Degree project

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# The Neural Correlates of Burnout: A Systematic Review

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## Abstract

Burnout is a condition that results from chronic work-related stress, and it is associated with impairments in cognitive and emotion-related functions, such as impaired executive functions and emotion regulation. This thesis aimed to conduct a systematic review of the neural correlates of burnout. The thesis investigates the following research question: do the neural correlates of burnout involve the same brain regions and/or functions as those implicated in the cognitive functions affected by burnout? The systematic literature search resulted in seven studies which studied either the functional, structural, or electrophysiological correlates of burnout. The results showed that burnout involves functional and structural alterations in regions involved in various higher-order cognitive functions. Structural findings indicate alterations in brain regions involved with emotion processing, memory and attention (i.e., medial prefrontal cortex, caudate, amygdala). Electrophysiological findings indicate differences in alpha power in burnout individuals compared to controls, suggesting that alpha power is reduced when burnout's specific symptoms (i.e., exhaustion) increase. Evident are also findings on functional differences in working memory (dorsolateral prefrontal cortex) and reduced functional connectivity between emotion processing areas (the amygdala and anterior cingulate cortex) and areas such as the motor cortex. The presented findings answer the research question. It can be concluded that the brain regions implicated in the cognitive functions affected by burnout resemble many of the regions affected in the neural correlates of burnout. Future studies should take into account the methodological issues of the existing studies.



*Keywords:* burnout, neural correlates, exhaustion, cynicism

## The Neural Correlates of Burnout: A Systematic Review

Burnout is a serious condition constituting a significant health risk for today's working-age population. It is estimated that 18% of the psychiatric diagnoses in Swedish women are caused by burnout and 46% of employees in America are highly affected by stress, to the extent of burnout (Försäkringskassan, 2020; Kalia, 2002). Burnout results from poorly managed work-related stress and it has been suggested that the latter is due to the rapid change in work-life in western countries (Ahola et al., 2006; Heinemann & Heinemann, 2017; WHO, 2019). It is the burden of high demands of flexibility, higher education and broader knowledge that affects the workers. Burned-out workers experience physical and mental problems, such as exhaustion, concentration difficulties, reduced capacity to work under time pressure, and emotional instability (Glise et al., 2020; Krabbe et al., 2017; Stenlund et al., 2012). Research has also shown that burnout is associated with the increased prevalence of various diseases, such as coronary heart disease (Toker et al., 2012).

Research interest in burnout has increased since the 1970s and today there is abundant literature on the phenomenon in occupational health psychology (Bakker & Costa, 2014) and clinical psychology (Schonfeld & Bianchi, 2016). Research regarding the cognitive consequences of burnout is also extensive and has demonstrated how burnout negatively affects executive functions such as memory and attention (Grossi et al., 2015). However, much less is known about the neural correlates of burnout, which could possibly help distinguish burnout from other similar disorders (e.g., depression).

### Definition of Burnout

Burnout was first described in 1974 by Herbert Freudenberger, causing the phenomenon to thrive and large numbers of burnout studies to get published (Heinemann & Heinemann, 2017). Even though burnout is a well-known phenomenon in organizations and workplaces as well as in the general population, the concept is still debated amongst researchers. Burnout is not included in the Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM–5; American Psychiatric Association, 2013). However, burnout is included in the International Statistical Classification of Diseases and Related Health Problems (ICD-11; World Health Organization, 2019) as an occupational phenomenon, though it is not a medical diagnosis. Burnout is defined as an occupational syndrome caused by chronic work-related stress and is characterized by three dimensions; feelings of exhaustion, mental distance from work and lack of professional efficacy (World Health Organization, 2019). Burnout has been studied for more than four decades, though a medical diagnosis or a clear agreed-on definition is still not evident. The reason for the ambiguity is the lack of consistency regarding the description of burnout which speaks for the need for a clarified definition (Heinemann & Heinemann, 2017; Maslach et al., 2001).

One definition of burnout describes it as a state of depletion of one's energy resulting from exposure to work-related stress. This state consists of physical fatigue, cognitive weariness (i.e., feelings of reduced mental agility), and emotional exhaustion (Melamed et al., 2006). However, the definition which has become the most dominant comes from Maslach et al. (2001), who state that burnout has three dimensions. The first dimension is exhaustion, which reflects long-term stress and causes people to withdraw from the stressor (i.e., work), both cognitively and emotionally. Cynicism or "depersonalization" refers to having a distant attitude towards work and is the second dimension that is often combined with exhaustion. Lastly, as a result of overwhelming negative feelings, comes a lack of professional efficacy (Maslach et al., 2001).

Despite different definitions, exhaustion is central to many definitions. Studies often use different terms to describe the feeling of being overwhelmed by negative aspects of work, e.g., "overstrain" or "fatigue". Some define burnout as not only being related to work-related stress, but instead a consequence of different demanding situations in life. However, the lack of a clear agreed-on definition causes uncertainty regarding the symptomatology of burnout and complicates the research (Grossi et al., 2015; Schaufeli & Enzmann, 2020). According to Heinemann and Heinemann (2017), there are only very few studies attempting to identify the biomarkers of burnout as a way to define burnout. Therefore, further scientific investigation on burnout is needed to clarify the concept. This is important due to the high prevalence and the resulting risk factors of burnout that negatively affect the working population (Heinemann & Heinemann, 2017).

## Assessing Burnout

There are several different instruments used to measure and identify burnout but these differ in how burnout has been conceptualized.

Since the 1980s, burnout has mainly been measured with the Maslach Burnout Inventory (MBI; see Appendix A). The first version of MBI, the MBI-Human Services Survey (Maslach et al., 2001), measures aspects of burnout based on interviews and questionnaires with employees in the human service sector, e.g., nurses, social workers, and psychologists. Professionals in the human service sector are intensely involved with clients and their associated problems which are thought to pose a risk for burnout (Maslach & Jackson, 1981). The inventory consists of 25 items which are written statements about attitudes and feelings. The scale contains three subscales: exhaustion (feelings of being emotionally drained by work), depersonalization (feelings of impersonality towards one's work tasks), and personal accomplishment (feelings of achievement in one's work). The inventory measures two dimensions of each statement, the frequency and intensity of feelings and situations (i.e., "how often have you felt this?" or "how strongly have you felt that?"; Maslach & Jackson, 1981).

Burnout later became apparent in other occupations, such as among police officers, the military force, and students (Heinemann & Heinemann, 2017), and a new version of the MBI was developed. MBI-General Survey (MBI-GS; Maslach & Jackson, 1981) measures "exhaustion, cynicism (a distant attitude toward the job), and reduced professional efficacy" (p. 402) but also includes personal relationships toward one's work and the work itself. Items are slightly revised to suit various occupations (Maslach & Jackson, 1981).

The Copenhagen Burnout Inventory (Kristensen et al., 2005) differs from MBI because it measures three burnout forms: personal burnout, work-related burnout, and client-related burnout. The scale of personal burnout is created so that everyone would be able to answer the questions: the employed/unemployed, pensioners, and young people. It is a generic scale with questions regarding personal feelings concerning burnout. The work-related scale measures symptoms related to work, which enables researchers to distinguish between work- and non-work-related factors. And lastly, the client-related burnout scale measures the extent to which employees' fatigue is associated with their work with clients (Kristensen et al., 2005).

The Oldenburg Burnout Inventory (OLBI; Halbesleben & Demerouti, 2005) assesses two dimensions: disengagement and exhaustion. OLBI includes questions assessing both physical and cognitive aspects of exhaustion, which extends the MBI and yields a broader understanding of burnout. OLBI is designed to be applicable for all occupations and is, therefore, a general inventory. One limitation is that it has not been used in many English-speaking studies (Halbesleben & Demerouti, 2005).

The problem with the existence of several measurement instruments in burnout research is the type of burnout they measure. Since there is no standard definition or classification of burnout, it may be that the questionnaires do not measure the same phenomenon. As a result, findings from studies using different instruments are difficult to compare (Heinemann & Heinemann, 2017). The lack of clarity and the use of different measurement instruments also causes more confusion surrounding the diagnosis (Heinemann & Heinemann, 2017; Maslach et al., 2001).

## Cognitive and Emotional Consequences of Burnout

Burnout is associated with impairments in cognitive and emotion-related functions. Disorganization and disturbances in concentration and memory are often described as worse in burnout subjects than in their age-matched peers, which could be associated with a high stress level (Rönnlund et al., 2013). An excessive level of stress relates to cognitive difficulties, causing the memory to be particularly affected in those with burnout, though it is not the only affected function (Rönnlund et al., 2013; Weber & Jaekel-Reinhard, 2000). The executive functions, episodic memory and attention are cognitive systems that, according to Deligkaris et al. (2014), are linked to burnout. The executive system is the cognitive control mechanism in the brain, and its main task is to modulate our cognitive processes (i.e., language, perception and attention). The functioning of the executive system is impaired in individuals with burnout and the dysfunction could show by an insufficient prepotent response (e.g., pain response; Deligkaris et al., 2014; Miyake et al., 2000). Individuals with burnout may also show dysfunction in episodic memory, resulting from cognitive impairment in the memory system. Overall, memory and attention lapses are highly experienced in burnout, which negatively affects the people experiencing these symptoms (Deligkaris et al., 2014; Rönnlund et al., 2013).

A theory conceived by Deligkaris et al. (2014) suggests that the working memory system could be the main impaired system in burnout. It has four components, the central executive, the visuospatial sketchpad, the episodic buffer and the phonological loop. These components have different roles, such as the phonological loop, which is involved in retaining information. The cognitive impairments mainly affect the more demanding functions, such as the central executive component (Deligkaris et al., 2014), which suggests that the more complex the function, the more vulnerable it is to chronic stress. The working memory system is connected to all the affected systems in burnout, i.e., the executive, attention and memory systems. This link could explain the association between cognitive impairments and burnout (Deligkaris et al., 2014).

Cognitive control deficits (CCD) such as errors in perception, self-regulation and memory can appear more regularly in burnout subjects. Diestel and Schmidt (2011) propose that employees with CCDs are more vulnerable to emotional labour and its harmful impacts, such as limited resource capacity. Emotional labour is described as regulating feelings in one's workplace. It is essential to be able to differentiate between expressed feelings versus felt emotions in some sectors (e.g., service sectors; working with other people). The ability is called emotional dissonance, which is a form of self-regulation. The emotional dissonance capacity could be limited in burnout subjects due to the possibility of impaired self-regulation, which would complicate the emotional aspect of one's work. The findings on CCDs causing emotional problems in burnout are supported by data from Golonka et al. (2017). They studied error monitoring; a component of behavioural regulation needed to adjust to situations. The study shows that CCDs might influence behavioural adjustments in burnout individuals. Other emotional symptoms in burnout are personality changes such as aggressiveness, lack of interest and drive, which could be connected to cynicism. Burnout could also affect private life in terms of social isolation, relationship problems, and a negative self-image (Weber & Jaekel-Reinhard, 2000).

As a result of cognitive and emotional impairments, both physical and mental health is affected in those suffering from burnout (Honkonen et al., 2006; Sapolsky, 1996). Burnout is associated with sleep problems, such as poor sleep, frequent awakenings, and fatigue during the day. Since sleep is vital for cognitive functions and emotion regulation (Saleh & Shapiro, 2008; Wagner et al., 2004), poor sleep can further worsen burnout. Besides negatively affected sleep, burnout subjects may have an increased risk of immune dysfunction, diabetes, allergies, and metabolic disorders (Grossi et al., 2015; Honkonen et al., 2006).

## The Neural Basis of the Cognitive Deficits of Burnout

The neurobiology of the cognitive impairments of burnout is highly associated with the brain's frontal regions. The prefrontal cortex (PFC), in particular, is the brain region regulating our higher-order cognitive abilities and has extensive connections with many other cortical and subcortical regions (Arnsten, 2009). The dorsolateral PFC (dlPFC) is connected to the motor and sensory cortices that regulate attention and thought. Event-related functional magnetic resonance imaging findings speak for the possibility of diminishing dlPFCs activity just by exposing a person to a stressor (e.g., a social stressor; Dolcos & McCarthy, 2006). The dlPFC is crucial for working memory which is highly affected in burnout subjects (Deligkaris et al., 2014). Chronic stress in burnout causes impairment in working memory, which is associated with dysfunction in PFC.

The structural architecture of the PFC network has also been suggested to be altered as a consequence of burnout. Animal studies suggest that this seems to be due to dendritic changes, such as decreased amount and length of dendrites (Radley et al., 2006). These changes are associated with impairments in working memory and attentional set-shifting (Arnsten, 2009). Magnetic resonance imaging (MRI) studies also show that the volume of the caudate and putamen are significantly smaller in burnout subjects (Gavelin et al., 2020)

The relationship between PFC and other brain regions is important for our cognition, where stress also causes disruptions. Between the hippocampus and PFC, a plastic relationship is required for flexible memory consolidation. The working memory is affected by burnout, suggesting that stress disrupts the relationship between the hippocampus and the PFC (Arnsten, 2009).

Impaired cognitive processes in the executive system are associated with frontal cortex dysfunction more generally. According to Sandström et al. (2005), both the prefrontal cortex and the hypothalamic-pituitary-adrenal (HPA) axis are linked to cognitive dysfunction due to chronic stress in burnout. Increased activity in the HPA axis is linked to cognitive dysfunction and other symptoms such as fatigue. Symptoms such as high stress led to stronger functional connectivity between the amygdala, thalamus and hypothalamus. The statement is supported by the finding of stress being the causal factor in the activation of HPA. Leading to connectivity between the amygdala and the paraventricular hypothalamic nuclei (Golkar et al., 2014).

Error monitoring, as well as the response evaluation process, is shown to be associated with the anterior cingulate cortex (ACC) and especially the dorsal ACC (Debener et al., 2005; Golonka et al., 2017). The ACC is a brain structure involved in response selection (i.e., choosing a response to stimuli) and regulation of affect (i.e., emotion/mood expression; Hajcak et al., 2004).

Electroencephalogram (EEG) studies show that burnout subjects indicate changed event-related potential patterns in error processing; decreased error positivity and enhanced error-related negativity amplitudes. The error processing is therefore impaired. The finding of ACC underlying error monitoring is supported by Golkar et al. (2014) where it is stated that the amygdala, mesial prefrontal cortex and ACC are needed to regulate emotional conflict. In burnout, these regions could be altered, causing impairments in emotional and behavioural regulation structures.

To conclude, burnout-related stress may cause disruption in emotion processing limbic networks as well as structural changes in cognitive control areas, i.e., thinning of grey matter volume in dlPFC, ACC, and mesial PFC. Structures such as the ACC risk being altered and stress may cause the activity in dlPFC to diminish. Due to dysfunction in dlPFC, higher-order executive functions such as working memory and attention are affected. Other regions involved in emotion regulation and error monitoring are also affected by this (i.e., ACC; Arnsten, 2009; Dolcos & McCarthy, 2006; Golkar et al., 2014). Amygdala is reported to have a key role in stress responses and the heavy stress caused by burnout could be problematic in that sense. Findings show that the amygdala's functional connectivity with e.g., ACC could be altered and impaired in burnout (Sandström et al., 2005).

## The Present Thesis

The current thesis aims to conduct a systematic review of the neural correlates of burnout. The existing literature brings much insight into the cognitive consequences of burnout, such as; impairments in attention, self-regulation and episodic memory (Deligkaris et al., 2014; Rönnlund et al., 2013). Existing research stresses the importance of shedding light on the underlying structural and functional changes in the brain to understand how the brain is affected by burnout. This could yield a broader understanding of the causal mechanisms of burnout and more certainty regarding its symptoms. Due to the negative impact burnout has in our society, a more precise description of burnout, its characteristics and how it differs from other stress-related conditions, is needed since it will help tackle the problem (Blix et al., 2013; Deligkaris et al., 2014). The thesis will investigate the research question: Do the neural correlates of burnout involve the same brain regions and/or functions as those implicated in the cognitive functions affected in burnout?

# Methods

## Search Strategy

A literature search was conducted in the databases Web of Science, Medline EBSCO and PubMed on the 15th of February 2022. In Medline EBSCO and PubMed, the following keyword string was used: ("burnout") AND ((ERP OR "event-related potential*") OR (EEG OR "electroencephalography") OR ("magnetic resonance imaging" OR MRI) OR ("functional magnetic resonance imaging" OR fMRI) OR (PET OR "positron emission tomography") OR (DTI OR "Diffusion tensor imaging") OR (MEG OR "Magnetoencephalography")). On Web of Science, another keyword string was applied: (TS=("burnout")) AND ALL= ((ERP OR "event-related potential*") OR (EEG OR "electroencephalography") OR ("magnetic resonance imaging" OR MRI) OR ("functional magnetic resonance imaging" OR fMRI) OR (PET OR "positron emission tomography") OR (DTI OR "Diffusion tensor imaging") OR (MEG OR "Magnetoencephalography")).

In total N=312 articles were found using the above-mentioned databases and manually added articles were included from reference lists during the initial search (see Figure 1). All articles were imported to Rayyan, a web and mobile app made for conducting systematic reviews (Ouzzani et al., 2016). Articles were then screened by excluding and including articles with reason, see Figure 1 for further details on exclusion etc.

## Inclusion and Exclusion Criteria

The inclusion criteria included a) Studies with participants with average to high scores on burnout scales (i.e., burnout, due to work-related stress), b) Adults (i.e., at least 18 years old), c) Both healthy and clinical populations, d) Controls are healthy, with low or no scores on burnout scales (i.e., no burnout), e) Empirical and peer-reviewed articles written in English, (f) Included studies use different brain imaging techniques, such as structural neuroimaging (MRI, DTI), functional neuroimaging (fMRI, PET) and electrophysiological recordings (EEG, ERP, MEG).

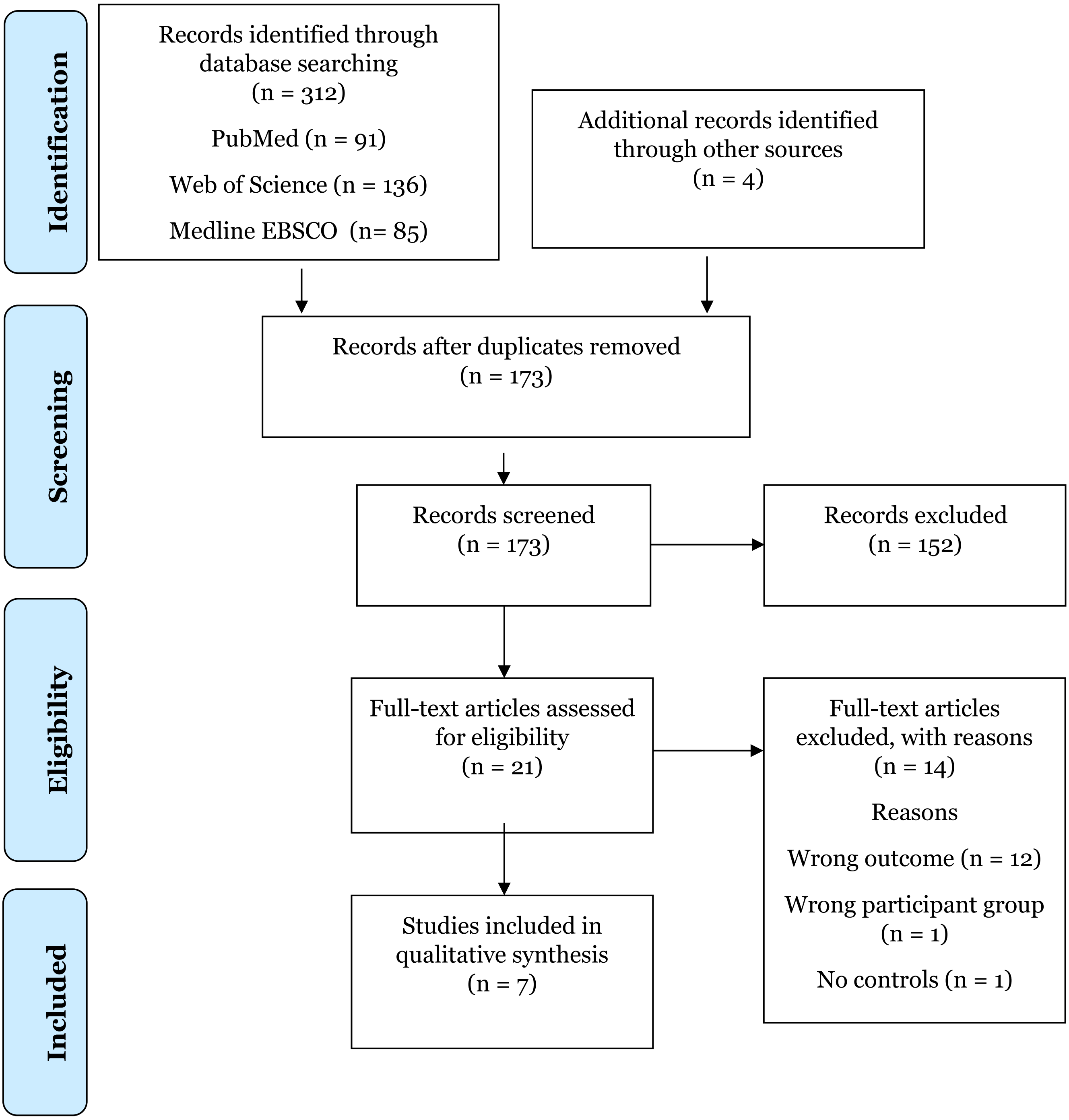
The exclusion criteria were studies in which a) participants have used drugs that could affect brain function or structure, b) methods not mentioned in the inclusion criteria.

## Data Extraction

The outcome measures of the systematic review are the structural and functional brain changes in burnout. The data extracted from the articles are; first author, publication year, sample characteristics (size, sex, mean age, health), type of burnout scale, task description, and study design.

**Figure 1**

PRISMA 2009 Flow Diagram




*Note*. The process of the literature search, PRISMA 2009 Flow Diagram (Moher et al., 2009).

# Results

## Study Characteristics

The descriptive information of the included studies is presented in Table 1. The total number of participants in all studies was N = 573 of which 66% were female and the mean age ranged from 19 to 55. All studies included healthy controls and all subjects were either diagnosed with "reaction to severe stress, and adjustment disorder" in accordance with the International Classification of Diseases (ICD-10, F43) or experiencing symptoms of exhaustion syndrome/stress reaction due to work. Only two studies matched their participant groups for socioeconomic status (i.e., years of education, occupation and position; Golkar et al., 2014; Savic, 2015). These two studies as well as two others also included similar gender distributions (Blix et al., 2013; Savic et al., 2018).

The majority of studies used a between-subjects design i.e., comparing the burnout group with the healthy control group (Blix et al., 2013; Golkar et al., 2014; Golonka et al., 2019; Jovanovic et al., 2011; Sandström et al., 2012; Savic, 2015). Only one study had a mixed design i.e., using both between-subjects and within-subjects designs. Savic et al. (2018) compared burnout subjects with controls but they also carried out a longitudinal test where only the burnout subjects were treated with cognitive therapy.

MBI-GS was the most used scale to measure burnout (Blix et al., 2013; Golkar et al., 2014; Savic, 2015; Savic et al., 2018). One study used the Polish version of MBI-GS and the Areas of Worklife Survey scale (AWS; Golonka et al., 2019). Two studies used the Shirom Melamed Burnout Questionnaire (SMBM) which tests exhaustion, as well as attention, memory and anxiety problems (Melamed et al., 1992). One of the studies used MBI-GS simultaneously with SMBM (Jovanovic et al., 2011; Sandström et al., 2012).

Four studies used MRI as the neuroimaging method (see Table 2). In one study the authors used voxel-morphometry with (1) the whole brain as a search space to discover regional white matter and grey matter changes and (2) restricted areas thought to be involved in stress regulation. Structural volumetry analyses were used on structures with poor white and grey matter distinction such as basal ganglia (Blix et al., 2013). The two other MRI studies imaged cortical thickness and subcortical volumes (Savic, 2015; Savic et al., 2018). The fourth MRI study analyzed structural images of the whole brain and hippocampal volume. Hypothesized functional changes in the binding potential to the 5-hydroxytryptamine (5-HT) receptor in specific regions in burnout subjects were also investigated and conducted with PET images focusing on the amygdala, hippocampus and insular cortex etc., (Jovanovic et al., 2011).

Two studies investigated functional correlates of burnout using fMRI. One of those used region-of-interest analysis of the left and right amygdala (Golkar et al., 2014). The second study used whole-brain analysis (without region of interest) in relation to subjects performing two cognitive tasks (i.e., the *n*-back task and a visual long-term memory task; Sandström et al., 2012).

Finally, one study used resting-state EEG to study the electrophysiological correlates of burnout. The brain electrical activity was measured in three minutes separately for both conditions i.e., eyes-open and eyes-closed. The study aimed to analyze differences in resting-state EEG in the mentioned conditions and to investigate the alpha and beta power in the burnout group versus controls (Golonka et al., 2019).

**Table 1**

*Individual Study Characteristics*

| Author | Participants | Health | Mean age (SD) | Study Design | Burnout Scale | Task description |
|---|---|---|---|---|---|---|
| Blix et al., 2013 | N=98 (76 females) Nationality: Swedish | Subjects: diagnosed (severe stress due to work) Controls: healthy | Subjects: 41.3 (6.6) Controls: 37.5 (7.2) | Between subjects | MBI-GS. Average score: Subject's >3.0 Controls: 2 | No task |
| Savic, 2015 | N=80 (40 females) Nationality: Swedish | Subjects: diagnosed (severe stress due to work) Controls: healthy | Subjects: 38 (6) Controls: 36 (6) | Between subjects | MBI-GS. Average score: Subject's >3.0 Controls: 2 | No task |
| Savic et al., 2018 | N=128 (76 females) Nationality: Swedish | Subjects: symptoms of occupational exhaustion syndrome (ES) Controls: healthy | Subjects: 38 (6) Controls: 32 (7) | Between subjects, within-subjects | MBI-GS. Average score: Subject's >3.0 Controls: 2 | No task |
| Golkar et al., 2014 | N=110 (72 females) | Subjects: diagnosed | Subjects: 38 (6) | Between subjects | MBI-GS. | Emotion regulation |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Nationality: Swedish | (severe stress due to work) Controls: healthy | Controls: 33 (6) | | Average score: Subject's >3.0 Controls: 2 | task: upregulate, maintain, down-regulate emotion |
| Jovanovic et al., 2011 | N=32 (22 females) Nationality: Swedish | Subjects: diagnosed (severe stress due to work) Controls: healthy | Subjects: 38 (5) Controls: 34 (9) | Between subjects | MBI-GS, SMBM. Average score: Subject's >3.0 (MBI-GS), >4.6 (SMBM) Controls: 2 (MBI-GS), 4 (SMBM) | Digits span test, Three-back verbal working memory test, Verbal encoding and retrieval test |
| Sandström et al., 2012 | N=30 (10 LTSL, 10 depression, 10 controls). Nationality: Swedish | Subjects: diagnosed (severe stress due to work) Controls: healthy | Subjects (LTSL): 37.3 (4.1) Subjects (depression): 25.2 (3.6) Controls: 29.2 (2.5) | Between subjects | SMBM. Average score: Subject's >4.6 Controls: 4 | The n-back task – working memory. Visual long-term memory task – continuous recognition task |
| Golonka et al., 2019 | N=95 (57 females) Nationality: Polish | Subjects: not diagnosed Controls: healthy | Total: 36.14 (7.89) | Between subjects | MBI-GS. (Polish version). Average score: Subject's >3.0 Controls: 2 | Eyes open - focus on the fixation point. Eyes closed – sit still, eyes closed |

*Note*. Lines separating the studies into groups indicate their neuroimaging method, see Table 2. LTSL= long term sick leave. SD= standard deviation. MBI-GS= Maslach burnout inventory-general survey (Maslach & Jackson, 1981). SMBM= Shirom Melamed burnout questionnaire (Melamed et al., 1992).

## Structural Brain Correlates in Burnout

Three studies investigated mainly structural brain alterations in burnout (see Table 2). Blix et al. (2013) found that burnout subjects had significantly lower structural volume in their bilateral caudate and putamen compared with controls. The observation is partly supported by Savic (2015) and Savic et al. (2018) who showed that the caudate is bilaterally smaller in burnout subjects than in matched controls. The reduced caudate volume was negatively correlated with the MBI-GS scores of exhaustion, indicating that a reduced caudate volume implies a higher level of burnout (Blix et al., 2013; Savic, 2015; Savic et al., 2018).

Contrary to the alterations found in the putamen by Blix et al. (2013), Savic (2015) reported no significant differences in the structural volume of the putamen between the burnout and healthy control groups. Neither were there any differences in the hippocampus, cerebellum or thalamus (Savic, 2015). However, in Savic et al. (2018) the right amygdala volume was significantly larger in burnout subjects and the caudate volume was smaller than in controls. Moreover, there was a positive correlation between the scores of MBI-GS and the amygdala volume. MBI-GS scores and the volume of the amygdala are therefore thought to be associated (Savic, 2015; Savic et al., 2018).

Burnout subjects also showed a thinner cortex in the right PFC, more specifically the inferior frontal, opercular, bilateral subgenual cortices, as well as in the left superior temporal gyrus (STG). The thinning of these regions was found to correlate with the score of MBI-GS inversely (Savic et al., 2018). Additionally, reduced grey matter volume in the medial prefrontal cortex (mPFC; Savic, 2015), the ACC and the right and left middle frontal gyrus, (Blix et al., 2013) were reported. Regarding the brain being greatly impacted by the structural alterations caused by burnout, it is stated that age could be negatively correlated with the alterations in mainly the frontal and parietal lobes. The correlation was significantly stronger among the burnout subjects, an indication of the impact of stress on the structure of the brain (Savic, 2015).

## Functional Brain Correlates in Burnout

Three studies investigated functional brain changes in burnout. Sandström et al. (2012) measured brain activity during the n-back task and the visual long-term memory task with fMRI. Results showed reduced activation in prefrontal regions during the *n*-back task, a working memory task. Mainly the left ventrolateral cortex and the dlPFC showed a lesser degree of activation in a burned-out brain than in healthy controls. These findings indicate that burnout subjects involve fewer regions in the prefrontal cortex during working memory usage. Additionally, it was found that the frontoparietal network was highly activated during the n-back task in both burnout and controls.

Whereas in the visual long term memory task the temporal polar and dorsal occipital regions were more involved in burnout subjects and controls. Results show similarities in that a large amount of the functional networks in burnout subjects still function in the same way as in controls. Though, in burnout subjects, the prefrontal cortex showed reduced activation during e.g., n-back task, unlike controls (Sandström et al., 2012).

Golkar et al., (2014) found significantly weaker functional connectivity between the right and left amygdala and clusters in the dlPFC, the mPFC, and the motor cortex in burnout subjects. However, burnout subjects' functional connectivity was more robust with clusters of the anterior cerebellum, the insular cortex and vermis cerebelli than in controls. The MBI-GS scores were positively correlated with activity in the left amygdala, the insular cortex and the thalamus functional connectivity (Golkar et al., 2014). Reduced functional connectivity between the amygdala and mPFC is problematic due to the involvement of this network in emotion and stress regulation. Burnout subjects also showed a significantly higher startle response during the down-regulation of negative emotions. This indicates that emotion regulation, especially the regulation of negative emotions, is impaired in those who experience burnout.

Jovanovic et al. (2011) tested 5-HT 1A receptor binding in burnout subjects and did not find significantly reduced 5-HT 1A receptor binding in the amygdala in the burnout group as compared to the healthy controls. The finding was surprising due to the amygdala's involvement in stress perception. Instead, the ACC, hippocampus and the insular cortex demonstrated significant reductions in 5-HT 1A receptor BP (Jovanovic et al., 2011).

## Electrophysiological Correlates of Burnout

Only one study investigated the electrophysiological correlates of burnout using EEG. Specifically, Golonka et al. (2019) analyzed the alpha frequency band (8.5-13.0 Hz) during two conditions; eyes open and eyes closed. Significantly lower alpha power was measured in the eyes open condition in the burnout group as compared to controls indicating cortical hyperactivity which can be seen in e.g., fatigue and depression.

The analysis also showed a negative correlation between alpha power and exhaustion and cynicism. A significant negative correlation was found between alpha power and exhaustion in the eyes-open condition for the global central (-0.2598), global anterior (-0.2952) and posterior regions (-0.3050; i.e., correlation is presented for the global effect, left and right of all areas). A significant negative correlation between alpha power and the closed-eyes condition was only found in the central left (-0.2184), anterior (-0.2130; globally), posterior global (-0.2139) and left areas (-0.2250). A significant negative correlation was detected in the eyes open condition between alpha power and cynicism over the posterior areas for both right (-0.2583) and left (-0.2818) sides and the global anterior regions (-0.2761; Golonka et al., 2019). No significant effects were found for beta, delta, or theta bands.

**Table 2**

*Structural, Functional and Electrophysiological Correlates of Burnout*

| **Study** | **Neuroimaging Method/Analysis** | **Results (Burnout vs Controls)** |
|---|---|---|
| Structural neuroimaging correlates (Volume) | | |
| Blix et al., 2013 | MRI, VBM, VOI = hippocampus, caudate, putamen | Caudate ↓<br>Putamen ↓<br>ACC ↓<br>dlPFC ↓<br>Basal ganglia ↓<br>Hippocampus NS<br>Amygdala NS |
| Savic, 2015 | MRI, VOI/TIV = thalamus, cerebellum, amygdala, hippocampus, basal ganglia | Amygdala ↑<br>Caudate ↓<br>Hippocampus NS<br>Putamen NS<br>Thalamus NS<br>Cerebellum NS |
| Savic et al., 2018 | MRI, VOI/TIV = amygdala, hippocampus, caudate, putamen | Right amygdala ↑<br>Caudate ↓<br>Hippocampus NS<br>Putamen NS |
| Functional neuroimaging correlates (Functional connectivity/Activity/+ PET results BP) | | |
| Golkar et al., 2014 | fMRI, ROI = left and right amygdala | **Connectivity between the amygdala and:**<br>mPFC ↓<br>dlPFC ↓<br>Motor Cortex ↓<br>Cerebellum ↑<br>Insular Cortex ↑ |
| Jovanovic et al., 2011 | (MRI), PET, Whole brain volumes, VOI = amygdala, hippocampus, insular cortex, the temporal neocortex, dlPFC, the orbitofrontal and parietal cortex, raphe nuclei, cerebellum, mPFC (BA10) | **BP**<br>Hippocampus ↓<br>ACC ↓<br>Insular cortex ↓<br>Amygdala NS<br>dlPFC NS<br>Parietal cortex NS<br>Temporal cortex NS<br>Orbitofrontal cortex NS<br>Cerebellum NS<br>Raphe nuclei NS |

| | | |
|---|---|---|
| Sandström et al., 2012 | fMRI, whole brain analysis | **n-back task:**<br>Left ventrolateral PFC ↓<br>Left dlPFC ↓<br>**CVMT:**<br>Temporal polar, dorsal occipital regions ↑<br>Left middle occipital ↑ |
| Electrophysiological correlates | | |
| Golonka et al., 2019 | EEG, Alpha band power | CE = ↑ ($\alpha$ dB)<br>OE = ↓ ($\alpha$ dB)<br>$\alpha$ + exhaustion (OE) = negative correlation<br>$\alpha$ + exhaustion (CE) = sig correlation<br>$\alpha$ + cynicism (OE) = negative correlation |

*Note.* Results demonstrate differences in burnout as compared to healthy controls. ↓ shows reduced volume/activity/connection. ↑ shows increased volume/activation/connection. VBM=Voxel-Based Morphometry. ROI=Region of interest. VOI=Volume of interest. TIV=Total intracranial volume. BP=Binding potential. $\alpha$ dB=Alpha power. BA10=Brodmann areas 10. GM=grey matter. NS=not significant. Sig=significant. ACC=Anterior cingulate cortex. dlPFC=dorsolateral prefrontal cortex. mPFC=mesial prefrontal cortex. OE=Open eyes condition. CE=Closed eyes condition. MRI=Magnetic resonance imaging. fMRI=functional magnetic resonance imaging. EEG=Electroencephalography. PET= Positron emission tomography.

## Discussion

The aim of this thesis was to conduct a systematic review on the existing literature on the neural correlates of burnout. The research question was whether the neural correlates of burnout involve the same brain regions and/or functions as those implicated in the cognitive functions affected in burnout.

Burnout is associated with impairments in higher-order cognitive abilities, such as working memory and attention (Arnsten, 2009; Deligkaris et al., 2014). Research suggests that these impairments are associated with alterations in the PFC, especially the dlPFC (Deligkaris et al., 2014). Results of this systematic review showed that the cortex in the right PFC (e.g., the inferior frontal cortices) is thinner in burnout subjects and negatively correlated with MBI-GS scores (Savic et al., 2018). The mPFC and the right and left frontal gyrus are other regions of the PFC in which the grey matter volume is reduced in burnout as compared to controls (Blix et al., 2013; Savic, 2015). It has been argued that these differences in PFC may have been caused by stress (Arnsten, 2009; Deligkaris et al., 2014).

Stress regulation, emotion and motivation are functions often affected in a burnout subject, and these have been shown to be related to the caudate and the putamen (Blix et al., 2013). Findings on regions implicated in the cognitive functions in burnout showed evidence of how both regions are significantly smaller in individuals with burnout (Gavelin et al., 2020). Blix et al. (2013) report resembling evidence stating that the volumes of the caudate and the putamen were smaller in burnout, while Savic (2015) and Savic et al. (2018) only reported the reduction of the caudate in burnout individuals.

Burnout is also associated with problems in emotion regulation, a function that relies on ACC (Debener et al., 2005; Golonka et al., 2017). Indeed, Jovanovic et al. (2011) found that the ACC, amongst others, is affected in burnout subjects. Specifically, the ACC had significant reductions in 5-HT 1A receptor binding potential in burnout subjects. The activity reductions in ACC were negatively correlated with stress, suggesting that the degree of stress and reduction of the 5-HT 1A receptor is related. The interaction between stress and 5-HT 1A receptor has earlier been reported in animal experiments and gives an insight into stress and its effects on the brain (Jovanovic et al., 2011).

Emotion regulation involves the down-regulation of the amygdala by the prefrontal cortical areas (Sandström et al., 2005). Stress has been shown to affect functional connectivity between the amygdala and prefrontal regions in burnout subjects (Golkar et al., 2014). Findings indicate a reduced connection between the dlPFC, motor cortex, mPFC and the amygdala. Though the functional connection between the ACC and amygdala is still intact. The amygdala is also found to be significantly larger in burnout subjects than in controls and the volume was positively correlated with MBI-GS scores (Savic, 2015; Savic et al., 2018). Amygdala is involved in the processing of emotions, especially negative emotions and stress. The finding seems to suggest an elevated need of emotion processing, due to the prolonged/severe stress which causes enlargement of the amygdala structure.

EEG studies on alpha power is of interest due to the arousal patterns which could be demonstrated in relation to different burnout characteristics such as exhaustion (Golonka et al., 2019). Findings showed a negative correlation between alpha power and exhaustion for posterior regions and a negative correlation between the alpha and cynicism for the global anterior regions etc. Golonka et al. (2019) also report that the reduced alpha power in burnout subjects suggests that cortical activity was hyperactive which could be a characteristic for burnout. This could be associated with a compensatory effort that burnout individuals are developing while trying to keep up a good performance. The burned-out brain is working hard to still function properly.

Burnout individuals experience cognitive dysfunctions daily and according to the findings above, the condition is associated with alterations in brain areas involved in these functions.

## Methodological Issues of Studies

A major limitation in some of the studies (Jovanovic et al., 2011; Sandström et al., 2012) was that the participant groups (burnout vs. controls) were not gender-or age-matched, nor matched by socioeconomic status. This could introduce a bias. If participants differ in their employment status and education level it may imply that the resulting differences in the structural and functional brain correlates between burnout individuals and controls may be due to these underlying differences and not due to burnout itself. To eliminate such biases future studies should match participants based on socioeconomic statuses such as occupation and education level.

The fact that the majority of the included studies used MBI-GS to measure burnout is a strength due to its consistent definition of burnout and its symptoms. However, Sandström et al. (2012) used only SMBM (Melamed et al., 1992), while Jovanovic et al. (2011) used SMBM additionally to MBI-GS. The problem with using different burnout scales across different studies is that these scales do not necessarily measure the same aspects of burnout, which makes it difficult to compare the results. Future studies need to make a more consistent use of the scales to measure burnout.

It is also worth mentioning that all studies were conducted in Sweden, except one in Poland (Golkar et al., 2014). This means that all studies are based on western, educated, industrialized, rich and democratic (WEIRD) samples making the results limited to only a few populations (Henrich et al., 2010). The generalizability is even lower due to the large number of studies based in Sweden, which only show findings from one population of people. The standard of living in Sweden could differ from many other countries in the western world as well as the rest of the world. In future studies, it would be important to study burnout also in other countries and cultural contexts to investigate the possible differences in neural correlates.

Another possible limitation is the number of participants in some of the studies. The greatest number of participants was N=128 (Savic et al., 2018), while Sandström et al. (2012) included only N=10 burnout participants. Studies with few participants are less generalizable and the true effect is harder to find (Brysbaert, 2019). Researchers should consider the number of participants in the study and eventually include more participants.

A limitation in this systematic review is the low number of earlier studies on the neural correlates of burnout. The use of different neuroimaging methods in the existing studies is a limitation as well. Different methods and analyses used make it difficult to compare the studies.

## Societal and Ethical Aspects

All studies included in this review included only adult participants, followed the ethical guidelines and asked participants to give written consent, which indicates adequate ethical standards. On a societal level, research on the neural correlates of burnout could lead to the development of necessary interventions, support preventative work and raise more awareness of the condition and its adverse consequences in society. Burnout is affecting the brain in many ways and the need for a deeper understanding is evident to be able to handle the consequences and decrease its occurrence.

## Conclusion

The aim of this thesis was to investigate the neural correlates of burnout. Results showed that the neural basis of burnout involves structural and functional alterations in the same brain regions as those affected in the cognitive functions impaired in burnout. Structural changes are reported in brain areas involved in e.g., attention, memory and emotion processing (i.e., mPFC, STG, caudate and the amygdala). As well as functional differences in working memory (dlPFC), and reduced functional connectivity between brain areas regulating stress and behaviour (the ACC and the amygdala) and other regions such as the motor cortex involved with bodily movements. EEG findings showed that symptoms of burnout, such as exhaustion, were negatively correlated with alpha power, indicating that the frequency patterns are changed in the brains of burnout individuals. In order to limit the structural and functional impact on brain regions and functions, it is important to proceed with the research on neural correlates of burnout. Further research could also contribute to a final definition of burnout which is needed for reliable results and to make the research field more confident. Future studies should take into account the methodological issues of the existing studies.

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# Appendix A

Format of Maslach Burnout Inventory

| | | A few times a year | Monthly | A few times a month | Every week | A few times a week | Every day |
|---|---|---|---|---|---|---|---|
| Never | How often: | 1 | 2 | 3 | 4 | 5 | 6 |

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| How strong: | Very mild, barely noticeable | | | Moderate | | | Very strong, major |