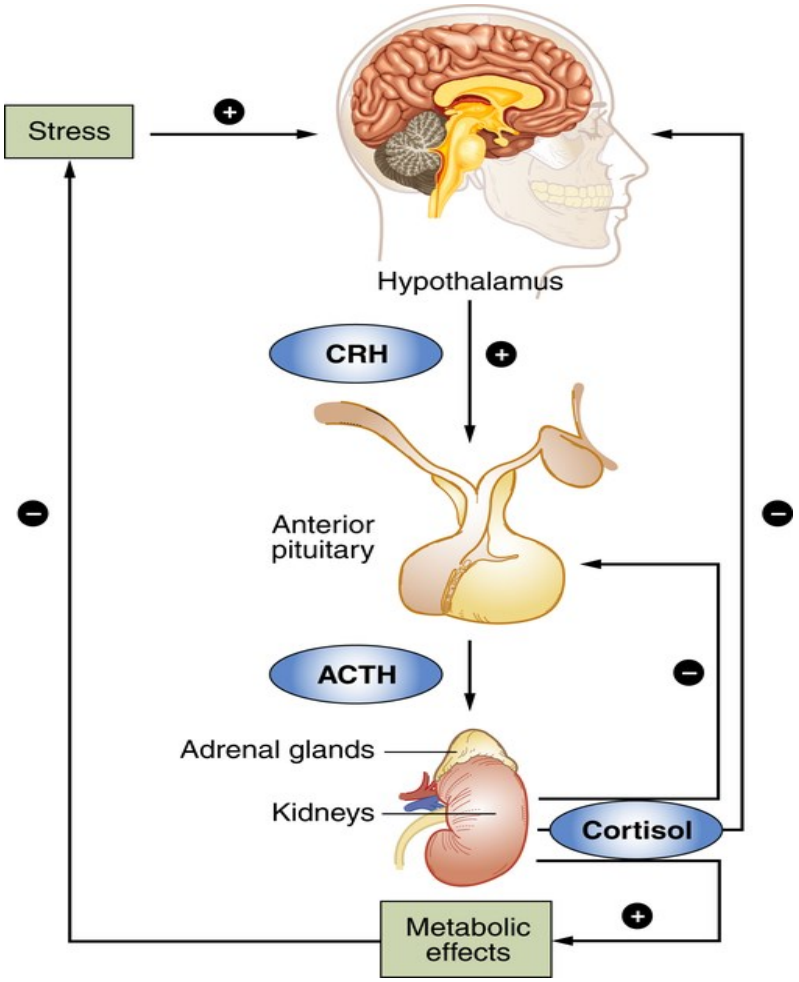

***Figure 2**: The HPA Axis. The neurohormonal feedback loop, reproduced from (Smyth et al., 2013).*

The HPA axis's activation by various stressors, including thermal and emotional, prompts a dynamic neuroendocrine response characterised by releasing hormones like arginine vasopressin and corticosterone (G. Russell & Lightman, 2019). Chronic stress leads to adaptations in the HPA axis, altering its sensitivity and reactivity to subsequent stressors. This modified response is crucial for

understanding the differential impacts of stress based on factors like sex, cognitive appraisal, and the nature of the stressor (Jasnić et al., 2013; Ostrander et al., 2006).

Stress-related neurological pathways mediated by the HPA axis significantly influence heart rate variability, an autonomic nervous system function marker. Chronic stress, mediated through HPA axis activation, can alter HRV and breathing patterns, demonstrating the comprehensive impact of stress on body health (Cvijetić et al., 2022; Lin et al., 2023). Furthermore, cortisol, a primary stress hormone regulated by the HPA axis, is directly associated with changes in HRV, reflecting alterations in autonomic activity and the cardiovascular stress response (G. Kuyper & Honig, 2008).

Alterations in the HPA axis lead to impaired stress processing and emotional regulation in disorders such as PTSD. Dysregulation can adversely affect brain functions in managing stress, illustrating the complex integration between the HPA axis and brain functions in stress regulation (von Majewski et al., 2023).

The HPA axis collaborates with various brain regions to modulate stress-related cardiovascular and respiratory responses. The paraventricular nucleus of the hypothalamus, receiving inputs from stress-responsive brain areas like the medial prefrontal cortex, hippocampus, and amygdala, coordinates a comprehensive response to stress (Horii-Hayashi et al., 2015; Jamieson et al., 2022; Melis et al., 1999). This intricate interaction is essential for maintaining homeostasis and adapting behavioural and physiological responses to environmental demands (Mooney-Leber et al., 2021).

2.3.2 The Autonomic Nervous System

The Autonomic Nervous System is a principal executor of the brain and plays a vital role in metabolic regulation across the body, which leads to a perfect setting for solving a particular task. The ANS comprises the sympathetic and parasympathetic nervous systems, each playing critical roles in stress response. The sympathetic nervous system mobilises the body's resources during stress, often called the "fight or flight" response (Roos et al., 2017). In contrast, the parasympathetic nervous system orchestrates the "rest and digest" activities, restoring the body to calm (Shimizu & Okabe, 2007).

When facing stress, concurrently with the HPA axis, the sympathetic system is activated, releasing neurotransmitters like noradrenaline that enhance the body's ability to cope with stress. This dual activation illustrates the interconnectedness of the HPA axis and ANS, ensuring a comprehensive response to stressors (Fig. 3) (Hinds & Sánchez, 2022; Johnson et al., 1992; S. M. Smith & Vale, 2006).

The amygdala detects threatening stimuli and communicates with the hypothalamus to enhance the stress response. This interaction influences autonomic functions such as pupil dilation and changes in heart and respiratory rates, integrating emotional and physiological responses to stress (Hendrix, 2008). On the other hand, the hypothalamus serves as a central regulator that communicates with various parts of the body, including the ANS, to control functions like blood pressure, heart rate, and the immune system (Messina et al., 2016).

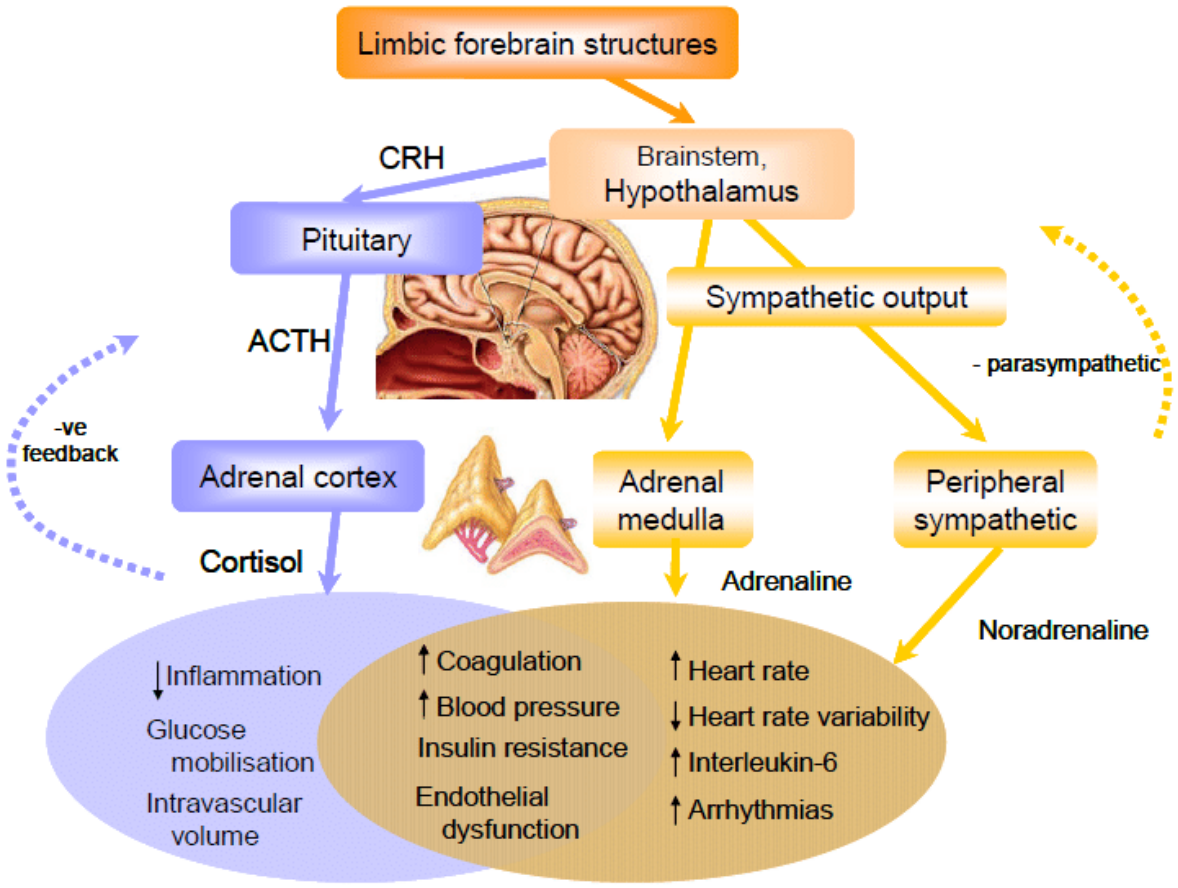

***Figure 3**: The activation of the HPA axis is in purple, and the activation of the SNS axis is in yellow, reproduced from (Hackett, 2016).*

The sympathetic nervous system activation during stress increases the release of norepinephrine, which acts on the heart and blood vessels to increase heart rate and blood pressure, meeting the body's heightened metabolic demands (Roos et al., 2017). Norepinephrine acts on beta-1 adrenergic receptors in the heart, increasing heart rate and the force of myocardial contraction (Motiejunaite et al., 2021). This sympathetic activation increases cardiac output, which helps to meet the body's increased metabolic demands during the stress response (Lívea Dornela Godoy et al., 2018). Additionally, norepinephrine stimulates alpha-1 and alpha-2 adrenergic receptors in vascular smooth muscle, causing vasoconstriction and increased blood pressure (Goldstein, 2010).

In the respiratory system, norepinephrine acts on beta-2 adrenergic receptors in the bronchioles, leading to bronchodilation and increased airflow (Lívea Dornela Godoy et al., 2018; Ocklenburg et al., 2016). Norepinephrine leads to a higher breathing frequency and greater tidal volume, allowing for more efficient gas exchange and increased tissue oxygen delivery (Larocca et al., 2011). Research has shown that noradrenaline released from the pontine noradrenergic A5 nuclei can modulate respiratory frequency, indicating the intricate involvement of central structures in regulating breathing patterns (Viemari et al., 2004). Elevated cortisol levels, a hallmark of the stress response, can further influence the rate and rhythm of breathing, underscoring the close connection between stress responses and respiratory control (Doussard-Roosevelt et al., 2003).

Conversely, following the acute stress response, the parasympathetic nervous system facilitates physiological recovery, reducing heart rate and promoting energy conservation and digestion. This shift to parasympathetic dominance is critical for long-term health, preventing chronic stress and aiding in the recovery from temporary stressors (Tindle & Tadi, 2020). The parasympathetic nervous system, as reviewed in (Berto, 2014), is mediated by the vagus nerve, which counteracts the effects of the sympathetic nervous system by slowing down heart rate, dilating blood vessels, and activating digestion and energy storage.

Post-stress cortisol levels typically decrease, signalling the parasympathetic nervous system to initiate recovery processes. This transition from stress to relaxation involves complex feedback mechanisms between the HPA axis and the ANS, which is essential for maintaining homeostasis (Richer et al., 2022). Variations in this feedback can significantly impact emotional and physical health, influencing everything from cardiovascular health to psychological well-being. For instance, individual differences in autonomic feedback can influence emotional and behavioural outcomes, with higher autonomic feedback intensifying reactions to stress and potentially leading to burnout and reduced job performance (Klein & Verbeke, 1999). Chronic stress can lead to persistent activation of the HPA axis and the amygdaloid corticotropin-releasing hormone system, resulting in anxiety and stress-associated disorders (Makino et al., 2002).

2.4 Processing of Diverse Stress Stimuli

2.4.1 Classification and Characteristics of Stress Stimuli

Stress stimuli can be broadly categorized into two primary types: physiological stressors and psychological stressors. While these categories are not mutually exclusive, they differ significantly in how the brain perceives, registers, and processes them.

Physiological stressors target homeostatic parameters and are processed primarily through viscerosensory pathways (K. J. Kovács et al., 2005). These stressors directly impact physiological parameters such as oxygen levels, temperature, and metabolic states (Kagias et al., 2012). Examples from animal experiments include bacterial lipopolysaccharide injection, predator scent exposure, food deprivation, and acute heat shock (K. Kovács, 2013). Physiological stressors activate autonomic circuits and stress-related motoneurons with minimal involvement of higher cortical processes, leading to immediate, reflexive responses to restore homeostasis (O'Riordan et al., 2023).

On the other hand, Psychological stressors engage more complex processing mechanisms, recruiting somatosensory and nociceptive afferent pathways (K. J. Kovács et al., 2005). In animal experiments, psychological stressors are usually presented in immobilization, foot shock, restraint, and forced swimming (Lívea Dornela Godoy et al., 2018). Psychological stressors are processed through cortical and limbic circuits, integrating cognitive, emotional, and learned components (Lívea Dornela Godoy et al., 2018). Laboratory stressors such as the Trier Social Stress Test (TSST) and the Social Evaluation Test are examples of psychological stressors used in human research (Campbell & Ehlert, 2012; Ho et al., 2014; S. M. Smith & Vale, 2006).

Stress stimuli can be presented through sensory modalities, including visual, auditory, and haptic inputs. The modality of a stimulus significantly influences its emotional impact and the physiological responses it elicits (Polo et al., 2024). For example, studies have shown that emotional sounds can trigger more robust physiological responses than visual or audio-visual stimuli, indicating the sensory pathway's role in stress processing (Horvat et al., 2015; Polo et al., 2024).

The emotional valence of a stimulus, whether perceived as positive, negative, or neutral, plays a crucial role in processing it. Negative stimuli consistently trigger stronger cerebral activation across different stimulus types (e.g., pictures, faces, and words) than neutral stimuli (Lea Marie Reisch et al., 2020; Pan et al., 2023). Positive emotional states, particularly when contingent on task performance, can enhance cognitive flexibility, while non-contingent positive affect promotes cognitive stability (Senne Braem et al., 2013).

The intensity of a stressor affects the brain's response, with high-intensity stressors leading to more pronounced physiological and neural changes (Tadayon et al., 2018). High arousal states, especially

those associated with negative emotions, can impair context processing and lead to heightened stress responses (Thomas Maran et al., 2018).

2.4.2 Cognitive and Emotional Mechanisms in Stress Processing

The processing of stress stimuli involves complex cognitive and emotional mechanisms influenced by various theoretical frameworks. These mechanisms are central to understanding how the brain interprets and responds to stressors.

Cognitive Control and Emotional Modulation

Cognitive control mechanisms, particularly those mediated by the prefrontal cortex, are pivotal in managing stress responses (M. C. Anderson & Green, 2001; Koussis et al., 2023). Emotional states, whether positive or negative, can modulate these cognitive processes. For instance, negative affect triggered by a challenging situation can enhance cognitive effort, leading to increased focus and task performance, a phenomenon explained by the affect-congruent modulation of cognitive control (Pan et al., 2023; Van Steenbergen, 2015). Conversely, depending on their context, positive emotions can facilitate cognitive flexibility or promote cognitive stability (Senne Braem et al., 2013).

Attentional Bias

Attentional bias is the tendency for emotionally salient stimuli, especially negative ones, to capture attention (Amanda W. Calkins et al., 2011). This bias is particularly evident in individuals with anxiety or depression, where there is a heightened focus on negative stimuli, which can exacerbate symptoms (Sep et al., 2019). Cognitive control processes manage this bias, preventing emotionally charged distractors from interfering with task performance (Manuel Petrucci & Anna Pecchinenda, 2017).

Stress Reactivity Patterns

Individual differences, personality traits, prior experiences, and age significantly influence stress reactivity (K. J. Kovács et al., 2005). These differences manifest in distinct patterns of physiological and behavioural responses to stress (Kiecolt-Glaser et al., 2020). For example, research has identified multiple stress reactivity patterns in children, ranging from moderate reactivity to parasympathetic-specific responses, each associated with different developmental and environmental factors (K. E. Smith & Pollak, 2020).

2.4.3 Theoretical Paradigms Shaping Stress Research

Several theoretical models provide a framework for understanding the complex interplay between physiological and psychological stress processing. These paradigms guide research by highlighting different aspects of stress responses and shaping the interpretation of findings.

Polyvagal Theory and Neurovisceral Integration Model

These frameworks emphasize the role of heart rate variability in emotional response and regulation (Appelhans & Luecken, 2006). The polyvagal theory highlights the vagus nerve's role in connecting the brain to the heart, influencing HRV and thus regulating physiological and emotional states during stress (Heilman et al., 2012). The neurovisceral integration model further suggests that HRV reflects the dynamic interaction between cognitive, affective, and physiological systems, measuring how well these systems are integrated during stress (Thayer et al., 2009).

Interoceptive Predictive Coding

This model, often called the "Bayesian Brain," posits that the brain continuously predicts and interprets incoming sensory information, including internal bodily signals, to maintain homeostasis and guide behaviour (Barrett & Simmons, 2015; Hugo D. Critchley et al., 2018). According to this framework, physiological signals, such as heartbeats, can significantly influence cognitive processes, selectively enhancing or inhibiting information processing based on the body's current state. Emotions, deeply connected to these physiological states, pervasively affect cognition and behaviour, shaping how stress is perceived and managed. The concept of interoceptive predictive coding also suggests that emotions are interoceptive inferences, and disruptions in this predictive process may contribute to psychiatric disorders related to selfhood, such as anxiety and depression(Seth & Critchley, 2013).

Affect-as-Cognitive-Feedback Account

This framework challenges traditional views of the relationship between affect and cognition, suggesting that affect acts as feedback that shapes cognitive strategies (Jeffrey R. Huntsinger et al., 2014). The influence of affect on cognition is context-dependent. This account proposes that affective experiences impact cognitive outcomes by assigning a positive or negative value to dominant processing styles, thereby affecting information processing (Isbell et al., 2016).

Affective Signalling Hypothesis

This hypothesis focuses on how affective signals, particularly negative ones, modulate cognitive control and adaptation. It posits that negative affective cues can enhance cognitive control by signalling potential threats or errors, thus preparing the individual for more focused and adaptive

responses (Miklos Bognar et al., 2023). This hypothesis is integrated within conflict monitoring theories, introducing the concept of affective signals related to conflict as a motivator for increased cognitive control and processing (Dignath et al., 2020). This integration emphasizes the interplay between affective responses and cognitive functions in conflict resolution and decision-making.

2.5 Methods Review for Studying Stress Processing

Neuroimaging Techniques

Functional magnetic resonance imaging and magnetoencephalography are commonly employed to visualize brain activity during stress. fMRI offers high spatial resolution, making it ideal for pinpointing specific brain regions involved in stress processing (Rinaldi et al., 2011). However, its limited temporal resolution poses challenges in capturing rapid changes in brain activity (J. Wang et al., 2007). With superior temporal resolution, magnetoencephalography is better suited for studying real-time interactions between brain regions during stress (Emi Yamano et al., 2016). Both methods, while powerful, require specialized equipment and expertise, making them resource-intensive. Neuroimaging also presents interpretation challenges due to the complexity of brain activity and the artificial nature of laboratory settings.

Physiological Measures

Techniques such as heart rate variability, salivary cortisol levels, galvanic skin response, and electroencephalography provide objective and quantifiable data on the body's physiological responses to stress. HRV, for instance, reflects the balance between the sympathetic and parasympathetic branches of the autonomic nervous system, offering insights into autonomic regulation during stress (Sparrow & Golianu, 2014). However, external factors unrelated to stress can influence this measurement, such as physical activity or medication use, which may confound the results (Ragonesi & Antick, 2008). The timing of physiological assessments is also crucial, as stress responses can vary over time, complicating the interpretation of data.

Behavioural Tasks

Tasks like the Trier Social Stress Test, the Decision-Making under Uncertainty and Stress virtual reality task, and the Stroop task with incorporated social-evaluative elements are used to assess the impact of stress on cognitive functions such as attention, memory, and decision-making (Giles et al., 2024; Henk van Steenbergen, 2015; Mueller et al., 2022; S. M. Smith & Vale, 2006). These tasks are valuable for understanding the functional consequences of stress on behaviour. However, individual differences in task performance, influenced by factors such as motivation, fatigue, or prior experience, can complicate the interpretation of results (J. Wang et al., 2007). The ecological validity of these tasks is also a concern, as they may not fully capture the complexity of real-world stressors (Giles et al., 2024).

Self-Report Questionnaires

Self-report measures, including tools like the Interpersonal Reactivity Index and the Temperament and Character Inventory, offer insights into individual experiences of stress and related traits (Emi Yamano et al., 2016). While these questionnaires provide valuable subjective data, they are prone to biases such as social desirability and recall inaccuracies, which can affect the reliability and validity of findings (Stephanie S. Rude et al., 2002). The subjective nature of self-reports may not always align with objective physiological or neural measures of stress.

Animal Models vs. Human Studies

Animal models of chronic stress, such as the social defeat stress model and chronic mild stress model, are fundamental in dissecting physiological, neurobiological, and genetic aspects of stress responses. These models provide a controlled environment to study stress mechanisms and therapeutic interventions (Bali & Jaggi, 2015; A. Toyoda, 2017). However, the applicability of findings from these animal models to human conditions is limited due to physiological and genetic differences between species and ethical considerations (Ashokan et al., 2016; Delaleu et al., 2011; Pace et al., 2022).

Human studies, utilizing subjective and objective methods, offer a richer understanding of stress processing directly applicable to human experiences. Laboratory-based stress paradigms like the TSST and the Montreal Imaging Stress Task, along with biomarkers such as cortisol and HRV, are commonly used in these studies (Bali & Jaggi, 2015). However, the ecological validity of these laboratory settings can be limited, and the artificiality of the experimental environment may not fully represent real-life stressors (Sep et al., 2019). A recent review (Arsalan et al., 2022) highlighted the potential of wearable devices to effectively measure stress in everyday environments. Integrating these wearable devices with precise laboratory methods could enhance stress measurements' accuracy and ecological validity.

Multimodal Approaches

A multimodal approach offers a complex solution to address the limitations of individual methods. Combining neuroimaging with physiological measures, behavioural assessments, and self-report data provides a more comprehensive understanding of how stress affects the brain and behaviour (Giorgos Giannakakis et al., 2019). This integrated approach allows researchers to capture the complexity of stress responses across different levels of analysis, offering a complete picture of the dynamic processes involved in stress processing (Giorgos Giannakakis et al., 2019).

3. Experimental Part

3.1 Aims and Hypotheses

The main aim of the experimental study is to investigate the neurophysiological and neuronal mechanisms underlying the processing of various types of naturalistic stress stimuli. The research focuses on identifying the differences in brain and body responses to highly affective negative stimuli, which are primarily processed automatically, compared to negative stimuli subject to greater cognitive control.

Specific Objectives and Hypotheses:

Hypothesis 1: Neurophysiological Mechanisms of Stress Stimuli Processing

Objective: To describe the neurophysiological mechanisms underlying the processing of different types of stress stimuli, specifically distinguishing between neutral stimuli, highly affective negative stimuli (DISTURBING), and negative stimuli requiring greater cognitive control (CONCERNING).

Hypotheses**:**

- We hypothesize that DISTURBING stimuli will elicit widespread activation across brain regions associated with emotional processing.
- CONCERNING stimuli are expected to engage more distributed brain regions involved in cognitive processing and regulation.

Hypothesis 2: Physiological Responses to Different Types of Stress Stimuli

Objective**:** To determine the physiological responses, specifically heart rate and respiratory patterns, to different types of stress stimuli, distinguishing between highly affective and cognitively regulated stressors.

Hypotheses**:**

- We hypothesize that DISTURBING stimuli will result in a heightened sympathetic response, as reflected by an increased heart rate and changes in respiratory patterns.
- CONCERNING stimuli are expected to result in a more moderated physiological response, with less pronounced changes in heart rate and breathing patterns.

3.2 Methods

3.2.1 Participants

The study's inclusion criteria were being a university student, older than eighteen, and fluent in Czech. Initially, 89 participants registered for our experiment through online tests. We included data from 80 participants in the final analysis. Nine participants were excluded due to anatomical or psychological anomalies or technical issues related to data recording errors or mistakes in the visual stimuli presentation. The participants were equally divided by sex, with a mean age of 22.27 years (SD = 2.11).

We recruited participants over nine months through advertisements on the National Institute of Mental Health and Charles University's social media platforms.

Exclusion Criteria

The following criteria led to exclusion from participation in the study:

Left-handedness: Participants in this study must be right-handed due to hemispheric lateralisation of brain functions. In right-handed individuals, language and other cognitive functions are predominantly localised in the left hemisphere, whereas left-handed individuals may have more variable hemispheric specialisation. Ensuring a homogeneous sample in terms of handedness minimises variability in brain activation patterns, thus enhancing the reliability and interpretability of the fMRI data (Karolis et al., 2019).

Psychiatric History: The exclusion of participants with a personal or immediate family history of severe psychiatric illness is crucial to control for potential confounding variables. Psychiatric conditions, such as major depressive disorder, schizophrenia, and bipolar disorder, can alter brain function and structure, thereby affecting the neural mechanisms of stress processing. This criterion ensures that underlying psychiatric conditions do not influence observed neural responses (van Dijk et al., 2021).

Head Injury: A history of head injury resulting in loss of consciousness can lead to long-term alterations in brain structure and function, which might confound the study results. Traumatic brain injuries can cause diffuse axonal injury, affecting neural connectivity and cognitive functions. Excluding individuals with such histories helps maintain the integrity of the data by ensuring that neural responses to stimuli are not affected by prior brain trauma (Sharp et al., 2014).

Active Medical Conditions: Participants with active and untreated medical conditions, such as cerebrovascular disease, are excluded to avoid confounding effects on brain function and physiological responses. Conditions like stroke or transient ischemic attacks can significantly alter

cerebral blood flow and neural activity, which would interfere with the study's aims to investigate typical neural mechanisms of stress processing (Gorelick et al., 2011).

Substance Use: Individuals with any substance-related disorder or long-term dependence on addictive substances within the past six months were excluded because substance use can have profound and lasting effects on brain function. Substances such as alcohol and illicit drugs can alter neural circuitry involved in stress processing and cognitive control. This exclusion criterion ensures that participants' brain responses are not influenced by recent substance use or withdrawal (Koob & Volkow, 2016).

Neurological Conditions: A history of neurological disease, including epilepsy, multiple sclerosis, or Parkinson's disease, is an exclusion criterion due to the potential impact of these conditions on brain function. Neurological diseases can cause structural and functional brain changes that confound the interpretation of fMRI results related to stress processing (McNamara, 1991).

MRI Contraindications: Participants with MRI contraindications, such as metal implants, pacemakers, and extensive tattoos, are excluded for safety reasons and to prevent artefacts in the imaging data. Metal objects can interfere with the magnetic field of the MRI machine, causing distortions or posing safety risks. Pregnant women are also excluded due to potential risks associated with strong magnetic fields (Kanal et al., 2013; Shellock & Crues, 2004).

Visual Impairment: Uncorrectable visual impairment not resolvable with diopters up to size five or contact lenses is a criterion for exclusion because visual stimuli are central to the experiment. Accurate and consistent visual perception is necessary to ensure that all participants similarly process the stimuli, enabling reliable interpretation of the fMRI data. For participants with visual acuity within the range of ±5 diopters, we provided them with special MRI-compatible glasses to ensure optimal visual clarity during the experiment.

Claustrophobia: Participants were in a narrow fMRI during the experiment. Claustrophobic reactions can induce significant anxiety and stress, potentially confounding the results by introducing additional variables unrelated to the experimental conditions.

Ethics

The National Institute of Mental Health Ethics Committee approved the study (project number 115/19), adhering to the 1964 Helsinki Declaration. Participants received informed consent and study details before participation, including data processing for research. At the beginning of the study, all respondents signed an informed consent to participate and process the data for research purposes.

Participation in the study was voluntary, and participants were rewarded with 1000 CZK. All gathered data was handled confidentially, and the subject´s identity was kept anonymous.

3.2.2 Visual Stimuli Preparation

The selection of visual stimuli for this fMRI study was a carefully designed multi-stage process to ensure the chosen images, photos, and media graphics effectively evoked a range of emotional responses, particularly those related to stress and worry. To achieve this, we conducted a preliminary experiment to identify and validate appropriate stimuli for the main fMRI study.

***Figure 4**: Three examples of stimuli: Cognitive, Disturbing, and Neutral.*

In this preliminary experiment, we collected 379 visual stimuli from various online newspapers, each consisting of an image accompanied by a short text headline. These stimuli were then categorized into three groups: Cognitive, Disturbing, and Neutral (Fig. 4). To ensure that the stimuli within each category differed minimally from one another, we carefully selected and standardized the stimuli (Fig. 5). To evaluate the effectiveness of these stimuli, we presented them to 157 participants, who rated the stimuli online using arousal and valence scales. This separate experiment allowed us to select the most suitable stimuli later used in the primary fMRI study.

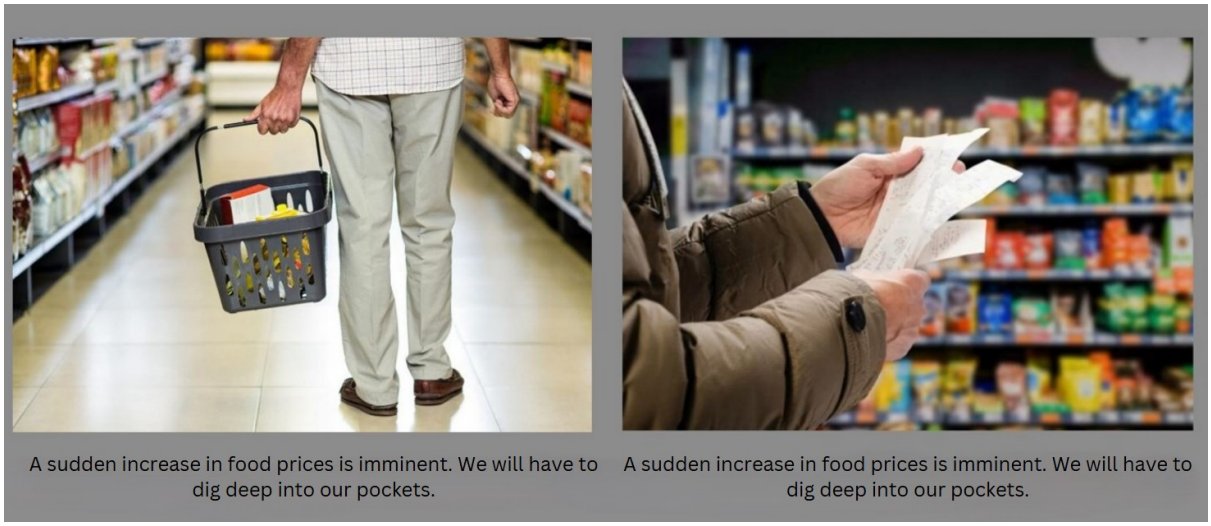

***Figure 5**: Examples of Concerning stimuli from two groups of visual stimuli.*

Disturbing visual stimuli included images of injured or dead bodies, blood, acts of violence, and natural disasters, accompanied by explanatory texts. These stimuli are intended to activate fast and unconscious stress responses, and they received the highest ratings for both arousal and negative valence.

In contrast, negative cognitive-controlled visual stimuli did not contain explicit images and were designed not to elicit automatic stress responses without contextual information. We designed the headers for these stimuli to provoke stress reactions, covering economic crises, housing unaffordability, disinformation, climate change, nuclear war, geopolitical risks, and political extremism. Participants rated these stimuli as having negative valence and moderately high arousal.

Neutral visual stimuli were intended to isolate the impact of content type on brain responses. These stimuli featured soft news with a neutral tone, such as information about local events, attractions, and scientific findings. They do not evoke strong emotional responses or induce worry. Participants rated them with slightly positive valence and moderate arousal.

3.2.3 Experiment Design

Before the experiment, participants completed an online questionnaire hosted on the National Institute of Mental Health's platform. The questionnaire covered demographic data, news media consumption (frequency, types, trust, impact), and assessments of self-reported personality traits and thinking styles. We conducted the experiment at the National Institute of Mental Health in the Czech Republic. Each day, the experiment was conducted with one or two participants, starting at 1:00 PM.

Before and after fMRI measurement, participants completed the Positive and Negative Affect Schedule (PANAS) (Watson et al., 1988) to assess their emotional state before entering the MRI scanner. We instructed participants to turn off or silence their mobile phones and remove all metallic objects. We informed participants about the safety procedures regarding the MRI environment. A pulse oximeter was attached to the participant's left index finger to record heart rate activity. A respiratory belt was placed around the participant's chest to monitor breathing patterns.

We used a block design for the fMRI study, alternating between blocks of different stimulus categories. We grouped each category into distinct blocks based on the specific topics of stimuli. Each fMRI session included 18 blocks of 5 images, with both blocks and the images within them presented randomly. Each stimulus was displayed for 8 seconds, followed by a black fixation cross on a grey background between the blocks, which we presented as a control condition for two seconds.

Psychological Intervention

Participants underwent two fMRI scanning sessions, with an intervention between them. Interventions that occurred after the first fMRI session involved training participants to either upregulate (UP) or downregulate (DOWN) their emotional responses to concerning media content. Participants were randomly divided into two groups for this purpose.

Psychologists arranged the training through a simulated online media platform designed to resemble a popular Czech news portal. During the training, participants read six short news articles on the economic crisis, housing unaffordability, disinformation, climate change, nuclear war, and geopolitical risks. After reading each article, they rated their emotional response using arousal and valence scales. The training included guided practice, supervised by psychologists, and independent practice, ensuring participants could effectively internalize and apply the strategies in preparation for the second fMRI session.

Participants employed a de-catastrophising technique commonly used in cognitive-behavioural therapy for the downregulation strategy.

For the upregulation strategy, participants used catastrophising questions to focus on negative potential outcomes. However, because this thesis focused on the differential processing of different types of negative stimuli, the effect of the intervention was not analysed.

Once the training was complete, participants read the remaining articles independently, applying their assigned cognitive strategy without direct supervision. They then underwent a third PANAS assessment to gauge their affective state post-training.

Following the intervention, participants had a second fMRI scanning session, during which they were exposed to a new set of stimuli that maintained thematic and visual consistency with the first set (fig. 2). Participants were instructed to apply their trained cognitive strategy while viewing the stimuli. After this session, a final PANAS assessment was conducted to evaluate their affective state.

The study concluded with a debriefing session for participants in the upregulation group. During this session, a psychologist emphasised that catastrophising is not recommended for everyday media consumption, addressed ethical considerations, and ensured participant well-being.

3.2.4 Data Acquisition

fMRI

We collected structural and functional neuroimaging data in this study using a Siemens Prisma 3T scanner equipped with a 64-channel head coil. The magnetic field's 3T (Tesla) strength balances signal strength and safety, making it ideal for detailed neuroimaging studies. The 64-channel head

coil enhances signal quality and allows faster image acquisition than coils with fewer channels, making it well-suited for capturing detailed neuroimaging data.

Visual stimuli were presented to participants through a mirror system attached to the head coil, projecting images from behind the participant. This setup ensures participants remain comfortably supine while viewing the stimuli, crucial for maintaining consistent and stable imaging conditions.

Functional images were acquired using a gradient-echo echo-planar imaging sequence, optimal for capturing blood oxygenation level-dependent (BOLD) signals. BOLD fMRI measures brain activity by detecting changes in blood flow; as neurons consume more oxygen, the local response is an increase in blood flow to these regions. This leads to a change in the oxygenated to deoxygenated haemoglobin ratio, which the scanner can detect (Fazal et al., 2022; Yen et al., 2023).

The functional imaging covered the entire brain with 46 slices per volume and a voxel size of 2 × 2 × 2 mm^3, providing comprehensive brain coverage. The voxel size of 2 × 2 × 2 mm^3 offers high spatial resolution, allowing for detailed brain activity mapping and ensuring that even small regions of interest are accurately captured.

The Field of View (FOV) was set at 208 mm to ensure comprehensive coverage of the entire brain during scanning. This dimension is critical for capturing the full extent of brain activity, particularly in studies involving complex cognitive tasks. The Repetition Time (TR) was 1,000 ms, which is relatively short and allows for high temporal resolution.

We chose an Echo Time (TE) of 30 ms to optimise the BOLD contrast, enhancing the sensitivity and specificity of the fMRI data. The TE influences the sensitivity of the sequence to detect changes in the ratio of oxygenated to deoxygenated haemoglobin, making 30 ms an appropriate choice for capturing robust BOLD signals. We set the flip angle at 52 degrees. The flip angle, which is the angle to which the net magnetisation vector is flipped during the radiofrequency pulse, affects the signal intensity and contrast. A 52-degree angle compromises between maximising signal and minimising saturation effects, ensuring clear and high-contrast images (J. Wang et al., 2006).

We set the bandwidth at 2,004 Hz/pixel. Bandwidth in MRI refers to the range of frequencies collected during the imaging process. A wider bandwidth reduces distortions and artefacts, resulting in more transparent images. This setting is critical in echo-planar imaging, which is prone to artefacts (Zou et al., 2005).

We used an Integrated Parallel Acquisition Technique factor of 2, which effectively doubles data acquisition speed using parallel imaging techniques. This reduces the overall scan time and minimises motion artefacts by shortening participants' time to remain still.

We recorded 1,029 brain volumes over approximately 29 minutes and 11 seconds. Recording many volumes provides a rich dataset with excellent temporal resolution, allowing for the detailed analysis of brain activity over time. We maintained the same gradient-echo echo-planar imaging parameters for the resting state sequence but increased the number of slices per volume to 60, enhancing spatial resolution and coverage. We recorded 500 brain volumes over about 8 minutes and 40 seconds to analyse functional connectivity during rest.

During functional and resting state sessions, participants were exposed to medial image-text presentations, and resting state data was collected. The second session also included high-resolution anatomical scans to provide detailed structural information for precise brain mapping and co-registration with functional data.

High-resolution anatomical scans included a 3D T1-weighted magnetisation-prepared rapid gradient-echo (MP-RAGE) sequence and a 3D T2-weighted Sampling Perfection with Application-optimised Contrasts using different flip angle Evolutions (SPACE) sequences. The MP-RAGE sequence yielded 240 sagittal slices with a $0.7 \times 0.7 \times 0.7$ mm³ resolution. This ultra-high resolution is essential for capturing fine anatomical details and accurate brain structure mapping. The sequence parameters were TR/TE/TI of 2,400/2.34/1,000 ms, a FOV of 224 mm, and a total acquisition time of 7 minutes and 40 seconds. These parameters ensure the images are detailed and high-quality, suitable for subsequent structural analyses.

The SPACE sequence also matched the MP-RAGE's resolution, with a TR/TE of 3,200/564 ms and a total acquisition time of 7 minutes and 55 seconds. The SPACE sequence provides excellent contrast for brain tissue, making it particularly useful for distinguishing between grey and white matter.

The advantages of these settings include high spatial and temporal resolution, comprehensive brain coverage, and minimised artefacts, all contributing to the detailed and accurate mapping of brain activity. However, a potential drawback is the long scan duration, which could lead to participant fatigue and increased movement artefacts. To mitigate this, we could consider using higher Integrated Parallel Acquisition Technique factors or reducing the number of recorded volumes in future studies to optimise scan time and enhance participant comfort without compromising data quality.

Pulse and Respiratory Activity Monitoring

We recorded pulse and respiratory activity using a pulse oximeter and a respiratory belt during the fMRI experiment. These devices are non-invasive, comfortable, and compatible with simultaneous MRI recording, ensuring minimal interference with the imaging process and maintaining participant comfort.

The pulse oximeter was placed on the participant's left index finger. This device measures blood oxygen levels and pulse rate by emitting light through the fingertip and detecting changes in light absorption, which correlate with blood volume changes. Continuous heart rate and oxygen saturation monitoring provide crucial real-time data on the cardiovascular responses to the media stimuli presented during the experiment.

The respiratory belt was placed around the participant's ribcage. It measures respiratory effort by detecting changes in the circumference of the chest during breathing. The belt operates pneumatically, where the expansion and contraction of the ribcage alter the volume inside a pneumatic balloon connected to a pressure sensor. These volume changes are converted into pressure changes, which the sensor records as electrical signals corresponding to the respiratory rate and pattern.

These specific sensors, a pulse oximeter and a pneumatic respiratory belt, are highly suitable for simultaneous MRI recording. They are designed to be MRI-compatible, meaning they do not contain metal components that could interfere with the magnetic field or produce artefacts in the images.

fMRI data analysis

The fMRI data were processed and analysed using the Statistical Parametric Mapping software (SPM12, version 12; available at the SPM12 website), operating within MATLAB R2016b (MathWorks). This software package is widely used in neuroimaging for its robust and comprehensive tools for analysing brain imaging data.

For each participant, the preprocessing of functional data involved several critical steps:

Realignment: This step corrects for head motion by aligning all the images in the time series to a reference image, typically the first image. This ensures that each voxel represents the same part of the brain across all scans.

Normalisation: The realigned images were transformed into a standardised space, typically based on the Montreal Neurological Institute (MNI) system. This spatial normalisation allows for comparing brain activity across participants by aligning individual brain anatomies to a standard template.

Spatial Smoothing: The normalised images were smoothed with a Gaussian kernel with a full width at a half-maximum of 6 × 6 × 6 mm. This step increases the signal-to-noise ratio and compensates for anatomical differences by averaging the signal over neighbouring voxels.

High-pass Filtering: The time series data were subjected to a high-pass filter with a cutoff period of 128 seconds to remove low-frequency noise and drifts that could confound the analysis.

After preprocessing, the data were subjected to a first-level analysis using a generalised linear model. The design matrix in this analysis incorporated factors modelling the hemodynamic response function for different experimental conditions: Neutral, Disturbing, and Concirning stimuli, and each contrasted against a control condition (fixation cross). This analysis generated contrast images, linear combinations of β-images (parameter estimates), representing the brain's response to each condition.

These first-level contrast images were then entered into a second-level, group-wise analysis to identify condition-specific regional brain responses. The second-level analysis used a full-factorial model, which accounted for the following factors:

Group: This factor had two levels, representing the data collected before and after the intervention (Pre- and Post-intervention).

Intervention Type: This factor also had two levels, distinguishing between participants trained in upregulating (enhancing) and downregulating (diminishing) their emotional responses.

Stimuli Type: This factor included Neutral, Disturbing, and Concerning.

Statistical significance in the second-level analysis was determined at a p-value threshold of ≤ 0.05, corrected for family-wise error across all grey matter voxels. This correction method accounts for multiple comparisons and controls the overall type I error rate, ensuring that the observed effects are unlikely to be due to chance.

Physiological data analysis

The physiological data processing for this study involved several meticulous steps to ensure accurate analysis and interpretation. This section outlines the procedures, providing a clear path for replicating the analysis. The data included measures of respiration (RESP) and heart rate (PULS) across two groups labelled "DOWN" and "UP" under different stimulus conditions. The primary objective of this processing phase was to prepare the data for statistical testing to determine whether there were significant differences in physiological responses across various stimulus types.

The initial dataset consisted of raw physiological measurements captured during the experiment. The data were divided into groups based on different experimental conditions: "DOWN" and "UP." Each group's dataset contained RESP and PULS measurements before and after applying various stimuli.

The first step involved removing any incomplete records to ensure the integrity of the analysis. Rows containing missing values were dropped from both datasets to avoid introducing bias or inaccuracies in subsequent analyses. This step resulted in two cleaned datasets, one for each group.

Before proceeding with the core analysis, an exploratory data analysis was conducted to understand the dataset's distribution, central tendencies, and variability. Descriptive statistics were computed for each physiological measure (RESP and PULS) in both groups, providing a summary of the data in terms of mean, standard deviation, minimum, and maximum values.

Visual tools such as pair plots were used to explore potential relationships between variables and detect anomalies or patterns in the data. These initial visualisations helped identify the data's non-normal distribution, which was confirmed through statistical tests.

The data distribution was examined using histograms and the Shapiro-Wilk test to determine the appropriate statistical tests for the analysis. The Shapiro-Wilk test results indicated that all measured variables (first and second RESP, first and second PULS) were non-normally distributed, with p-values significantly below the 0.05 threshold.

Given the non-normal distribution, a log transformation was applied to the data to normalise the distributions as much as possible. Log transformation is a standard technique to stabilise variance and make the data more suitable for statistical testing. However, the data remained non-normal even after transformation, necessitating non-parametric tests for further analysis.

The RESP and PULS values before and after the stimulus were combined for each participant to form aggregated measures. The average of the first and second RESP values was calculated to create a combined RESP score, and similarly, the PULS values were combined. These combined scores were further summed to create a total physiological score for each participant, representing their overall physiological response to the stimuli.

Given the non-normality of the data, non-parametric tests were employed. The Kruskal-Wallis test, a non-parametric alternative to ANOVA, was used to determine if there were any statistically significant differences in physiological responses across different stimulus types. The Kruskal-Wallis test was conducted separately for the "DOWN" and "UP" groups. The results of these tests indicated whether there were significant differences between the stimulus types in either group.

The data processing phase successfully prepared the physiological data for analysis by addressing missing data issues, non-normal distributions, and variance homogeneity. Despite extensive preprocessing and transformation efforts, the inherent non-normality of the data necessitated the use of non-parametric methods for statistical testing. This careful and thorough approach ensured the analysis was based on reliable and well-prepared data, allowing for accurate interpretation of the physiological responses to stimuli.

3.3 Results

3.3.1 Brain Data Analysis

We analyzed fMRI data to investigate the differential brain activation elicited by various types of visual stimuli: neutral, concerning, and disturbing for the pre-intervention session. This analysis focused on identifying brain regions that exhibited differential activation in response to these stimuli. The results revealed several key contrasts, highlighting significant differences in brain activation patterns across the various types of stimuli.

The table below (Table 1) summarizes the MNI coordinates and Z-scores for brain regions that showed significant activation differences. Corrections for multiple comparisons were applied using both Family-Wise Error and False Discovery Rate methods.

Table 1: Summary of significant brain activations during the fMRI experiment.

Stimuli Comparison	Region	MNI Coordinates	Z-score
Concerning > Neutral	Left ventral posterior cingulate and left dorsal Posterior Cingulate Cortex	(-6, -52, 32)	6.18
Disturbing > Neutral	Right fusiform gyrus	(54, -62, 2)	5.09
Disturbing > Neutral	Left angular gyrus	(-42, -60, 16)	4.44
Concerning > Disturbing	Left angular gyrus	(-42, -70, 46)	4.36
Disturbing > Concerning	Left visual association cortex	(-44, -76, 14)	5.64
Disturbing > Concerning	Right visual association cortex	(44, -66, 14)	5.21

Neural Activation of Concerning vs. Neutral Stimuli (Contrast 37)

We observed a significant difference in brain activation during the pre-intervention session compared to neutral stimuli (Fig. 6). Specifically, concerning stimuli elicited greater activation in the following regions:

- Left ventral and dorsal posterior cingulate cortex (MNI coordinates: x = −6, y = −52, z = 32; Z = 6.18)

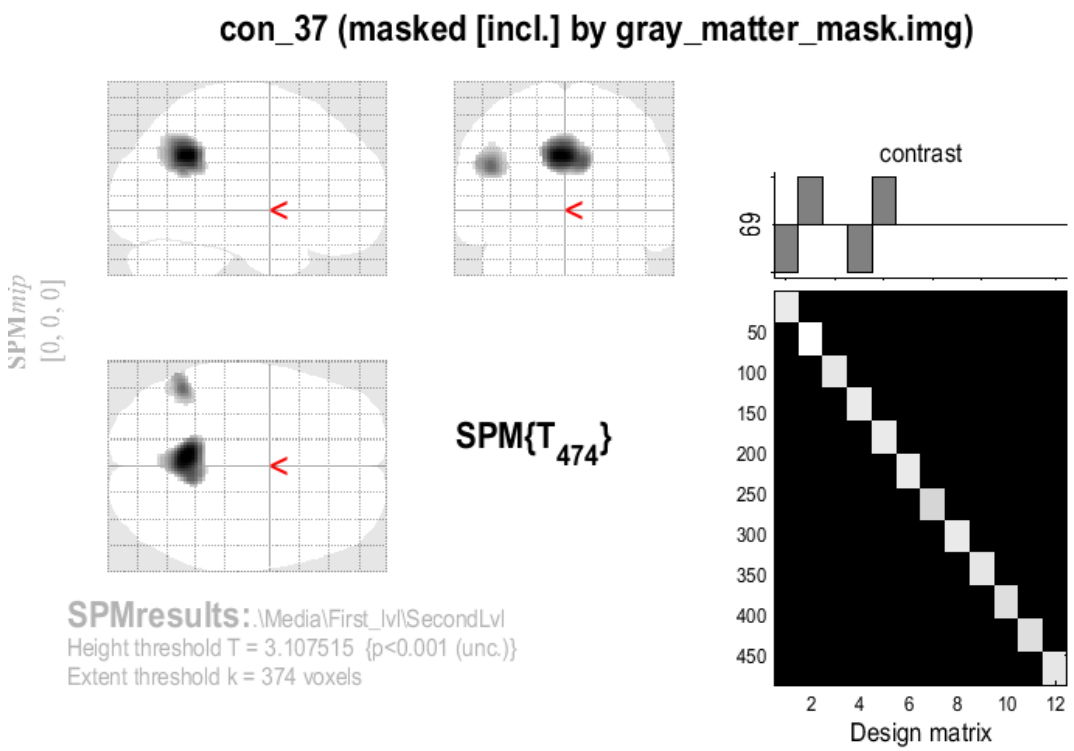

Figure 6. *Statistical Parametric Mapping (SPM) results for contrast 37 (Concerning vs. Neutral in pre-interventions session). The left panel shows the areas of significant activation in the brain, with the height threshold set at T=3.11 ($p < 0.001$ uncorrected) and an extent threshold of 374 voxels. The right panel displays the corresponding design matrix for the contrast.*

Neural Activation of Disturbing vs. Neutral Stimuli (Contrast 38)

In the comparison of disturbing against neutral stimuli, the analysis identified significant activations in two key regions(Fig. 7):

- Right fusiform gyrus (MNI coordinates: x = 54, y = −62, z = 2; Z = 5.09)
- Left angular gyrus (MNI coordinates: x = −42, y = −60, z = 16; Z = 4.44)

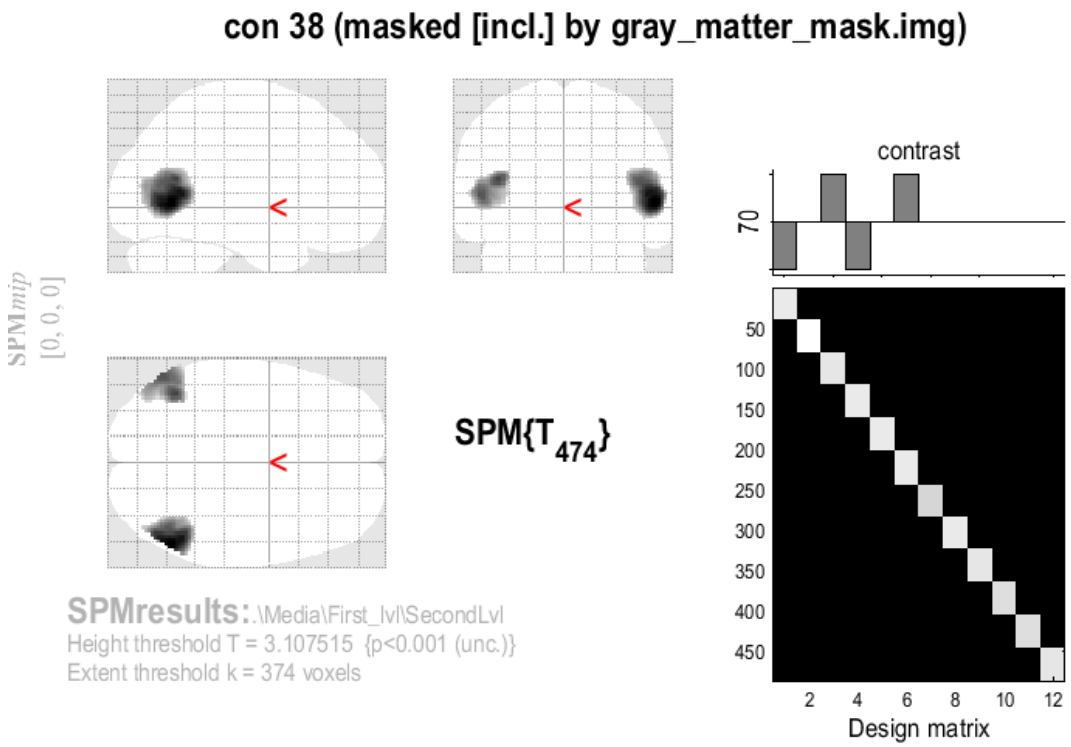

Figure 7. *Statistical Parametric Mapping (SPM) results for contrast 38 (Disturbing vs. Neutral in pre-interventions session). The left panel shows the areas of significant activation in the brain, with the height threshold set at T=3.11 ($p < 0.001$ uncorrected) and an extent threshold of 374 voxels. The right panel displays the corresponding design matrix for the contrast.*

Neural Activation of Concerning vs. Disturbing Stimuli (Contrast 41)

Concerning compared to disturbing stimuli elicited significantly greater activation in (Fig. 8):

- Left angular gyrus (MNI coordinates: x = −42, y = −70, z = 46; Z = 4.36)

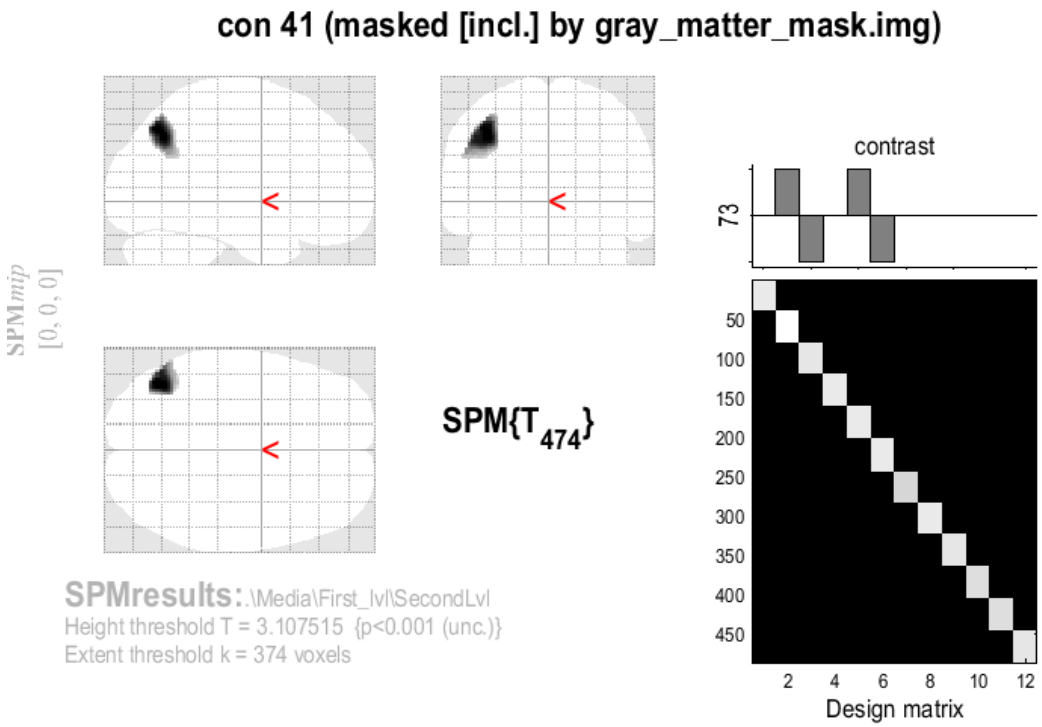

Figure 8. *Statistical Parametric Mapping (SPM) results for contrast 41 (Concerning vs. Disturbing) in pre-intervention session). The left panel shows the areas of significant activation in the brain, with the height threshold set at T=3.11 (p < 0.001 uncorrected) and an extent threshold of 374 voxels. The right panel displays the corresponding design matrix for the contrast.*

Neural Activation of Disturbing vs. Concerning Stimuli (Contrast 42)

Contrasting disturbing against concerning stimuli, we found significant changes in brain activation in the following regions (Fig. 9):

- Right visual association cortex (MNI coordinates: x = 44, y = −66, z = 14; Z = 5.21)
- Left visual association cortex (MNI coordinates: x = −44, y = −76, z = 14; Z = 5.64)

These visual association cortices showed heightened activation in response to concerning stimuli, indicating that such stimuli may engage more visual processing resources than disturbing stimuli.

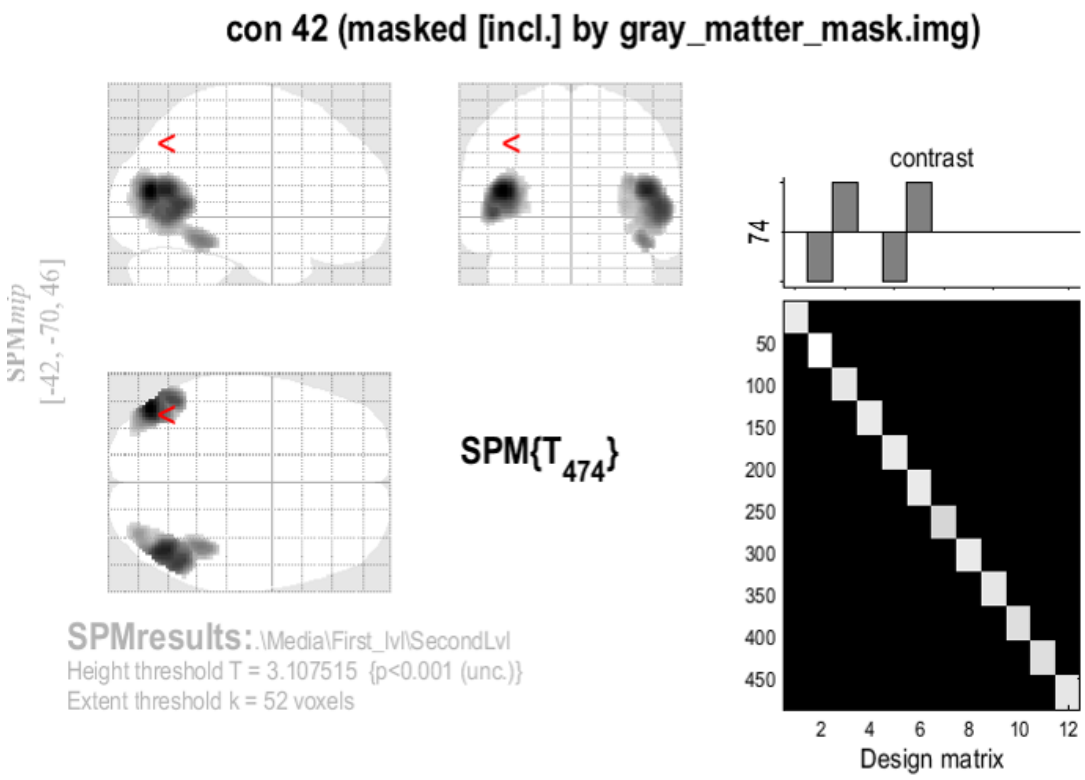

***Figure 9**: Statistical Parametric Mapping (SPM) results for contrast 42 (Disturbing vs. Concerning stimuli). The left panel shows the areas of significant activation in the brain, with the height threshold set at T = 3.107515 (p < 0.001 uncorrected) and an extent threshold of 52 voxels. The right panel displays the corresponding design matrix for the contrast.*

3.3.2 Physiological Data Analysis

We analyzed the physiological data focused on two primary measures, respiratory rate (RESP) and heart rate (PULS), across two intervention groups (DOWN and UP) under three stimulus conditions: Concerning, Neutral, and Disturbing. The goal was to determine whether there were significant differences in these physiological responses based on the type of stimuli, both before and after applying log transformations to address non-normality.

Initial Data Assessment:

The Shapiro-Wilk Test for Normality:

- The initial Shapiro-Wilk test revealed significant deviations from normality across all four measured variables during pre-intervention and post-intervention sessions for the DOWN group. Specifically, in the pre-intervention session, the following variables deviated from normal distribution: first session mean respiratory rate with a p-value of less than 0.001. First, the session mean pulse rate also has a p-value of less than 0.001. In the post-intervention session, we observed similar deviations in the variables of the second session mean respiratory rate and the second session mean pulse rate, both with p-values of less than 0.001.

- Similarly, the Shapiro-Wilk test indicated non-normal distributions in the same set of variables for the UP group. During the pre-intervention session, the first session's mean respiratory rate and the first session's mean pulse rate both had p-values of less than 0.001, indicating significant deviations from normality. These non-normal distributions persisted into the post-intervention session, where the second session mean respiratory rate and second session mean pulse rate also had p-values of less than 0.001.

Given the data's non-normal distribution, we applied log transformations to all variables. Post-transformation, the data approached normality, although some deviations persisted.

Log-Transformed Data Analysis:

The Levene's Test for Homogeneity of Variances:

- For the DOWN group, Levene's test indicated homogeneity of variances across the different stimulus types ($p = 0.694$), suggesting that variance was consistent across groups.
- The test similarly confirmed the homogeneity of variances ($p = 0.941$) in the UP group, further supporting the suitability of parametric tests on the log-transformed data.

Comparative Analysis of Stimulus Types:

Kruskal-Wallis Test (Non-parametric):

- The Kruskal-Wallis test for the DOWN group yielded a statistic of 0.0078 with a p-value of 0.9961, indicating no significant differences in the combined physiological scores across the stimulus types.
- For the UP group, the test resulted in a Kruskal-Wallis statistic of 0.1860 with a p-value of 0.9112, showing no significant differences between the stimulus conditions.

ANOVA (Parametric):

- The ANOVA for the DOWN group returned a statistic of 0.1242 with a p-value of 0.8833, consistent with the Kruskal-Wallis results, indicating no statistically significant differences in physiological responses across the stimulus types.
- Similarly, in the UP group, ANOVA yielded a statistic of 0.0427 with a p-value of 0.9583, reaffirming the lack of significant differences.

The box plots below (Fig. 10) illustrate the distribution of combined RESP and PULS scores by stimulus type for the DOWN and UP groups after outlier treatment. These plots confirm the statistical analysis, showing similar distributions across stimulus types with no significant variations.

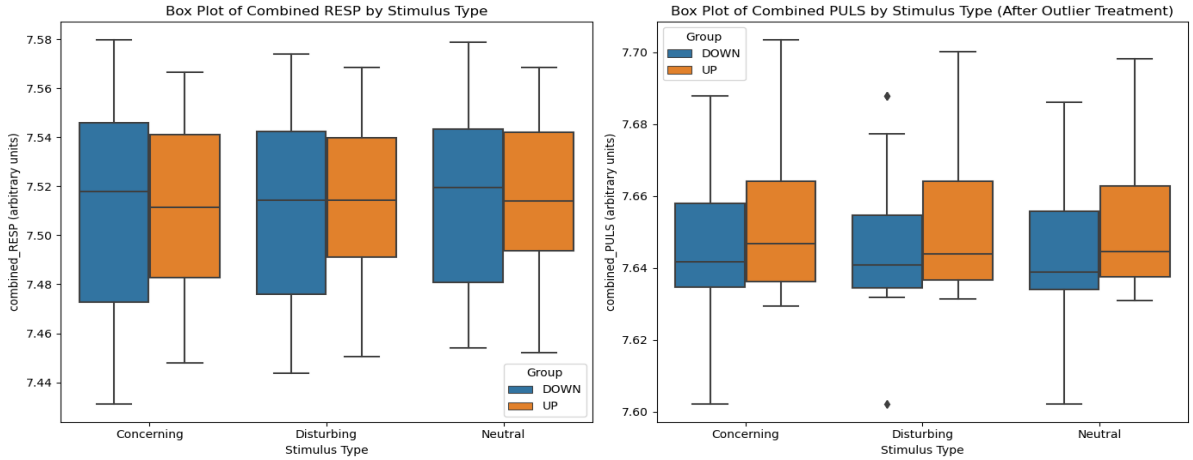

***Figure 10**: Combined box plots of respiratory rate (RESP) and pulse rate (PULS) in arbitrary units across different stimulus types (Concerning, Disturbing, Neutral) for DOWN and UP groups. The left plot shows RESP, while the right plot shows PULS after outlier treatment.*

The plots illustrated the median values, interquartile ranges, and the spread of the data, which further confirmed the statistical findings:

- Combined RESP Scores: There was a consistent overlap in the interquartile ranges and median values across stimulus types, with no significant outliers detected post-treatment.
- Combined PULS Scores: The box plots revealed that the distributions were uniform across stimulus types, with only minimal variations between the DOWN and UP groups.

In conclusion, the analysis demonstrated that all three stimulus types did not lead to statistically significant differences in physiological responses, as measured by RESP and PULS, in either the DOWN or UP groups. This was consistent across non-parametric and parametric tests, suggesting a robust outcome. The visual analysis further supported these findings, showing minimal variation in the physiological scores across different stimuli.

3.4 Discussion

The primary aim of this thesis was to investigate the neurophysiological and neuronal mechanisms underlying the processing of different stress stimuli. Specifically, we aimed to identify differences in brain and physiological responses to highly affective negative stimuli (DISTURBING) and those stimuli requiring greater cognitive control (CONCERNING).

We anticipated that processing negatively valenced stimuli, particularly concerning and disturbing types, would engage key brain regions traditionally associated with emotional processing and regulation, such as the amygdala, prefrontal cortex, insula, and anterior cingulate cortex. These regions are well-documented in the literature for their roles in managing emotional responses, detecting threats, and regulating cognitive control during stress (Dixon et al., 2017; Malena Mielke et al., 2021; Rigney et al., 2017). Specifically, the amygdala is known for its involvement in fear and emotional salience (H. Toyoda et al., 2011), the PFC for its role in cognitive control and emotion regulation (Paschke et al., 2016), the insula for interoceptive awareness and emotional experience, and the ACC for integrating emotional and cognitive processing (Simmons et al., 2012).

However, the fMRI data revealed an unexpected pattern of neural activation that did not align with these anticipated regions.

Neural Responses to Stimuli

The posterior cingulate cortex (PCC) was significantly activated when comparing CONCERNING stimuli to neutral stimuli. This region primarily involves self-referential thought and emotional regulation (Sinha et al., 2004). The activation of the PCC suggests that CONCERNING stimuli may have required more cognitive evaluation, particularly in relation to the self, rather than being processed through immediate emotional responses. This finding aligns with the Interoceptive Predictive Coding model (Hugo D. Critchley et al., 2018), where the brain continuously interprets incoming sensory information, including a cognitive appraisal of stimuli, to guide behaviour and maintain homeostasis. The presence of text likely intensified the need for cognitive processing, leading to this unexpected activation in the PCC.

The angular gyrus showed significant activation in two key contrasts: DISTURBING stimuli compared to neutral stimuli and CONCERNING stimuli compared to DISTURBING stimuli. This region is associated with cognitive processes such as attention, memory retrieval, and information integration (Grob et al., 2024; Horwitz et al., 1998; Ramanan et al., 2017). The heightened activation suggests that both CONCERNING and DISTURBING stimuli, which were initially hypothesized to be processed more automatically, may have required substantial cognitive evaluation. This supports the Affective Signalling Hypothesis, which posits that negative affective cues can enhance cognitive

control by signalling potential threats, thus preparing the individual for more adaptive responses (Dignath et al., 2020; Miklos Bognar et al., 2023). The cognitive complexity introduced by the text might have led to the unexpected involvement of the angular gyrus.

The fusiform gyrus was notably activated when DISTURBING stimuli were compared to neutral stimuli. This region critically processes complex visual stimuli, such as facial recognition (Weiner & Zilles, 2016). The involvement of the fusiform gyrus suggests that DISTURBING stimuli require more detailed visual processing, possibly due to their emotional content and visual complexity. This finding is consistent with the Interoceptive Predictive Coding model (Hugo D. Critchley et al., 2018), where the brain integrates visual information with emotional responses to guide behaviour.

Activation in the visual association cortex (VAC) was observed when DISTURBING stimuli were compared to CONCERNING stimuli. The VAC is known for processing complex or ambiguous visual stimuli (Rosen et al., 2018). However, its involvement here may also indicate its role in prioritizing emotionally significant stimuli. This aligns with the Affective signalling hypothesis, where the VAC collaborates with the amygdala and PFC to enhance cognitive control, particularly in response to emotionally charged stimuli (Dignath et al., 2020; Miklos Bognar et al., 2023). The strong engagement of VAC suggests that DISTURBING stimuli captured attention more effectively, drawing on cognitive and perceptual resources to a greater extent than CONCERNING stimuli.

Physiological Responses to Stimuli

Despite our expectations, the heart and respiratory rates data did not reveal significant differences across the stimulus types. This uniformity might be attributed to the cognitive demands introduced by the accompanying text, which likely required significant semantic processing and engaged cognitive pathways rather than eliciting physiological solid responses. The Interoceptive Predictive Coding model could help explain this, as the brain's focus on cognitive interpretation might have moderated physiological arousal, leading to uniform responses across stimuli (Hugo D. Critchley et al., 2018). The uniformity in physiological responses observed might also be related to the influence of individual differences in personality traits, such as neuroticism and extraversion, as well as the emotion regulation strategies employed, which were not accounted for in this initial analysis. For instance, cognitive reappraisal is associated with more adaptive physiological responses, such as lower heart rate and higher heart rate variability (Denson et al., 2011; Troy et al., 2019). Conversely, expressive suppression might have led to increased physiological arousal and could have masked differences in responses to the different stimuli (Pizzie & Kraemer, 2021). Additionally, the functional coupling between the ventrolateral prefrontal cortex and the amygdala, which modulates emotional responses, might not have been strongly activated, contributing to the lack of differentiation in heart rate and respiratory patterns across stimuli (Morawetz et al., 2016).

Influence of Emotion Regulation Strategies

The observed outcomes likely reflect the impact of different emotion regulation strategies that participants may have employed. If participants predominantly used cognitive reappraisal, where they reinterpret the meaning of a stressor to alter its emotional impact, this could have led to more uniform physiological responses (Volokhov & Demaree, 2010). However, if expressive suppression was more commonly employed, it might have masked physiological differences that could otherwise have been observed (Pizzie & Kraemer, 2021). This highlights the importance of assessing emotion regulation strategies in future research better to understand their impact on neural and physiological outcomes.

Influence of Early Life Experiences and Genetic Predispositions

The uniformity in physiological responses might also be influenced by individual differences shaped by early life experiences and genetic predispositions. For instance, early adversity or prenatal stress can significantly shape an individual's stress response system (Pizzie & Kraemer, 2021). Genetic variations, such as those in the serotonin transporter gene (5-HTTLPR), could predispose individuals to specific stress reactivity patterns (Plieger et al., 2017). These factors suggest that a more personalised approach, considering genetic and environmental influences, is necessary to fully understand the variability in stress responses observed in our study.

Sensory Processing Differences

Individual differences in sensory processing likely influenced how participants responded to the stimuli (Caitlin Bloomer et al., 2014; Gatti et al., 2018). Given the reliance on text-visual stimuli in this study, it is possible that the stimuli were not equally effective across all participants. Future studies could benefit from exploring multimodal stimuli that combine visual, auditory, and tactile elements to create more engaging and stress-inducing scenarios that better reflect real-world experiences. The nature of the stimuli used in this study might have been more cognitively demanding than emotionally salient, which is supported by the increased activation in regions like the PCC and angular gyrus.

Methodological Considerations

Methodological issues such as habituation and order effects could have influenced the results. Repeated exposure to similar stimuli might have led to habituation, reducing the stress response over time (Loeffler et al., 2016). Additionally, the fMRI environment could have introduced stress, potentially confounding the results. This underscores the need for careful consideration of such factors in future studies.

Ecological Validity and Future Directions

While laboratory settings are valuable for isolating specific variables, they limit the ecological validity of stress research. The artificial and predictable nature of lab stressors contrasts sharply with real-world stressors, which are multifaceted and unpredictable. Ecological Momentary Assessment methods and virtual reality, as demonstrated in the meta-analysis by (Coban et al., 2022), present paradigms to address this limitation by creating more immersive and realistic stress simulations. Additionally, (Weber et al., 2022) provide a systematic review of physiological reactions to acute stressors and subjective stress during daily life, highlighting the effectiveness of Ecological Momentary Assessment in capturing real-world stress responses. This approach would enhance the ecological validity of lab-based research, potentially leading to more significant and generalizable findings.

4. Conclusion

This thesis explored the neurophysiological and neuronal mechanisms involved in processing different types of stress stimuli, focusing on distinguishing between more automatic versus rather cognitively controlled responses. While we hypothesized that negatively valenced stimuli, mainly those disturbing and concerning, would engage key brain regions traditionally associated with emotional processing and regulation, such as the amygdala, prefrontal cortex, insula, and anterior cingulate cortex, the results presented a more complex picture.

The fMRI data revealed significant activations in the posterior cingulate cortex, angular gyrus, fusiform gyrus, and visual association cortices rather than the expected regions. These findings suggest that the stimuli employed in the study, which included visual and textual components, likely engaged cognitive processing mechanisms more than purely emotional ones. The involvement of these regions points to the role of cognitive evaluation, self-referential processing, and detailed visual processing in response to stress stimuli, challenging traditional models that primarily focus on the amygdala and prefrontal cortex.

The absence of significant physiological differences across the different types of stimuli further underscores the influence of cognitive processing in this context. It is possible that the cognitive demands introduced by the textual content led to a more uniform physiological response, as the brain's focus on semantic interpretation might have moderated the expected variations in heart and respiratory rates.

The results suggest that cognitive and sensory processing mechanisms might play a more significant role in stress responses than previously thought, especially in contexts where stimuli are complex and require substantial cognitive evaluation. This finding challenges traditional models that emphasize the amygdala and prefrontal cortex as the primary regions involved in stress processing.

The engagement of regions like the posterior cingulate cortex and angular gyrus underscores the importance of cognitive appraisal and self-referential processing in stress responses. Future research should investigate how these cognitive processes interact with emotional regulation mechanisms during stress. Understanding the cognitive components of stress processing could inform the development of more personalized stress management strategies.

The uniform physiological responses observed across stimuli types highlight the importance of considering cognitive demands and individual differences in future research. Additionally, the artificial and controlled laboratory setting might not fully capture the nuances of real-world stressors, suggesting a need for more ecologically valid methodologies.

Overall, this study contributes to a deeper understanding of the complexity of stress responses, emphasizing the interplay between cognitive and sensory processing alongside emotional regulation. Future research should continue to explore these interactions, particularly in more ecologically valid contexts, to better understand the full scope of stress processing mechanisms and their implications for psychological interventions and stress management.

5. References

Aldhafeeri, F. M., Mackenzie, I., Kay, T., Alghamdi, J., & Sluming, V. (2012). Regional brain responses to pleasant and unpleasant IAPS pictures: Different networks. *Neuroscience Letters*, *512*(2), 94–98. https://doi.org/10.1016/j.neulet.2012.01.064

Amanda W. Calkins, Christen M. Deveney, Meara L. Weitzman, Bridget A. Hearon, Greg J. Siegle, & Michael Otto. (2011). The effects of prior cognitive control task exposure on responses to emotional tasks in healthy participants. *Behavioural and Cognitive Psychotherapy*, *39*(2), 205–220. https://doi.org/10.1017/S1352465810000652

Anderson, A. K., & Phelps, E. A. (2001). Lesions of the human amygdala impair enhanced perception of emotionally salient events. *Nature*, *411*(6835), 305–309. https://doi.org/10.1038/35077083

Anderson, M. C., & Green, C. (2001). Suppressing unwanted memories by executive control. *Nature*, *410*(6826), 366–369. https://doi.org/10.1038/35066572

Anthony Burgos-Robles, Eyal Y. Kimchi, Eyal Y. Kimchi, Ehsan M. Izadmehr, Mary Jane Porzenheim, William A Ramos-Guasp, Edward H. Nieh, Ada C. Felix-Ortiz, Praneeth Namburi, Christopher A. Leppla, Kara N. Presbrey, Kavitha K. Anandalingam, Pablo A Pagan-Rivera, Melodi Anahtar, Anna Beyeler, & Kay M. Tye. (2017). Amygdala Inputs to Prefrontal Cortex Guide Behavior Amid Conflicting Cues of Reward and Punishment. *Nature Neuroscience*, *20*(6), 824–835. https://doi.org/10.1038/NN.4553

Appelhans, B. M., & Luecken, L. J. (2006). Heart Rate Variability as an Index of Regulated Emotional Responding. *Review of General Psychology*, *10*(3), 229–240. https://doi.org/10.1037/1089-2680.10.3.229

Arsalan, A., Anwar, S. M., & Majid, M. (2022, January). *Human stress assessment: A comprehensive review of methods using wearable sensors and non-wearable techniques*. https://doi.org/10.48550/arxiv.2202.03033

Ashokan, A., Hegde, A., & Mitra, R. (2016). Short-term environmental enrichment is sufficient to counter stress-induced anxiety and associated structural and molecular plasticity in basolateral amygdala. *Elsevier BV*, *69*, 189–196. https://doi.org/10.1016/j.psyneuen.2016.04.009

Ashworth, E., Brooks, S. J., & Schiöth, H. B. (2021). Neural activation of anxiety and depression in children and young people: A systematic meta-analysis of fMRI studies. *Psychiatry Research: Neuroimaging*, *311*, 111272. https://doi.org/10.1016/j.pscychresns.2021.111272

Asim H. Gazi, Matthew T. Wittbrodt, Anna B. Harrison, Srirakshaa Sundararaj, Nil Z. Gurel, Jonathon A. Nye, Amit J. Shah, Viola Vaccarino, J. Douglas Bremner, & Omer T. Inan. (2021). Robust Estimation of Respiratory Variability Uncovers Correlates of Limbic Brain Activity and Transcutaneous Cervical Vagus Nerve Stimulation in the Context of Traumatic Stress. *IEEE Transactions on Biomedical Engineering*, 1–1. https://doi.org/10.1109/TBME.2021.3108135

Atilano-Barbosa, D., Paredes, L., Enciso, F., Pasaye, E. H., & Mercadillo, R. E. (2022). Moral emotions when reading quotidian circumstances in contexts of violence: An fMRI study. *Adaptive Behavior*, *30*(2), 119–145. https://doi.org/10.1177/1059712320939346

Bali, A., & Jaggi, A. S. (2015). Preclinical experimental stress studies: Protocols, assessment and comparison. *Elsevier BV*, *746*, 282–292. https://doi.org/10.1016/j.ejphar.2014.10.017

Barrett, L. F., & Simmons, W. K. (2015). Interoceptive Predictions in the Brain. *Nature Reviews Neuroscience*, *16*(7), 419–429. https://doi.org/10.1038/nrn3950

Ben-Zur, H., Gil, S., & Shamshins, Y. (2012). The relationship between exposure to terror through the media, coping strategies and resources, and distress and secondary traumatization. *International Journal of Stress Management*, *19*(2), 132–150. https://doi.org/10.1037/a0027864

Berto, R. (2014). The role of nature in coping with psycho-physiological stress: A literature review on restorativeness. *Multidisciplinary Digital Publishing Institute*, *4*(4), 394–409. https://doi.org/10.3390/bs4040394

Bodas, M., Siman-Tov, M., Peleg, K., & Solomon, Z. (2015). Anxiety-Inducing Media: The Effect of Constant News Broadcasting on the Well-Being of Israeli Television Viewers. *Psychiatry*, *78*(3), 265–276. https://doi.org/10.1080/00332747.2015.1069658

Brehl, A.-K., Kohn, N., Schene, A. H., & Fernández, G. (2020). A Mechanistic Model for Individualised Treatment of Anxiety Disorders Based on Predictive Neural Biomarkers. *Psychological Medicine*, *50*(5), 727–736. https://doi.org/10.1017/s0033291720000410

Burks, N., & Martin, B. (1985). Everyday Problems and Life Change Events: Ongoing versus Acute Sources of Stress. *Journal of Human Stress*, *11*(1), 27–35. https://doi.org/10.1080/0097840X.1985.9936735

Caetano, I., Amorim, L., Castanho, T. C., Coelho, A., Ferreira, S., Portugal-Nunes, C., Soares, J. M., Gonçalves, N., Sousa, R., Reis, J., Lima, C., Marques, P., Moreira, P. S., Rodrigues, A. J., Santos, N. C., Morgado, P., Esteves, M., Magalhães, R., Picó-Pérez, M., & Sousa, N. (2022). Association of amygdala size with stress perception: Findings of a transversal study across the lifespan. *European Journal of Neuroscience*, *56*(8), 5287–5298. https://doi.org/10.1111/ejn.15809

Caitlin Bloomer, Crystal Hitt, Douglas M. Olson, & Colin Wruck. (2014). *Stress responses due to application of audio or visual stimuli*.

Campbell, J., & Ehlert, U. (2012). Acute psychosocial stress: Does the emotional stress response correspond with physiological responses? *Psychoneuroendocrinology*, *37*(8), 1111–1134. https://doi.org/10.1016/j.psyneuen.2011.12.010

Cannon, W. B. (1915). *Bodily changes in pain, hunger, fear and rage: An account of recent researches into the function of emotional excitement* (pp. xiii, 311). D Appleton & Company. https://doi.org/10.1037/10013-000

Caspi, A., Bolger, N., & Eckenrode, J. (1987). Linking person and context in the daily stress process. *Journal of Personality and Social Psychology*, *52*(1), 184.

Chen, Y., Peng, H., Zhuang, K., Xie, W., Li, C., Xue, J., Chen, M., Huang, X., Zou, T., Wang, Y., Can, D., Li, H., Yuan, T., & Zhang, J. (2023, February). *A cingulate-hippocampal circuit mediates early depressive symptoms in Alzheimer's disease*. https://doi.org/10.1101/2023.02.07.527491

Cloutman, L. L., Binney, R. J., Drakesmith, M., Parker, G. J. M., & Lambon Ralph, M. A. (2012). The variation of function across the human insula mirrors its patterns of structural connectivity: Evidence from in vivo probabilistic tractography. *NeuroImage*, *59*(4), 3514–3521. https://doi.org/10.1016/j.neuroimage.2011.11.016

Coban, M., Bolat, Y. I., & Goksu, I. (2022). The potential of immersive virtual reality to enhance learning: A meta-analysis. *Educational Research Review*, *36*, 100452. https://doi.org/10.1016/j.edurev.2022.100452

Cohen, S., Janicki-Deverts, D., & Miller, G. E. (2007). Psychological Stress and Disease. *JAMA*, *298*(14), 1685–1687. https://doi.org/10.1001/jama.298.14.1685

Cvijetić, S., Keser, I., Jurasović, J., Orct, T., Babić, Ž., Boschiero, D., & Ilich, J. Z. (2022). Diurnal salivary cortisol in relation to body composition and heart rate variability in young adults. *Frontiers in Endocrinology*. https://doi.org/10.3389/fendo.2022.831831

Cynthia D. Fast & John P. McGann. (2017). Amygdalar Gating of Early Sensory Processing through Interactions with Locus Coeruleus. *The Journal of Neuroscience*, *37*(11), 3085–3101. https://doi.org/10.1523/JNEUROSCI.2797-16.2017

Davern, P. J., & Head, G. A. (2011). Role of the Medial Amygdala in Mediating Responses to Aversive Stimuli Leading to Hypertension. *Clinical and Experimental Pharmacology and Physiology*, *38*(2), 136–143. https://doi.org/10.1111/j.1440-1681.2010.05413.x

Delaleu, N., Nguyen, C. Q., Peck, A. B., & Jönsson, R. (2011). *Sjögren's syndrome: Studying the disease in mice*. *13*(3), 217–217.

Denson, T. F., Grisham, J. R., & Moulds, M. L. (2011). Cognitive reappraisal increases heart rate variability in response to an anger provocation. *Motivation and Emotion*, *35*(1), 14–22. https://doi.org/10.1007/s11031-011-9201-5

Derek Schaeuble, Amy E.B. Packard, Jessica M. McKlveen, Rachel Morano, Sarah M. Fourman, Brittany L. Smith, Jessie R. Scheimann, Ben A. Packard, Steven P. Wilson, Jeanne James, David Y. Hui, Yvonne M. Ulrich-Lai, James P. Herman, & Brent Myers. (2019). Prefrontal Cortex Regulates Chronic Stress-Induced Cardiovascular Susceptibility. *Journal of the American Heart Association*, *8*(24). https://doi.org/10.1161/JAHA.119.014451

Dick, A. S., Silva, K., Gonzalez, R., Sutherland, M. T., Laird, A. R., Thompson, W. K., Tapert, S. F., Squeglia, L. M., Gray, K. M., Nixon, S. J., Cottler, L. B., La Greca, A. M., Gurwitch, R. H., & Comer, J. S. (2021). Neural vulnerability and hurricane-related media are associated with post-traumatic stress in youth. *Nature Human Behaviour*, *5*(11), 1578–1589. https://doi.org/10.1038/s41562-021-01216-3

Diener, S. J., Nees, F., Wessa, M., Wirtz, G., Frommberger, U., Penga, T., Ruttorf, M., Ruf, M., Schmahl, C., & Flor, H. (2016). *Reduced amygdala responsivity during conditioning to trauma-related stimuli in posttraumatic stress disorder. 53*(10), 1460–1471.

Dignath, D., Eder, A. B., Steinhauser, M., & Kiesel, A. (2020). Conflict Monitoring and the Affective-Signaling Hypothesis—An Integrative Review. *Psychonomic Bulletin & Review*, *27*(2), 193–216. https://doi.org/10.3758/s13423-019-01668-9

DiMaggio, C., & Galea, S. (2006). The behavioral consequences of terrorism: A meta-analysis. *Academic Emergency Medicine: Official Journal of the Society for Academic Emergency Medicine*, *13*(5), 559–566. https://doi.org/10.1197/j.aem.2005.11.083

Dixon, M. L., Thiruchselvam, R., Todd, R., & Christoff, K. (2017). Emotion and the prefrontal cortex: An integrative review. *Psychological Bulletin*, *143*(10), 1033–1081. https://doi.org/10.1037/bul0000096

Doussard-Roosevelt, J. A., Montgomery, L. A., & Porges, S. W. (2003). Short-term stability of physiological measures in kindergarten children: Respiratory sinus arrhythmia, heart period, and cortisol. *Developmental Psychobiology*, *43*(3), 230–242. https://doi.org/10.1002/dev.10136

Emi Yamano, Akira Ishii, Masaaki Tanaka, Shusaku Nomura, & Yasuyoshi Watanabe. (2016). Neural basis of individual differences in the response to mental stress: A magnetoencephalography study. *Brain Imaging and Behavior*, *10*(4), 1160–1171. https://doi.org/10.1007/S11682-015-9479-0

Enneking, V., Dzvonyar, F., Dück, K., Dohm, K., Grotegerd, D., Förster, K., Meinert, S., Lemke, H., Klug, M., Waltemate, L., Goltermann, J., Hülsmann, C., Borgers, T., Böhnlein, J., Sindermann, L., Richter, M., Leehr, E. J., Repple, J., Opel, N., … Redlich, R. (2020). Brain functional effects of electroconvulsive therapy during emotional processing in major depressive disorder. *Elsevier BV*, *13*(4), 1051–1058. https://doi.org/10.1016/j.brs.2020.03.018

Estelle Blons, Laurent M. Arsac, Pierre Gilfriche, Heather McLeod, Véronique Lespinet-Najib, Eric Grivel, & Veronique Deschodt-Arsac. (2019). Alterations in heart-brain interactions under mild stress during a cognitive task are reflected in entropy of heart rate dynamics. *Scientific Reports*, *9*(1), 18190. https://doi.org/10.1038/S41598-019-54547-7

Eunjoo Kim & Jeansok J. Kim. (2019). Amygdala, Medial Prefrontal Cortex and Glucocorticoid Interactions Produce Stress-Like Effects on Memory. *Frontiers in Behavioral Neuroscience*, *13*, 210–210. https://doi.org/10.3389/FNBEH.2019.00210

Fazal, Z., Gomez, D. E. P., Llera, A., Marques, J. P. R. F., Beck, T., Poser, B. A., & Norris, D. G. (2022). A comparison of multiband and multiband multiecho gradient-echo EPI for task fMRI at 3 T. *Human Brain Mapping*, *44*(1), 82–93. https://doi.org/10.1002/hbm.26081

Fevre, M. L., Matheny, J., & Kolt, G. S. (2003). Eustress, Distress, and Interpretation in Occupational Stress. *Journal of Managerial Psychology*, *18*(7), 726–744. https://doi.org/10.1108/02683940310502412

Fossati, P. (2012). Neural correlates of emotion processing: From emotional to social brain. *European Neuropsychopharmacology*, *22*, S487–S491. https://doi.org/10.1016/j.euroneuro.2012.07.008

Frot, M., Mauguière, F., & Garcia-Larrea, L. (2022). Insular dichotomy in the implicit detection of emotions in human faces. *Oxford University Press*, *32*(19), 4215–4228. https://doi.org/10.1093/cercor/bhab477

G. Kuyper, A. M., & Honig, A. (2008). Treatment of post-myocardial infarction depressive disorder. *Expert Review of Neurotherapeutics*. https://doi.org/10.1586/14737175.8.7.1115

Garfin, D. R., Poulin, M. J., Blum, S., & Silver, R. C. (2018). Aftermath of Terror: A Nationwide Longitudinal Study of Posttraumatic Stress and Worry Across the Decade Following the September 11, 2001 Terrorist Attacks. *Journal of Traumatic Stress*, *31*(1), 146–156. https://doi.org/10.1002/jts.22262

Gatti, E., Calzolari, E., Maggioni, E., & Obrist, M. (2018). Emotional ratings and skin conductance response to visual, auditory and haptic stimuli. *Scientific Data*, *5*(1), 180120. https://doi.org/10.1038/sdata.2018.120

Giles, G. E., Cantelon, J. A., Navarro, E., & Brunyé, T. T. (2024). State and trait predictors of cognitive responses to acute stress and uncertainty. *Military Psychology: The Official Journal of the Division of Military Psychology, American Psychological Association*, 1–8. https://doi.org/10.1080/08995605.2024.2370708

Giorgos Giannakakis, Dimitris Grigoriadis, Katerina Giannakaki, Olympia Simantiraki, Alexandros Roniotis, & Manolis Tsiknakis. (2019). Review on psychological stress detection using biosignals. *IEEE Transactions on Affective Computing*, 1–1. https://doi.org/10.1109/TAFFC.2019.2927337

Girotti, M., Carreno, F. R., & Morilak, D. A. (2022). Role of Orbitofrontal Cortex and Differential Effects of Acute and Chronic Stress on Motor Impulsivity Measured With 1-Choice Serial Reaction Time Test in Male Rats. *International Journal of Neuropsychopharmacology*, *25*(12), 1026–1036. https://doi.org/10.1093/ijnp/pyac062

Goldin, P. R., McRae, K., Ramel, W., & Gross, J. J. (2008). The neural bases of emotion regulation: Reappraisal and suppression of negative emotion. *Biological Psychiatry*, *63*(6), 577–586. https://doi.org/10.1016/j.biopsych.2007.05.031

Goldring, M. (2022). *A Componential Model of Stress Reactivity in Daily Life* [Columbia University]. https://doi.org/10.7916/7dz8-cw18

Goldstein, D. S. (2010). Adrenal responses to stress. *Springer Science+Business Media*, *30*(8), 1433–1440. https://doi.org/10.1007/s10571-010-9606-9

Gorelick, P. B., Scuteri, A., Black, S. E., Decarli, C., Greenberg, S. M., Iadecola, C., Launer, L. J., Laurent, S., Lopez, O. L., Nyenhuis, D., Petersen, R. C., Schneider, J. A., Tzourio, C., Arnett, D. K., Bennett, D. A., Chui, H. C., Higashida, R. T., Lindquist, R., Nilsson, P. M., … American Heart Association Stroke Council, Council on Epidemiology and Prevention, Council on Cardiovascular Nursing, Council on Cardiovascular Radiology and Intervention, and Council on Cardiovascular Surgery and Anesthesia. (2011). Vascular contributions to cognitive impairment and dementia: A statement for healthcare professionals from the american heart association/american stroke association. *Stroke*, *42*(9), 2672–2713. https://doi.org/10.1161/STR.0b013e3182299496

Greco, J. A., & Liberzon, I. (2016). Neuroimaging of Fear-Associated Learning. *Neuropsychopharmacology*, *41*(1), 320–334. https://doi.org/10.1038/npp.2015.255

Grob, A.-M., Heinbockel, H., Milivojevic, B., Doeller, C. F., & Schwabe, L. (2024). Causal Role of the Angular Gyrus in Insight-Driven Memory Reconfiguration. *Elife*, *12*. https://doi.org/10.7554/elife.91033

Hackett, R. (2016). *The role of psychosocial wellbeing and biological stress processes in linking type II diabetes and cardiovascular disease*.

Heilbronner, S. R., & Hayden, B. Y. (2016). Dorsal Anterior Cingulate Cortex: A Bottom-Up View. *Annual Review of Neuroscience*, *39*, 149–170. https://doi.org/10.1146/annurev-neuro-070815-013952

Heilman, K. J., Connolly, S. D., Padilla, W. O., Wrzosek, M., Graczyk, P. A., & Porges, S. W. (2012). Sluggish Vagal Brake Reactivity to Physical Exercise Challenge in Children With Selective Mutism. *Development and Psychopathology*, *24*(1), 241–250. https://doi.org/10.1017/s0954579411000800

Hendrix, S. (2008). Neuroimmune Communication in Skin: Far From Peripheral. *Journal of Investigative Dermatology*, *128*(2), 260–261. https://doi.org/10.1038/sj.jid.5701171

Henk van Steenbergen. (2015). *Affective Modulation of Cognitive Control: A Biobehavioral Perspective*. 89–107. https://doi.org/10.1007/978-1-4939-1236-0_7

Hinds, J. A., & Sánchez, E. R. (2022). The Role of the Hypothalamus–Pituitary–Adrenal (HPA) Axis in Test-Induced Anxiety: Assessments, Physiological Responses, and Molecular Details. *Stresses*, *2*(1), 146–155. https://doi.org/10.3390/stresses2010011

Ho, S. S., Konrath, S., Brown, S., & Swain, J. E. (2014). Empathy and stress related neural responses in maternal decision making. *Frontiers in Neuroscience*, *8*. https://doi.org/10.3389/fnins.2014.00152

Holman, E. A., Garfin, D. R., Lubens, P., & Silver, R. C. (2020). Media Exposure to Collective Trauma, Mental Health, and Functioning: Does It Matter What You See? *Clinical Psychological Science*, *8*(1), 111–124. https://doi.org/10.1177/2167702619858300

Hooker, C. I., Germine, L. T., Knight, R. T., & D'Esposito, M. (2006). Amygdala response to facial expressions reflects emotional learning. *The Journal of Neuroscience: The Official Journal of the Society for Neuroscience*, *26*(35), 8915–8922. https://doi.org/10.1523/JNEUROSCI.3048-05.2006

Horii-Hayashi, N., Sasagawa, T., Hashimoto, T., Kaneko, T., Takeuchi, K., & Nishi, M. (2015). A Newly Identified Mouse Hypothalamic Area Having Bidirectional Neural Connections With the Lateral Septum: The Perifornical Area of the Anterior Hypothalamus Rich in Chondroitin Sulfate Proteoglycans. *European Journal of Neuroscience*, *42*(6), 2322–2334. https://doi.org/10.1111/ejn.13024

Horvat, M., Kukolja, D., & Ivanec, D. (2015). *Comparing affective responses to standardized pictures and videos: A study report*.

Horwitz, B., Rumsey, J. M., & Donohue, B. C. (1998). Functional Connectivity of the Angular Gyrus in Normal Reading and Dyslexia. *Proceedings of the National Academy of Sciences*, *95*(15), 8939–8944. https://doi.org/10.1073/pnas.95.15.8939

Hugo A. Tejeda & Patricio O'Donnell. (2014). Amygdala Inputs to the Prefrontal Cortex Elicit Heterosynaptic Suppression of Hippocampal Inputs. *The Journal of Neuroscience*, *34*(43), 14365–14374. https://doi.org/10.1523/JNEUROSCI.0837-14.2014

Hugo D. Critchley, Hugo D. Critchley, Sarah N. Garfinkel, & Sarah N. Garfinkel. (2018). The influence of physiological signals on cognition. *Current Opinion in Behavioral Sciences*, *19*, 13–18. https://doi.org/10.1016/J.COBEHA.2017.08.014

Huiyan Lin, Miriam Müller-Bardorff, Bettina Gathmann, Jaqueline Brieke, Martin Mothes-Lasch, Maximilian Bruchmann, Wolfgang H. R. Miltner, & Thomas Straube. (2020). Stimulus arousal drives amygdalar responses to emotional expressions across sensory modalities. *Scientific Reports*, *10*(1), 1898. https://doi.org/10.1038/S41598-020-58839-1

Ironside, M., Browning, M., Ansari, T. L., Harvey, C. J., Sekyi-Djan, M. N., Bishop, S. J., Harmer, C. J., & O'Shea, J. (2019). Effect of Prefrontal Cortex Stimulation on Regulation of Amygdala Response to Threat in Individuals With Trait Anxiety. *JAMA Psychiatry*, *76*(1), 71–78. https://doi.org/10.1001/jamapsychiatry.2018.2172

Isbell, L. M., Rovenpor, D. R., & Lair, E. C. (2016). The Impact of Negative Emotions on Self-Concept Abstraction Depends on Accessible Information Processing Styles. *Emotion*, *16*(7), 1040–1049. https://doi.org/10.1037/emo0000193

James P. Herman. (2010). *Regulation of the HPA Axis by Acute and Chronic Stress*. 149–153. https://doi.org/10.1016/B978-0-08-045396-5.00230-X

James P. Herman & Jeffrey G. Tasker. (2016). Paraventricular Hypothalamic Mechanisms of Chronic Stress Adaptation. *Frontiers in Endocrinology*, *7*, 137–137. https://doi.org/10.3389/FENDO.2016.00137

Jamieson, B. B., Kim, J. S., & Iremonger, K. J. (2022). Cannabinoid and Vanilloid Pathways Mediate Opposing Forms of Synaptic Plasticity in Corticotropin-releasing Hormone Neurons. *Journal of Neuroendocrinology*, *34*(4). https://doi.org/10.1111/jne.13084

Janet, R., Costes, N., Mérida, I., Derrington, E., & Dreher, J. (2023). Relationships between serotonin availability and frontolimbic response to fearful and threatening faces. *Nature Portfolio*, *13*(1). https://doi.org/10.1038/s41598-023-28667-0

Jasnić, N., Djordjević, J., Vujović, P., Lakić, I., Đurašević, S., & Cvijič, G. (2013). The effect of vasopressin 1b receptors (V1bRs) blockade on the HPA axis activity in rats exposed to acute heat stress. *Journal of Experimental Biology*. https://doi.org/10.1242/jeb.082842

Jeffrey R. Huntsinger, Linda M. Isbell, & Gerald L. Clore. (2014). The affective control of thought: Malleable, not fixed. *Psychological Review*, *121*(4), 600–618. https://doi.org/10.1037/A0037669

Jessica McFadyen, Jason B. Mattingley, & Marta I. Garrido. (2019). An afferent white matter pathway from the pulvinar to the amygdala facilitates fear recognition. *eLife*, *8*. https://doi.org/10.7554/ELIFE.40766

Jhang, J., Lee, H., Kang, M. S., Lee, H.-S., Park, H., & Han, J.-H. (2018). Anterior cingulate cortex and its input to the basolateral amygdala control innate fear response. *Nature Communications*, *9*(1), 2744. https://doi.org/10.1038/s41467-018-05090-y

Jobson, D. D., Hase, Y., Clarkson, A. N., & Kalaria, R. N. (2021). The role of the medial prefrontal cortex in cognition, ageing and dementia. *Brain Communications*, *3*(3), fcab125. https://doi.org/10.1093/braincomms/fcab125

Joëls, M., Karst, H., & Sarabdjitsingh, R. A. (2018). The stressed brain of humans and rodents. *Acta Physiologica*, *223*(2), e13066. https://doi.org/10.1111/apha.13066

Johnson, E. O., Kamilaris, T. C., Chrousos, G. P., & Gold, P. W. (1992). Mechanisms of stress: A dynamic overview of hormonal and behavioral homeostasis. *Elsevier BV*, *16*(2), 115–130. https://doi.org/10.1016/s0149-7634(05)80175-7

Kagias, K., Nehammer, C., & Pocock, R. (2012). Neuronal Responses to Physiological Stress. *Frontiers in Genetics*, *3*. https://doi.org/10.3389/fgene.2012.00222

Kanal, E., Barkovich, A. J., Bell, C., Borgstede, J. P., Bradley, W. G., Froelich, J. W., Gimbel, J. R., Gosbee, J. W., Kuhni-Kaminski, E., Larson, P. A., Lester, J. W., Nyenhuis, J., Schaefer, D. J., Sebek, E. A., Weinreb, J., Wilkoff, B. L., Woods, T. O., Lucey, L., & Hernandez, D. (2013). ACR guidance document on MR safe practices: 2013. *Journal of Magnetic Resonance Imaging: JMRI*, *37*(3), 501–530. https://doi.org/10.1002/jmri.24011

Kar, L. D. V. de, Piechowski, R. A., Rittenhouse, P. A., & Gray, T. S. (1991). Amygdaloid Lesions: Differential Effect on Conditioned Stress and Immobilization-Induced Increases in Corticosterone and Renin Secretion. *Neuroendocrinology*, *54*(2), 89–95. https://doi.org/10.1159/000125856

Karolis, V. R., Corbetta, M., & Thiebaut de Schotten, M. (2019). The architecture of functional lateralisation and its relationship to callosal connectivity in the human brain. *Nature Communications*, *10*(1), 1417. https://doi.org/10.1038/s41467-019-09344-1

Keller, J. B., Hedden, T., Thompson, T. W., Anteraper, S. A., Gabrieli, J. D. E., & Whitfield-Gabrieli, S. (2015). Resting-State Anticorrelations Between Medial and Lateral Prefrontal Cortex: Association With Working Memory, Aging, and Individual Differences. *Cortex*, *64*, 271–280. https://doi.org/10.1016/j.cortex.2014.12.001

Kiecolt-Glaser, J. K., Renna, M. E., Shrout, M. R., & Madison, A. A. (2020). Stress Reactivity: What Pushes Us Higher, Faster, and Longer – and Why It Matters. *Current Directions in Psychological Science*, *29*(5), 492–498. https://doi.org/10.1177/0963721420949521

Killgore, W. D. S., Britton, J. C., Schwab, Z. J., Price, L. M., Weiner, M. R., Gold, A. L., Rosso, I. M., Simon, N. M., Pollack, M. H., & Rauch, S. L. (2013). *Cortico-limbic responses to masked affective faces across ptsd, panic disorder, and specific phobia. 31*(2), 150–159.

Kim, M. J., Solomon, K. M., Neta, M., Davis, F. C., Oler, J. A., Mazzulla, E. C., & Whalen, P. J. (2016). A face versus non-face context influences amygdala responses to masked fearful eye whites. *Social Cognitive and Affective Neuroscience*, *11*(12), 1933–1941. https://doi.org/10.1093/scan/nsw110

Kirk, P. A., Holmes, A. J., & Robinson, O. J. (2022). Threat vigilance and intrinsic amygdala connectivity. *Human Brain Mapping*, *43*(10), 3283–3292. https://doi.org/10.1002/hbm.25851

Kirsch, D., Preston, A., Tretyak, V., Le, V., Weber, W., Strakowski, S. M., & Lippard, E. (2021). Neural Functional Connectivity Changes to Psychosocial Stress in Young Adults With Bipolar Disorder and Preliminary Associations With Clinical Trajectories. *Bipolar Disorders*, *24*(3), 298–309. https://doi.org/10.1111/bdi.13127

Kivimäki, M., & Kawachi, I. (2015). Work Stress as a Risk Factor for Cardiovascular Disease. *Current Cardiology Reports*, *17*(9), 630. https://doi.org/10.1007/s11886-015-0630-8

Klein, D. J., & Verbeke, W. (1999). Autonomic feedback in stressful environments: How do individual differences in autonomic feedback relate to burnout, job performance, and job attitudes in salespeople? *Journal of Applied Psychology*, *84*(6), 911–924. https://doi.org/10.1037/0021-9010.84.6.911

Kleshchova, O., Rieder, J. K., Grinband, J., & Weierich, M. R. (2019). Resting amygdala connectivity and basal sympathetic tone as markers of chronic hypervigilance. *Elsevier BV*, *102*, 68–78. https://doi.org/10.1016/j.psyneuen.2018.11.036

Knudson, A. G. (1971). Mutation and cancer: Statistical study of retinoblastoma. *Proceedings of the National Academy of Sciences of the United States of America*, *68*(4), 820–823. https://doi.org/10.1073/pnas.68.4.820

Kogler, L., Müller, V. I., Chang, A., Eickhoff, S. B., Fox, P. T., Gur, R. C., & Derntl, B. (2015). Psychosocial versus physiological stress—Meta-analyses on deactivations and activations of the neural correlates of stress reactions. *NeuroImage*, *119*, 235–251. https://doi.org/10.1016/j.neuroimage.2015.06.059

Koob, G. F., & Volkow, N. D. (2016). Neurobiology of addiction: A neurocircuitry analysis. *The Lancet. Psychiatry*, *3*(8), 760–773. https://doi.org/10.1016/S2215-0366(16)00104-8

Koolhaas, J. M., Bartolomucci, A., Buwalda, B., de Boer, S. F., Flügge, G., Korte, S. M., Meerlo, P., Murison, R., Olivier, B., Palanza, P., Richter-Levin, G., Sgoifo, A., Steimer, T., Stiedl, O., van Dijk, G., Wöhr, M., & Fuchs, E. (2011). Stress revisited: A critical evaluation of the stress concept. *Neuroscience and Biobehavioral Reviews*, *35*(5), 1291–1301. https://doi.org/10.1016/j.neubiorev.2011.02.003

Koussis, N. C., Burgher, B., Jeganathan, J., Scott, J. G., Cocchi, L., & Breakspear, M. (2023). Cognitive Control System Gates Insula Processing of Affective Stimuli in Early Psychosis. *Schizophrenia Bulletin*, *49*(4), 987–996. https://doi.org/10.1093/schbul/sbad010

Kovács, K. (2013). CRH: The Link Between Hormonal-, Metabolic- And Behavioral Responses to Stress. *Journal of Chemical Neuroanatomy*, *54*, 25–33. https://doi.org/10.1016/j.jchemneu.2013.05.003

Kovács, K. J., Miklós, I. H., & Bali, B. (2005). Chapter 6.1—Psychological and physiological stressors. In T. Steckler, N. H. Kalin, & J. M. H. M. Reul (Eds.), *Techniques in the Behavioral and Neural Sciences* (Vol. 15, pp. 775–792). Elsevier. https://doi.org/10.1016/S0921-0709(05)80041-0

Lanteaume, L., Khalfa, S., Régis, J., Marquis, P., Chauvel, P., & Bartolomei, F. (2007). Emotion Induction After Direct Intracerebral Stimulations of Human Amygdala. *Cerebral Cortex*, *17*(6), 1307–1313. https://doi.org/10.1093/cercor/bhl041

Larkin, K. T., Brown, L. A., & Tiani, A. G. (2020). Chapter 5—Autonomic and neuroendocrine response to stress. In P. D. Chantler & K. T. Larkin (Eds.), *Cardiovascular Implications of Stress and Depression* (pp. 87–110). Academic Press. https://doi.org/10.1016/B978-0-12-815015-3.00005-2

Larocca, N. E., Moreno, D., Garmendia, J. V., & Sanctis, J. B. D. (2011). *Role of beta2 agonists in respiratory medicine with particular attention to novel patents and effects on endocrine system and immune response*.

Laura Tartari Neves, Paula Fernanda Ribas Neves, Lisiê Valéria Paz, Mariana Zancan, Bruna Bueno Milanesi, Gabriele Zenato Lazzari, Rafaela Barboza da Silva, Marina Mena Barreto Peres de Oliveira, Gianina Teribele Venturin, Samuel Greggio, Jaderson Costa da Costa, Alberto A. Rasia-Filho, Régis Gemerasca Mestriner, & Léder Leal Xavier. (2019). Increases in dendritic spine density in BLA without metabolic changes in a rodent model of PTSD. *Brain Structure & Function*, *224*(8), 2857–2870. https://doi.org/10.1007/S00429-019-01943-4

Lazarus & Folkman. (1984). *Stress, Appraisal, and Coping*. Springer Publishing Company.

Lea Marie Reisch, Lea Marie Reisch, Martin Wegrzyn, Friedrich G. Woermann, Christian G. Bien, & Johanna Kissler. (2020). Negative content enhances stimulus-specific cerebral activity during free viewing of pictures, faces, and words. *Human Brain Mapping*, *41*(15), 4332–4354. https://doi.org/10.1002/HBM.25128

LeDoux, J. E., & Pine, D. S. (2016). Using Neuroscience to Help Understand Fear and Anxiety: A Two-System Framework. *The American Journal of Psychiatry*, *173*(11), 1083–1093. https://doi.org/10.1176/appi.ajp.2016.16030353

Liekefett, L., Christ, O., & Becker, J. C. (2023). Can Conspiracy Beliefs Be Beneficial? Longitudinal Linkages Between Conspiracy Beliefs, Anxiety, Uncertainty Aversion, and Existential

Threat. *Personality & Social Psychology Bulletin*, *49*(2), 167–179. https://doi.org/10.1177/01461672211060965

Lin, J., Namaky, N., Costello, M., Uchino, B. N., Allen, J. P., & Coan, J. A. (2023). Social regulation of the neural threat response predicts subsequent markers of physical health. *Psychosomatic Medicine*. https://doi.org/10.1097/psy.0000000000001238

Linton, S. R., & Levita, L. (2021). *Potentiated perceptual neural responses to learned threat during Pavlovian fear acquisition and extinction in adolescents*. *24*(5). https://doi.org/10.1111/desc.13107

Lívea Dornela Godoy, Matheus Teixeira Rossignoli, Polianna Delfino-Pereira, N. Garcia-Cairasco, & Eduardo H.L. Umeoka. (2018). A Comprehensive Overview on Stress Neurobiology: Basic Concepts and Clinical Implications. *Frontiers in Behavioral Neuroscience*, *12*, 127–127. https://doi.org/10.3389/FNBEH.2018.00127

Loeffler, S., Hennig, J., & Peper, M. (2016). Psychophysiological Assessment of Social Stress in Natural and Laboratory Situations: Using the Experience Sampling Method and Additional Heart Rate Measures. *Journal of Psychophysiology*, *31*, 1–11. https://doi.org/10.1027/0269-8803/a000170

Makino, S., Hashimoto, K., & Gold, P. W. (2002). Multiple feedback mechanisms activating corticotropin-releasing hormone system in the brain during stress. *Pharmacology Biochemistry and Behavior*, *73*(1), 147–158. https://doi.org/10.1016/S0091-3057(02)00791-8

Malena Mielke, Lea Marie Reisch, Alexandra Mehlmann, Sebastian Schindler, Christian G. Bien, & Johanna Kissler. (2021). Right medial temporal lobe structures particularly impact early stages of affective picture processing. *Human Brain Mapping*. https://doi.org/10.1002/HBM.25687

Manuel Petrucci & Anna Pecchinenda. (2017). The role of cognitive control mechanisms in selective attention towards emotional stimuli. *Cognition & Emotion*, *31*(7), 1480–1492. https://doi.org/10.1080/02699931.2016.1233861

Marques, D. B., Rossignoli, M. T., Mesquita, B. de A., Prizon, T., Zacharias, L. R., Ruggiero, R. N., & Leite, J. P. (2023). *Decoding Fear or Safety and Approach or Avoidance by Brain-Wide Network Dynamics* (p. 2022.10.13.511989). bioRxiv. https://doi.org/10.1101/2022.10.13.511989

Mason, L., Scrimin, S., Zaccoletti, S., Tornatora, M. C., & Goetz, T. (2018). Webpage reading: Psychophysiological correlates of emotional arousal and regulation predict multiple-text comprehension. *Computers in Human Behavior*, *87*, 317–326. https://doi.org/10.1016/j.chb.2018.05.020

Maureen Ritchey, Maureen Ritchey, Andrew M. McCullough, Charan Ranganath, & Andrew P. Yonelinas. (2017). Stress as a mnemonic filter: Interactions between medial temporal lobe encoding processes and post-encoding stress. *Hippocampus*, *27*(1), 77–88. https://doi.org/10.1002/HIPO.22674

McEwen, B. S. (2007). Physiology and neurobiology of stress and adaptation: Central role of the brain. *Physiological Reviews*, *87*(3), 873–904. https://doi.org/10.1152/physrev.00041.2006

McLaughlin, K. A., Busso, D. S., Duys, A., Green, J. G., Alves, S., Way, M., & Sheridan, M. A. (2014). Amygdala Response to Negative Stimuli Predicts Ptsd Symptom Onset Following a Terrorist Attack. *Depression and Anxiety*, *31*(10), 834–842. https://doi.org/10.1002/da.22284

McNamara, M. E. (1991). Psychological factors affecting neurological conditions. Depression and stroke, multiple sclerosis, Parkinson's disease, and epilepsy. *Psychosomatics*, *32*(3), 255–267. https://doi.org/10.1016/S0033-3182(91)72063-X

Melis, M. R., Succu, S., Spano, M. S., & Argiolas, A. (1999). Morphine Injected Into the Paraventricular Nucleus of the Hypothalamus Prevents Noncontact Penile Erections and

Impairs Copulation: Involvement of Nitric Oxide. *European Journal of Neuroscience*, *11*(6), 1857–1864. https://doi.org/10.1046/j.1460-9568.1999.00603.x

Messina, G., Chieffi, S., Viggiano, A., Tafuri, D., Cibelli, G., Valenzano, A., Triggiani, A. I., Messina, A., Luca, V. D., & Monda, M. (2016). Parachute Jumping Induces More Sympathetic Activation Than Cortisol Secretion in First-Time Parachutists. *Asian Journal of Sports Medicine*, *7*(1). https://doi.org/10.5812/asjsm.26841

Miklos Bognar, Mate Gyurkovics, Henk van Steenbergen, & Balazs Aczel. (2023). Phasic affective signals by themselves do not regulate cognitive control. *Cognition & Emotion*, *37*(4), 650–665. https://doi.org/10.1080/02699931.2023.2191172

Mooney-Leber, S. M., Caruso, M. J., Gould, T. J., Cavigelli, S. A., & Kamens, H. M. (2021). The impact of adolescent stress on nicotine use and affective disorders in rodent models. *European Journal of Neuroscience*. https://doi.org/10.1111/ejn.15421

Morawetz, C., Kellermann, T., Kogler, L., Radke, S., Blechert, J., & Derntl, B. (2016). Intrinsic functional connectivity underlying successful emotion regulation of angry faces. *Social Cognitive and Affective Neuroscience*, *11*(12), 1980–1991. https://doi.org/10.1093/scan/nsw107

Motiejunaite, J., Amar, L., & Vidal-Petiot, E. (2021). Adrenergic receptors and cardiovascular effects of catecholamines. *Annales D'endocrinologie*, *82*(3–4), 193–197. https://doi.org/10.1016/j.ando.2020.03.012

Motomura, Y., Kitamura, S., Oba, K., Terasawa, Y., Enomoto, M., Katayose, Y., Hida, A., Moriguchi, Y., Higuchi, S., & Mishima, K. (2013). Correction: Sleep Debt Elicits Negative Emotional Reaction Through Diminished Amygdala-Anterior Cingulate Functional Connectivity. *Plos One*, *8*(10). https://doi.org/10.1371/annotation/5970fff3-0a1c-4056-9396-408d76165c4d

Motomura, Y., Kitamura, S., Oba, K., Terasawa, Y., Enomoto, M., Katayose, Y., Hida, A., Moriguchi, Y., Higuchi, S., & Mishima, K. (2014). Sleepiness induced by sleep-debt

enhanced amygdala activity for subliminal signals of fear. *BioMed Central*, *15*(1). https://doi.org/10.1186/1471-2202-15-97

Mueller, V., Richer, R., Henrich, L., Berger, L., Gelardi, A., Jaeger, K. M., Eskofier, B. M., & Rohleder, N. (2022). The Stroop Competition: A Social-Evaluative Stroop Test for Acute Stress Induction. *2022 IEEE-EMBS International Conference on Biomedical and Health Informatics (BHI)*, 1–4. https://doi.org/10.1109/BHI56158.2022.9926835

Namkung, H., Kim, S.-H., & Sawa, A. (2017). The insula: An underestimated brain area in clinical neuroscience, psychiatry, and neurology. *Elsevier BV*, *40*(4), 200–207. https://doi.org/10.1016/j.tins.2017.02.002

Neufeld-Cohen, A., Tsoory, M., Evans, A. K., Getselter, D., Gil, S., Lowry, C. A., Vale, W., & Chen, A. (2010). A triple urocortin knockout mouse model reveals an essential role for urocortins in stress recovery. *Proceedings of the National Academy of Sciences*. https://doi.org/10.1073/pnas.1013761107

Neville, A. (2023). *[General adaptation syndrome]. In: Drandrewneville.com [online].* [Graphic]. https://drandrewneville.com/hans-selyes-general-adaptation-syndrome/

Nicholson, A. A., Rabellino, D., Densmore, M., Frewen, P., Paret, C., Kluetsch, R., Schmahl, C., Théberge, J., Neufeld, R. W. J., McKinnon, M. C., Reiss, J. P., Jetly, R., & Lanius, R. A. (2016). The neurobiology of emotion regulation in posttraumatic stress disorder: Amygdala downregulation via real-time fMRI neurofeedback. *Wiley*, *38*(1), 541–560. https://doi.org/10.1002/hbm.23402

Ochsner, K. N., Bunge, S. A., Gross, J. J., & Gabrieli, J. D. E. (2002). Rethinking Feelings: An fMRI Study of the Cognitive Regulation of Emotion. *Journal of Cognitive Neuroscience*, *14*(8), 1215–1229. https://doi.org/10.1162/089892902760807212

Ochsner, K. N., Ray, R. D., Cooper, J. C., Robertson, E. R., Chopra, S., Gabrieli, J. D. E., & Gross, J. J. (2004). For better or for worse: Neural systems supporting the cognitive down- and up-

regulation of negative emotion. *NeuroImage*, *23*(2), 483–499. https://doi.org/10.1016/j.neuroimage.2004.06.030

Ocklenburg, S., Korte, S. M., Peterburs, J., Wolf, O. T., & Güntürkün, O. (2016). Stress and laterality—The comparative perspective. *Physiology & Behavior*, *164*(Pt A), 321–329. https://doi.org/10.1016/j.physbeh.2016.06.020

O'Riordan, A., Young, D. A., & Ginty, A. T. (2023). Physiological reactivity and habituation to acute psychological stress: The influence of trait extraversion. *Biological Psychology*, *181*, 108599. https://doi.org/10.1016/j.biopsycho.2023.108599

Ostrander, M. M., Ulrich-Lai, Y. M., Choi, D. C., Richtand, N. M., & Herman, J. P. (2006). Hypoactivity of the hypothalamo-pituitary-adrenocortical axis during recovery from chronic variable stress. *Endocrinology*. https://doi.org/10.1210/en.2005-1041

Pace, L. D., Viviani, L., & Straccia, M. (2022). *Researchers and their experimental models: A pilot survey in the context of the european union health and life science research*. *12*(20), 2778–2778.

Pan, D.-N., Jentsch, V. L., Langer, K., Hagedorn, B., Höffken, O., Wolf, O. T., & Merz, C. J. (2023). What a difference timing makes: Cortisol effects on neural underpinnings of emotion regulation. *Neurobiology of Stress*, *25*, 100544. https://doi.org/10.1016/j.ynstr.2023.100544

Paschke, L. M., Dörfel, D., Steimke, R., Trempler, I., Magrabi, A., Ludwig, V. U., Schubert, T., Stelzel, C., & Walter, H. (2016). Individual Differences in Self-Reported Self-Control Predict Successful Emotion Regulation. *Social Cognitive and Affective Neuroscience*, *11*(8), 1193–1204. https://doi.org/10.1093/scan/nsw036

Passamonti, L., Crockett, M. J., Apergis-Schoute, A. M., Clark, L., Rowe, J. B., Calder, A. J., & Robbins, T. W. (2012). Effects of Acute Tryptophan Depletion on Prefrontal-Amygdala Connectivity While Viewing Facial Signals of Aggression. *Biological Psychiatry*, *71*(1), 36–43. https://doi.org/10.1016/j.biopsych.2011.07.033

Paula Neumeister, Katharina Feldker, Carina Yvonne Heitmann, Christine Buff, Leonie Brinkmann, Maximilian Bruchmann, & Thomas Straube. (2017). Specific amygdala response to masked fearful faces in post-traumatic stress relative to other anxiety disorders. *Psychological Medicine*, *48*(7), 1209–1217. https://doi.org/10.1017/S0033291717002513

Pedale, T., Macaluso, E., & Santangelo, V. (2019). Enhanced insular/prefrontal connectivity when resisting from emotional distraction during visual search. *Springer Science+Business Media*, *224*(6), 2009–2026. https://doi.org/10.1007/s00429-019-01873-1

Phelps, E. A., & LeDoux, J. E. (2005). Contributions of the Amygdala to Emotion Processing: From Animal Models to Human Behavior. *Neuron*, *48*(2), 175–187. https://doi.org/10.1016/j.neuron.2005.09.025

Phelps, E. A., Lempert, K. M., & Sokol-Hessner, P. (2014). Emotion and Decision Making: Multiple Modulatory Neural Circuits. *Annual Review of Neuroscience*, *37*(1), 263–287. https://doi.org/10.1146/annurev-neuro-071013-014119

Pizzie, R. G., & Kraemer, D. J. M. (2021). The Association Between Emotion Regulation, Physiological Arousal, and Performance in Math Anxiety. *Frontiers in Psychology*, *12*, 639448. https://doi.org/10.3389/fpsyg.2021.639448

Plieger, T., Melchers, M., Vetterlein, A., Görtz, J., Kuhn, S., Ruppel, M., & Reuter, M. (2017). The serotonin transporter polymorphism (5-HTTLPR) and coping strategies influence successful emotion regulation in an acute stress situation: Physiological evidence. *International Journal of Psychophysiology*, *114*, 31–37. https://doi.org/10.1016/j.ijpsycho.2017.02.006

Polo, E. M., Farabbi, A., Mollura, M., Paglialonga, A., Mainardi, L., & Barbieri, R. (2024). Comparative Assessment of Physiological Responses to Emotional Elicitation by Auditory and Visual Stimuli. *IEEE Journal of Translational Engineering in Health and Medicine*, *12*, 171–181. https://doi.org/10.1109/JTEHM.2023.3324249

Quaedflieg, C. W. E. M., & Schwabe, L. (2018). Memory dynamics under stress. *Memory (Hove, England)*, *26*(3), 364–376. https://doi.org/10.1080/09658211.2017.1338299

Ragonesi, A. J., & Antick, J. R. (2008). Physiological responses to violence reported in the news. *Perceptual and Motor Skills*, *107*(2), 383–395. https://doi.org/10.2466/pms.107.2.383-395

Ramanan, S., Piguet, O., & Irish, M. (2017). Rethinking the Role of the Angular Gyrus in Remembering the Past and Imagining the Future: The Contextual Integration Model. *The Neuroscientist*, *24*(4), 342–352. https://doi.org/10.1177/1073858417735514

Ressler, K. J., Berretta, S., Bolshakov, V. Y., Rosso, I. M., Meloni, E. G., Rauch, S. L., & Carlezon, W. A. (2022). Post-traumatic stress disorder: Clinical and translational neuroscience from cells to circuits. *Nature Reviews Neurology*, *18*(5), 273–288. https://doi.org/10.1038/s41582-022-00635-8

Richer, R., Zenkner, J., Küderle, A., Rohleder, N., & Eskofier, B. M. (2022). *Vagus Activation by Cold Face Test Reduces Acute Psychosocial Stress Responses*. https://doi.org/10.21203/rs.3.rs-1431139/v1

Ridner, S. H. (2004). Psychological Distress: Concept Analysis. *Journal of Advanced Nursing*, *45*(5), 536–545. https://doi.org/10.1046/j.1365-2648.2003.02938.x

Rieck, J., Wrobel, J., Porras, A. R., McRae, K., & Gowin, J. (2023). *Neural Signatures of Emotion Regulation* (p. 2023.06.12.544668). bioRxiv. https://doi.org/10.1101/2023.06.12.544668

Rigney, A. E., Koski, J., & Beer, J. S. (2017). The functional role of ventral anterior cingulate cortex in social evaluation: Disentangling valence from subjectively rewarding opportunities. *University of Oxford*, *13*(1), 14–21. https://doi.org/10.1093/scan/nsx132

Rinaldi, S., Fontani, V., & Castagna, A. (2011). *Brain activity modification produced by a single radioelectric asymmetric brain stimulation pulse: A new tool for neuropsychiatric treatments. Preliminary fMRI study*. 649–649.

Roos, L. E., Giuliano, R. J., Beauchamp, K. G., Gunnar, M., Amidon, B., & Fisher, P. A. (2017). Validation of autonomic and endocrine reactivity to a laboratory stressor in young children. *Psychoneuroendocrinology*, *77*, 51–55. https://doi.org/10.1016/j.psyneuen.2016.11.023

Rosen, M. L., Sheridan, M. A., Sambrook, K. A., Peverill, M. R., Meltzoff, A. N., & McLaughlin, K. A. (2018). The Role of Visual Association Cortex in Associative Memory Formation across Development. *Journal of Cognitive Neuroscience*, *30*(3), 365–380. https://doi.org/10.1162/jocn_a_01202

Russell, A. L., Tasker, J. G., Lucion, A. B., Fiedler, J. L., Munhoz, C. D., Wu, T., & Deak, T. (2018). Factors promoting vulnerability to dysregulated stress reactivity and stress-related disease. *Journal of Neuroendocrinology*. https://doi.org/10.1111/jne.12641

Russell, G., & Lightman, S. (2019). The human stress response. *Nature Reviews Endocrinology*, *15*(9), 525–534. https://doi.org/10.1038/s41574-019-0228-0

Schienle, A., Schäfer, A., Pignanelli, R., & Vaitl, D. (2009). Worry tendencies predict brain activation during aversive imagery. *Neuroscience Letters*, *461*(3), 289–292. https://doi.org/10.1016/j.neulet.2009.06.041

Selye, H. (1946). The general adaptation syndrome and the diseases of adaptation. *The Journal of Clinical Endocrinology & Metabolism*, *6*(2), 117–230. https://doi.org/10.1210/jcem-6-2-117

Selye, H. (1950). *The physiology and pathology of exposure to stress* (pp. xx, 822; 203). Acta, Inc.

Senne Braem, Joseph A. King, Franziska M. Korb, Ruth M. Krebs, Wim Notebaert, & Tobias Egner. (2013). Affective Modulation of Cognitive Control is Determined by Performance-Contingency and Mediated by Ventromedial Prefrontal and Cingulate Cortex. *The Journal of Neuroscience*, *33*(43), 16961–16970. https://doi.org/10.1523/JNEUROSCI.1208-13.2013

Sep, M. S. C., van Ast, V. A., Gorter, R., Joëls, M., & Geuze, E. (2019). Time-dependent effects of psychosocial stress on the contextualization of neutral memories. *Psychoneuroendocrinology*, *108*, 140–149. https://doi.org/10.1016/j.psyneuen.2019.06.021

Seth, A. K., & Critchley, H. (2013). Extending Predictive Processing to the Body: Emotion as Interoceptive Inference. *Behavioral and Brain Sciences*, *36*(3), 227–228. https://doi.org/10.1017/s0140525x12002270

Sharp, D. J., Scott, G., & Leech, R. (2014). Network dysfunction after traumatic brain injury. *Nature Reviews Neurology*, *10*(3), 156–166. https://doi.org/10.1038/nrneurol.2014.15

Sheffield, J. M., Huang, A. S., Rogers, B. P., Blackford, J. U., Heckers, S., & Woodward, N. D. (2021). Insula sub-regions across the psychosis spectrum: Morphology and clinical correlates. *Translational Psychiatry*, *11*(1), 1–13. https://doi.org/10.1038/s41398-021-01461-0

Shellock, F. G., & Crues, J. V. (2004). MR procedures: Biologic effects, safety, and patient care. *Radiology*, *232*(3), 635–652. https://doi.org/10.1148/radiol.2323030830

Sheth, S. A., Mian, M. K., Patel, S., Asaad, W. F., Williams, Z., Dougherty, D. D., Bush, G., & Eskandar, E. N. (2012, June). *Human dorsal anterior cingulate cortex neurons mediate ongoing behavioural adaptation* (7410; Vol. 488, pp. 218–221). https://doi.org/10.1038/nature11239

Shimizu, H., & Okabe, M. (2007). Evolutionary origin of autonomic regulation of physiological activities in vertebrate phyla. *Journal of Comparative Physiology. A, Neuroethology, Sensory, Neural, and Behavioral Physiology*, *193*(10), 1013–1019. https://doi.org/10.1007/s00359-007-0256-4

Silvestrini, N., Chen, J.-I., Piché, M., Roy, M., Vachon-Presseau, E., Woo, C.-W., Wager, T. D., & Rainville, P. (2020). Distinct fMRI patterns colocalized in the cingulate cortex underlie the after-effects of cognitive control on pain. *NeuroImage*, *217*, 116898. https://doi.org/10.1016/j.neuroimage.2020.116898

Šimić, G., Tkalčić, M., Vukić, V., Mulc, D., Španić, E., Šagud, M., Olucha-Bordonau, F. E., Vukšić, M., & Hof, P. R. (2021). Understanding emotions: Origins and roles of the amygdala. *Multidisciplinary Digital Publishing Institute*, *11*(6), 823–823. https://doi.org/10.3390/biom11060823

Simmons, W. K., Avery, J. A., Barcalow, J. C., Bodurka, J., Drevets, W. C., & Bellgowan, P. S. F. (2012). Keeping the body in mind: Insula functional organization and functional connectivity

integrate interoceptive, exteroceptive, and emotional awareness. *Wiley*, *34*(11), 2944–2958. https://doi.org/10.1002/hbm.22113

Sinha, R., Lacadie, C., Skudlarski, P., & Wexler, B. E. (2004). Neural circuits underlying emotional distress in humans. *Annals of the New York Academy of Sciences*, *1032*, 254–257. https://doi.org/10.1196/annals.1314.032

Skyberg, A. M., Newman, B. T., Graves, A. J., Goldstein, A. M., Brindley, S. R., Kim, M., Druzgal, T. J., Connelly, J. J., & Morris, J. P. (2023). An epigenetic mechanism for differential maturation of amygdala–prefrontal connectivity in childhood socio-emotional development. *Translational Psychiatry*, *13*(1), 1–9. https://doi.org/10.1038/s41398-023-02380-y

Slawomira J. Diener, Frauke Nees, Michèle Wessa, Gustav Wirtz, Ulrich Frommberger, Tina Penga, Michaela Ruttorf, Matthias Ruf, Christian Schmahl, & Herta Flor. (2016). Reduced amygdala responsivity during conditioning to trauma-related stimuli in posttraumatic stress disorder. *Psychophysiology*, *53*(10), 1460–1471. https://doi.org/10.1111/PSYP.12699

Smith, K. E., & Pollak, S. D. (2020). Early life stress and development: Potential mechanisms for adverse outcomes. *Journal of Neurodevelopmental Disorders*, *12*(1), 34. https://doi.org/10.1186/s11689-020-09337-y

Smith, S. M., & Vale, W. (2006). The role of the hypothalamic-pituitary-adrenal axis in neuroendocrine responses to stress. *Dialogues in Clinical Neuroscience*. https://doi.org/10.31887/dcns.2006.8.4/ssmith

Smyth, J., Zawadzki, M., & Gerin, W. (2013). Stress and Disease: A Structural and Functional Analysis. *Social and Personality Psychology Compass*, *7*(4), 217–227. https://doi.org/10.1111/spc3.12020

Soroka, S., Fournier, P., & Nir, L. (2019). Cross-national evidence of a negativity bias in psychophysiological reactions to news. *Proceedings of the National Academy of Sciences*, *116*(38), 18888–18892. https://doi.org/10.1073/pnas.1908369116

Sparrow, K., & Golianu, B. (2014). *Does acupuncture reduce stress over time? A clinical heart rate variability study in hypertensive patients*. *26*(5), 286–294.

Spencer, S. J., Buller, K. M., & Day, T. A. (2005). Medial prefrontal cortex control of the paraventricular hypothalamic nucleus response to psychological stress: Possible role of the bed nucleus of the stria terminalis. *The Journal of Comparative Neurology*, *481*(4), 363–376. https://doi.org/10.1002/cne.20376

Stefano Delli Pizzi, Piero Chiacchiaretta, Dante Mantini, Dante Mantini, Dante Mantini, Giovanna Bubbico, Antonio Ferretti, Richard A.E. Edden, Richard A.E. Edden, Camillo Di Giulio, Marco Onofrj, & Laura Bonanni. (2017). Functional and neurochemical interactions within the amygdala–medial prefrontal cortex circuit and their relevance to emotional processing. *Brain Structure & Function*, *222*(3), 1267–1279. https://doi.org/10.1007/S00429-016-1276-Z

Stein, M. B., Simmons, A. N., Feinstein, J. S., & Paulus, M. P. (2007). Increased amygdala and insula activation during emotion processing in anxiety-prone subjects. *The American Journal of Psychiatry*, *164*(2), 318–327. https://doi.org/10.1176/ajp.2007.164.2.318

Stephanie S. Rude, Richard M. Wenzlaff, Bryce Gibbs, Jennifer Vane, & Tavia Whitney. (2002). Negative processing biases predict subsequent depressive symptoms. *Cognition & Emotion*, *16*(3), 423–440. https://doi.org/10.1080/02699930143000554

Suzuki, Y., & Tanaka, S. C. (2021). Functions of the ventromedial prefrontal cortex in emotion regulation under stress. *Scientific Reports*, *11*(1), 18225. https://doi.org/10.1038/s41598-021-97751-0

Tadayon, R., Gupta, C., Crews, D., & McDaniel, T. (2018). Differences in Psychophysiological Reactions to Anxiety in Individuals with Varying Trait Anxiety Scores. *Proceedings of the 3rd International Workshop on Multimedia for Personal Health and Health Care*, 19–24. https://doi.org/10.1145/3264996.3265005

Thayer, J. F., Hansen, A. L., Saus-Rose, E., & Johnsen, B. H. (2009). Heart Rate Variability, Prefrontal Neural Function, and Cognitive Performance: The Neurovisceral Integration Perspective on Self-Regulation, Adaptation, and Health. *Annals of Behavioral Medicine*, *37*(2), 141–153. https://doi.org/10.1007/s12160-009-9101-z

Thomas Maran, Pierre Sachse, & Marco Furtner. (2018). Negative Arousal Reduces Sensitivity for Processing Context Information. *Social Behavior and Personality*, *46*(6), 985–994. https://doi.org/10.2224/SBP.6878

Thompson, R. R., Garfin, D. R., Holman, E. A., & Silver, R. C. (2017). Distress, worry, and functioning following a global health crisis: A national study of Americans' responses to Ebola. *Clinical Psychological Science*, *5*(3), 513–521. https://doi.org/10.1177/2167702617692030

Tindle, J., & Tadi, P. (2020). *Neuroanatomy, parasympathetic nervous system*. https://europepmc.org/article/MED/31985934

Toyoda, A. (2017). Social defeat models in animal science: What we have learned from rodent models. *Wiley-Blackwell*, *88*(7), 944–952. https://doi.org/10.1111/asj.12809

Toyoda, H., Li, X.-Y., Wu, L. J., Zhao, M., Descalzi, G., Chen, T., Koga, K., & Zhuo, M. (2011). Interplay of Amygdala and Cingulate Plasticity in Emotional Fear. *Neural Plasticity*, *2011*, 1–9. https://doi.org/10.1155/2011/813749

Troy, A. S., Saquib, S., Thal, J., & Ciuk, D. J. (2019). The regulation of negative and positive affect in response to daily stressors. *Emotion (Washington, D.C.)*, *19*(5), 751–763. https://doi.org/10.1037/emo0000486

Tsujimoto, M., Matsuzaki, Y., Yamaya, N., & Kawashima, R. (2023). Brain Activation and Functional Connectivity of Reappraisal and Acceptance for Anxious Events. *eNeuro*, *10*(6), ENEURO.0033-23.2023. https://doi.org/10.1523/ENEURO.0033-23.2023

Uddin, L. Q., Nomi, J. S., Hébert-Seropian, B., Ghaziri, J., & Boucher, O. (2017). Structure and function of the human insula. *Lippincott Williams & Wilkins*, *34*(4), 300–306. https://doi.org/10.1097/wnp.0000000000000377

van Dijk, M. T., Murphy, E., Posner, J. E., Talati, A., & Weissman, M. M. (2021). Association of Multigenerational Family History of Depression With Lifetime Depressive and Other Psychiatric Disorders in Children. *JAMA Psychiatry*, *78*(7), 1–11. https://doi.org/10.1001/jamapsychiatry.2021.0350

Van Steenbergen, H. (2015). Affective Modulation of Cognitive Control: A Biobehavioral Perspective. In G. H. E. Gendolla, M. Tops, & S. L. Koole (Eds.), *Handbook of Biobehavioral Approaches to Self-Regulation* (pp. 89–107). Springer New York. https://doi.org/10.1007/978-1-4939-1236-0_7

Veen, V., & Carter, C. (2002, December). *The anterior cingulate as a conflict monitor: fMRI and ERP studies* (4–5; Vol. 77, pp. 477–482). https://doi.org/10.1016/s0031-9384(02)00930-7

Viemari, J.-C., Bévengut, M., Coulon, P., & Hilaire, G. (2004). Nasal trigeminal inputs release the A5 inhibition received by the respiratory rhythm generator of the mouse neonate. *Journal of Neurophysiology*, *91*(2), 746–758. https://doi.org/10.1152/jn.01153.2002

Volokhov, R. N., & Demaree, H. A. (2010). Spontaneous emotion regulation to positive and negative stimuli. *Brain and Cognition*, *73*(1), 1–6. https://doi.org/10.1016/j.bandc.2009.10.015

von Dawans, B., Strojny, J., & Domes, G. (2021). The effects of acute stress and stress hormones on social cognition and behavior: Current state of research and future directions. *Neuroscience and Biobehavioral Reviews*, *121*, 75–88. https://doi.org/10.1016/j.neubiorev.2020.11.026

von Majewski, K., Kraus, O., Rhein, C., Lieb, M., Erim, Y., & Rohleder, N. (2023). Acute stress responses of autonomous nervous system, HPA axis, and inflammatory system in posttraumatic stress disorder. *Translational Psychiatry*, *13*(1), 36. https://doi.org/10.1038/s41398-023-02331-7

Wang, J., Korczykowski, M., Rao, H., Fan, Y., Pluta, J., Gur, R. C., McEwen, B. S., & Detre, J. A. (2007). Gender difference in neural response to psychological stress. *Social Cognitive and Affective Neuroscience*, *2*(3), 227–239. https://doi.org/10.1093/scan/nsm018

Wang, J., Mao, W., Qiu, M., Smith, M. B., & Constable, R. T. (2006). Factors influencing flip angle mapping in MRI: RF pulse shape, slice-select gradients, off-resonance excitation, and B0 inhomogeneities. *Magnetic Resonance in Medicine*, *56*(2), 463–468. https://doi.org/10.1002/mrm.20947

Wang, S., Tepfer, L. J., Taren, A. A., & Smith, D. V. (2020). Functional parcellation of the default mode network: A large-scale meta-analysis. *Scientific Reports*, *10*(1), 16096. https://doi.org/10.1038/s41598-020-72317-8

Wang, Y., Gao, H., & Qi, M. (2023). Left Dorsolateral Prefrontal Cortex Activation Can Accelerate Stress Recovery: A Repetitive Transcranial Stimulation Study. *Psychophysiology*, *60*(10). https://doi.org/10.1111/psyp.14352

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology*, *54*(6), 1063–1070. https://doi.org/10.1037/0022-3514.54.6.1063

Weber, J., Angerer, P., & Apolinário-Hagen, J. (2022). Physiological reactions to acute stressors and subjective stress during daily life: A systematic review on ecological momentary assessment (EMA) studies. *PLOS ONE*, *17*(7), e0271996. https://doi.org/10.1371/journal.pone.0271996

Weidenfeld, J., & Ovadia, H. (2017). The Role of the Amygdala in Regulating the Hypothalamic-Pituitary-Adrenal Axis. In B. Ferry (Ed.), *The Amygdala—Where Emotions Shape Perception, Learning and Memories*. InTech. https://doi.org/10.5772/67828

Weidenfeld, J., Siegal, T., & Ovadia, H. (2012). Delayed effects of brain irradiation – part 1: Adrenocortical axis dysfunction and hippocampal damage in an adult rat model. *Neuroimmunomodulation*. https://doi.org/10.1159/000342522

Weiner, K. S., & Zilles, K. (2016). The anatomical and functional specialization of the fusiform gyrus. *Neuropsychologia*, *83*, 48–62. https://doi.org/10.1016/j.neuropsychologia.2015.06.033

Wei-Zhu Liu, Chun Yan Wang, Yu Wang, Han-Qing Pan, Wenhua Zhang, & Bing-Xing Pan. (2023). Circuit- and laminar-specific regulation of medial prefrontal neurons by chronic stress. *Cell & Bioscience*, *13*(1). https://doi.org/10.1186/s13578-023-01050-2

Wei-Zhu Liu, Wenhua Zhang, Zhi-Heng Zheng, Jia-Xin Zou, Xiao-Xuan Liu, Shou-He Huang, Wen-Jie You, Ye He, Jun-Yu Zhang, Xiao-Dong Wang, & Bing-Xing Pan. (2020). Identification of a prefrontal cortex-to-amygdala pathway for chronic stress-induced anxiety. *Nature Communications*, *11*(1), 2221. https://doi.org/10.1038/S41467-020-15920-7

Wen, Z., Raio, C. M., Pace-Schott, E. F., Lazar, S. W., LeDoux, J. E., Phelps, E. A., & Milad, M. R. (2022). Temporally and anatomically specific contributions of the human amygdala to threat and safety learning. *Proceedings of the National Academy of Sciences*, *119*(26), e2204066119. https://doi.org/10.1073/pnas.2204066119

William Aubé, Arafat Angulo-Perkins, Isabelle Peretz, Luis Concha, & Jorge L. Armony. (2015). Fear across the senses: Brain responses to music, vocalizations and facial expressions. *Social Cognitive and Affective Neuroscience*, *10*(3), 399–407. https://doi.org/10.1093/SCAN/NSU067

William D.S. Killgore, Jennifer C. Britton, Zachary J. Schwab, Lauren M. Price, Melissa R. Weiner, Andrea L. Gold, Isabelle M. Rosso, Naomi M. Simon, Mark H. Pollack, & Scott L. Rauch. (2014). Cortico-limbic responses to masked affective faces across ptsd, panic disorder, and specific phobia. *Depression and Anxiety*, *31*(2), 150–159. https://doi.org/10.1002/DA.22156

Wu, Y., Besson, P., Azcona, E. A., Bandt, S. K., Parrish, T. B., Breiter, H. C., & Katsaggelos, A. K. (2022). A multicohort geometric deep learning study of age dependent cortical and subcortical morphologic interactions for fluid intelligence prediction. *Scientific Reports*, *12*(1), 17760. https://doi.org/10.1038/s41598-022-22313-x

Xu, P., Chen, A., Li, Y., Xing, X., & Lu, H. (2019). Medial prefrontal cortex in neurological diseases. *Physiological Genomics*, *51*(9), 432–442. https://doi.org/10.1152/physiolgenomics.00006.2019

Xu, X., Yun, J., Tang, T., Zhang, J., Lu, C., Salvi, R., & Teng, G. (2019). Sensorineural hearing loss and cognitive impairments: Contributions of thalamus using multiparametric MRI. *Wiley-Blackwell*, *50*(3), 787–797. https://doi.org/10.1002/jmri.26665

Yang, M., Tsai, S.-J., & Li, C.-S. R. (2020). Concurrent amygdalar and ventromedial prefrontal cortical responses during emotion processing: A meta-analysis of the effects of valence of emotion and passive exposure versus active regulation. *Brain Structure and Function*, *225*(1), 345–363. https://doi.org/10.1007/s00429-019-02007-3

Yen, C., Lin, C.-L., & Chiang, M.-C. (2023). Exploring the Frontiers of Neuroimaging: A Review of Recent Advances in Understanding Brain Functioning and Disorders. *Life*, *13*(7), 1472. https://doi.org/10.3390/life13071472

Yuan Zhou, Yuwen He, Yuening Jin, Peter Zeidman, Li-Fang Gao, Bei Rong, Huan Huang, Yuan Feng, Jianlei Cui, Shudong Zhang, Yun Wang, Gang Wang, Yu-Tao Xiang, & Huiling Wang. (2023). Amygdala connectivity related to subsequent stress responses during the COVID-19 outbreak. *Frontiers in Psychiatry*, *14*. https://doi.org/10.3389/fpsyt.2023.999934

Yuko Hakamata, Shotaro Komi, Yoshiya Moriguchi, Shuhei Izawa, Yuki Motomura, Eisuke Sato, Shinya Mizukami, Yoshiharu Kim, Takashi Hanakawa, Yusuke Inoue, & Hirokuni Tagaya. (2017). Amygdala-centred functional connectivity affects daily cortisol concentrations: A putative link with anxiety. *Scientific Reports*, *7*(1), 8313–8313. https://doi.org/10.1038/S41598-017-08918-7

Zhang, J., Su, J., Wang, M., Zhao, Y., Zhang, Q.-T., Yao, Q., Lu, H., Zhang, H., Li, G.-F., Wu, Y.-L., Liu, Y.-S., Liu, F.-D., Zhuang, M.-T., Shi, Y.-H., Hou, T.-Y., Zhao, R., Qiao, Y., Li, J., Liu, J.-R., & Du, X. (2017). The Posterior Insula Shows Disrupted Brain Functional

Connectivity in Female Migraineurs Without Aura Based on Brainnetome Atlas. *Scientific Reports*, *7*(1), 16868. https://doi.org/10.1038/s41598-017-17069-8

Zhang, R., Deng, H., & Xiao, X. (2024). The Insular Cortex: An Interface Between Sensation, Emotion and Cognition. *Neuroscience Bulletin*. https://doi.org/10.1007/s12264-024-01211-4

Zhiying Zhao, Or Duek, Rebecca Seidemann, Charles T. Gordon, Christopher Walsh, Emma Romaker, William N. Koller, Mark Horvath, Yao Wang, Erin O'Brien, Harlan M. Fichtenholtz, Michelle Hampson, & Ilan Harpaz-Rotem. (2023). Amygdala downregulation training using fMRI neurofeedback in post-traumatic stress disorder: A randomized, double-blind trial. *Translational Psychiatry*, *13*(1). https://doi.org/10.1038/s41398-023-02467-6

Zou, P., Hutchins, S. B., Dutkiewicz, R. M., Li, C.-S., & Ogg, R. J. (2005). Effects of EPI readout bandwidth on measured activation map and BOLD response in fMRI experiments. *NeuroImage*, *27*(1), 15–25. https://doi.org/10.1016/j.neuroimage.2005.01.004