Bachelor Degree Project

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SLEEP DEPRIVATION AND EMOTIONAL REACTIVITY

A Systematic Review

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Abstract

Sleep has become less important in western society during modern times, where many have the habit of prioritizing productive activities instead of sufficient sleep. However, recent studies have indicated the importance of sleep for emotional processing. A crucial finding in literature regarding sleep and emotions has been the enhancement of negative emotions after sleep deprivation. The aim of this systematic literature review was to investigate the neural basis of the effects of sleep deprivation on emotional reactivity. In order to conduct this review, three databases were used to obtain relevant articles. Out of the total 1041 articles, 11 fulfilled the inclusion criteria and were included in the review. The selected articles exclusively contained results regarding reactivity to visual emotional stimuli. Results showed that total and partial sleep deprivation result in enhanced amygdala activity in response to negative stimuli. Enhanced amygdala activity was also found in response to positive and neutral stimuli after sleep deprivation. The insula was another brain region that displayed enhanced activity toward all types of valenced stimuli after sleep deprivation. Moreover, weaker connectivity between the amygdala and prefrontal areas (specifically the medial prefrontal cortex) was found after total and partial sleep loss. Together, these results suggest that sleep deprivation induces hyperreactivity toward emotional stimuli and disrupts top-down regulation of emotional reactivity.

Keywords: Emotional reactivity, sleep deprivation, emotional stimuli, sleep loss, neural, brain

Table of Contents

Introduction

A growing body of evidence has emerged during recent years which suggest that sleep plays an important role in emotional processing (Tempesta et al., 2019). However, sleep has become less important for people in the western world during modern times. These days, many have the habit of prioritizing work or doing other productive activities instead of spending time getting adequate sleep (Basner et al., 2007).

The effects of sleep loss have been shown to be detrimental for our emotional well-being, where even one night of sleep deprivation is known to make us feel substantially more stressed, angry, and anxious (Minkel et al., 2012). Research on sleep deprivation and emotions has been gaining increasingly more attention. A key finding in the literature on sleep and emotions is the increase of negative emotions after sleep deprivation. For instance, it has been reported that one week of sleep deprivation, with less than 5 hours of sleep each night, increases emotional disturbance (Dinges et al., 1997). Furthermore, chronic sleep loss makes us feel more negative emotions toward adverse events, and less positive emotions toward pleasant events (Zohar et al., 2005).

While several behavioural studies have investigated the effects of sleep deprivation on emotional processing, relatively few studies have tried to discover the underlying brain mechanisms. One of the first known studies to explore the neural mechanisms of sleep deprivation on emotional processing was conducted by Yoo and colleagues (2007a). It was found that the amygdala showed an exaggerated response to negative emotional stimuli following one night of sleep deprivation (Yoo et al., 2007a).

There are important insights to gain from discovering the underlying brain mechanisms of how sleep deprivation affects emotional processing. First and foremost, studies on this subject can provide valuable knowledge to the research on psychopathology and well-being. For example, research that has investigated the effects of sleep deprivation on psychopathological symptoms in healthy adults suggests that a total of two nights without sleep lead to increased symptoms of emotional psychopathology, including anxiety and depression (Kahn-Greene et al., 2007).

The aim of this thesis is to conduct a systematic literature review on the neural basis of the effects of sleep deprivation on emotional reactivity, more specifically, on the processing of emotional stimuli. The focus is on studies that have used either functional magnetic resonance imaging (fMRI), positron emission tomography (PET), or near infrared spectroscopy.

This thesis will first present a background on sleep, the role of sleep in emotional processing, and emotional reactivity during sleep deprivation. Next, a method section will be presented about how the review was conducted, followed by a result section summarizing all the findings from the selected studies. Finally, a discussion will be presented that will discuss the results based on different conditions of sleep deprivation.

Sleep

Sleep Stages

Sleep in humans, as well as in other mammals, can be divided into two main states: rapid-eye movement (REM) sleep and non-rapid-eye movement (NREM) sleep. Whereas REM sleep consists of only one stage, NREM sleep consist of three stages (N1, N2, and N3), with each stage representing increased depth of sleep (Iber et al., 2007). In the human sleep cycle, REM and NREM sleep alternate in an ultradian rhythm every 90 minutes. Although the length of the REM-NREM cycle remains mostly stable during the sleeping period (i.e., night), the ratio of REM to NREM sleep changes every cycle. This means that NREM sleep, specifically N3 stage, dominates in the early night period, whereas REM sleep dominates in the late night (or early morning) period. However, the reasons for the organisation of sleep stages (late stages of NREM in the early sleeping phase, and REM with early NREM stage in the late sleeping phase) remain undiscovered (Walker & van der Helm, 2009). Adults sleep approximately 75% to 80% in NREM stages, and about 20% to 25% in REM stage. In NREM sleep, N1 is approximately 2% to 5% of sleep, whereas N2 is approximately 45% to 55% of sleep, and N3 is approximately 13% to 23% of sleep. Adults begin in NREM sleep, which progresses from N1 to N2, and lastly N3. The first REM stage occurs approximately 80 to 100 minutes later, and thereafter the episodes of REM appear approximately 90 minutes after NREM sleep (Carskadon & Dement, 2011).

REM sleep is characterized by muscle atonia, tonic/phasic events, and episodes of rapid-eye movements. A phasic event of REM sleep is depicted on the electroencephalography (EEG) when rapid-eye movements occur, whereas the tonic events of REM sleep illustrate the intervals between the rapid-eye movements. It is also during REM sleep when the brain is most activated and when dreaming is typical, whereas the body is paralyzed. In contrast, NREM sleep is characterized by a less active brain in a movable body. In NREM sleep, there are three different waveforms that are visible on the electroencephalogram: sleep spindles, K-complexes, and high-voltage slow waves. NREM stages have the lowest arousal thresholds during the first stage (N1). The highest arousal thresholds occur during the third stage (N3), a stage also referred to as slow wave sleep (SWS) (Carskadon & Dement, 2011).

Functional Neuroanatomy of Sleep

All sleep stages in REM and NREM are related to dramatic changes in functional brain activity. In particular, neuroimaging studies have revealed that during REM sleep there is increased activity in cortical and subcortical brain regions associated with emotions, including the insula, medial prefrontal cortex (MPFC), amygdala, hippocampus, and striatum (Dang-Vu et al., 2010; Goldstein & Walker, 2014; Miyauchi et al., 2009). Other brain areas have also been reported to be activated during REM sleep, including the occipital cortex, pontine tegmentum, thalamic nuclei, and mediobasal prefrontal lobes. However, during NREM and in particular SWS, temporal lobe, thalamus, brain stem, basal ganglia, and prefrontal areas a significantly decreased activity. In comparison, during REM sleep, decreased activity has been found in the parietal cortex, posterior cingulate cortex, and dorsolateral prefrontal cortex (DLPFC) (Walker & van der Helm, 2009).

Sleep and Emotional Processing

The Role of Sleep in Emotional Memory Processing

Several studies have investigated the role of sleep in regards to emotional memory processing, and in particular emotional memory encoding and emotional memory consolidation.

In experimental literature, studies on the impact of sleep on memory have been represented in two stages: before learning (encoding memory) and after learning (memory consolidation). Before learning, describes the initial formation (encoding) of new information, whereas after learning, describes the long-term solidification (consolidation) of new memories (Walker & van der Helm, 2009).

Sufficient sleep before learning has been shown to benefit memory encoding of episodic information (Van der Werf et al., 2009). In contrast, sleep deprivation before learning has shown to impair the ability for successful episodic memory encoding (Yoo et al., 2007b). Furthermore, research has also investigated the effects of sleep on emotional memory encoding. In a study conducted by Kaida and colleagues (2015), it was found that total sleep deprivation (i.e., avoidance of sleep for at least one night) impaired the ability to encode emotional information, whereas REM sleep deprivation (i.e., avoidance of REM sleep) did not affect emotional memory encoding.

Memory consolidation appears to be greatly affected by emotions. Although neutral memories become more difficult to remember over time (Frankland & Bontempi, 2005), emotional memories seem to be easier to remember (LaBar & Cabeza, 2006). Evidence has also emerged that indicates the important role of sleep in long-term consolidation of emotional memories (Holland & Lewis, 2007). For instance, Wagner and colleagues (2006) demonstrated that emotional memories after four years were better remembered by sleep-rested subjects compared to sleep-deprived subjects.

Sleep Deprivation and Emotional Reactivity: Behavioural Studies

There are different theories about the function of sleep on emotional processing. This review will focus on emotional reactivity, and more specifically how it is affected by sleep deprivation.

According to behavioural studies, partial sleep deprivation (i.e., less sleep than normal) has been linked with increased emotional disturbance following one week of restricted sleep (Dinges et al., 1997). Moreover, the effects of partial sleep deprivation have revealed an increase of negative emotions in experiencing adverse events, and dampened increase of positive emotions in experiencing pleasant events (Zohar et al., 2005).

In terms of one night of total sleep deprivation, it has been linked with greater subjective reports of anxiety, anger, and stress in response to mildly stressful situations (Minkel et al., 2012). It has also been reported that one night of sleep loss leads to increased impulsivity to negative stimuli (Anderson & Platten, 2011).

One night of sleep loss has also shown to affect emotional evaluation. Tempesta and colleagues (2010) reported that subjects perceived neutral pictures as more negative after sleep deprivation. In contrast, no significant effects of sleep deprivation were found in regards to positive and negative stimuli.

Method

The research question that was addressed in this systematic review was how sleep deprivation affects emotional reactivity with a focus on the neural mechanisms underlying these effects.

Database Sources and Searches

In the initial phase of conducting this review, the first step was to search for research articles in relevant databases. The databases PubMed, Scopus and Web of Science were used in this process. From the 5th to 13th of March 2020, the following keywords were used in all three databases: sleep deprivation, sleep loss, sleep disruption, sleep restriction, emotion, neural, brain, magnetic resonance imaging, positron emission tomography, and near infrared spectroscopy (for more details regarding the combination of keywords used, see Appendix A).

The next step was to find additional articles through other sources. In this phase, two recent review articles were used to find additional articles (Tempesta et al., 2018, 2019).

Inclusion and Exclusion Criteria

Studies were included in this review if they fulfilled the following criteria:

- Studies conducted on human subjects.
- Subjects were adults (+18 years) and healthy.
- Includes fMRI, PET, or near infrared spectroscopy.
- The experimental task involves emotional stimuli.

- Peer-reviewed articles published in journals, written in English.
- The conditions of sleep deprivation included either partial, total, or specific sleep stage deprivation.

Studies were excluded if they fulfilled the following criteria:

- Studies conducted on animals.
- Studies with drugs involved.
- Subjects with a sleep disorder (e.g., insomnia).
- Meta-analyses and reviews.

For the considerations of study design, in a within-subject study, there had to be a sleep-deprived condition and a sleep-rested condition. As for between-subject designs, there had to be either a sleep-deprived group and a sleep-rested group, or groups with other characteristics (e.g. age-groups) completing a sleep-deprived condition and a sleep-rested condition.

Study Screening and Selection Process

The steps in the study screening and selection process were followed according to the PRISMA flow diagram (Moher et al., 2009) (see Figure 1). All the collected articles found in the databases and through additional sources were exported to Rayyan, a software developed by Ouzzani and colleagues (2016) for conducting systematic reviews. Rayyan was used for handling all the references and for doing the screening and selection process according to the steps mentioned in the flow diagram. The first step in Rayyan was to remove all the duplicates. The next step was to screen the articles based on their titles and abstracts by following the inclusion and exclusion criteria. The last step was to read the full-texts of the remaining articles and exclude the ones that did not fulfill the inclusion and exclusion criteria. The studies that remained after this process were included in this qualitative review.

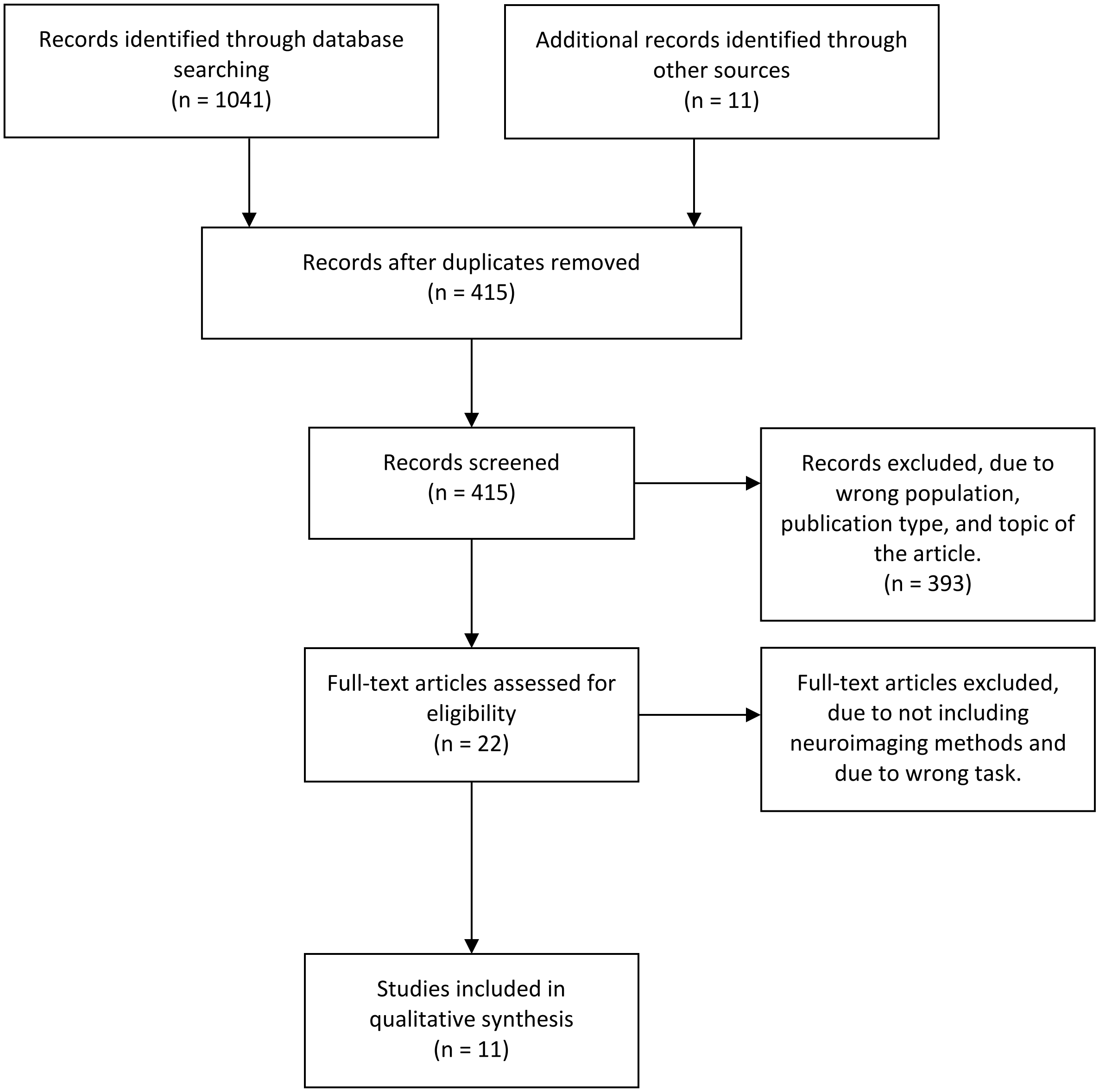

Figure 1. Study search, screening, and selection procedure according to the PRISMA flow diagram.

Results

Search Results

Searching in all three databases gave a total result of 1041 articles. Additionally, a total of 11 articles were collected from other sources. When searching in PubMed, no filters were used, which gave a total result of 129 articles. In Scopus, searching through titles, abstracts, and keywords, gave a total result of 523 articles. Searching in Web of Science through topics gave a total result of 389 articles. After having removed duplicates, a total of 415 articles were found. In the phase of screening articles based on their titles and abstracts, a total of 393 articles were excluded. The number of articles that remained for full-text assessment resulted in 22 articles. A total of 11 articles were included in the review, and 11 articles were excluded after full-text assessment.

Characteristics of Studies

The characteristics of the included studies are found in Table 1. Most studies included participants under 30 years of age (Table 1). The exceptions were one study with a mean age of 29.2±10.2 (Klumpers et al., 2015), and another study with a group of older adults between 65-75 years of age (Tamm et al., 2019). A total of eight studies (Chuah et al., 2010; Goldstein et al., 2013; Goldstein-Piekarski et al., 2015; Gujar et al., 2011; Klumpers et al., 2015; Simon et al., 2015; Tamm et al., 2019; Yoo et al., 2007a) involved both male and female participants, whereas three studies (Motomura et al., 2013; Motomura et al., 2014; Rosales-Lagarde et al., 2012) only involved male participants.

Three conditions of sleep deprivation were included in this review: total sleep deprivation, partial sleep deprivation, and REM sleep deprivation (Table 1). A total of seven studies had been identified with total sleep deprivation (Chuah et al., 2010; Goldstein et al., 2013; Goldstein-Piekarski et al., 2015; Gujar et al., 2011; Klumpers et al., 2015; Simon et al., 2015; Yoo et al., 2007a), whereas three studies had been identified with partial sleep deprivation (Motomura et al., 2013; Motomura et al., 2014; Tamm et al., 2019), and one study had been identified with REM sleep deprivation (Rosales-Lagarde et al., 2012).

In regards to total sleep deprivation, most studies were similar in the length of sleep loss, with 24 hours of no sleep. Two studies of total sleep deprivation had at least 30 hours of sleep loss (Gujar et al., 2011; Yoo et al., 2007a). In terms of partial sleep deprivation, two studies involved 4 hours of partial sleep loss (Motomura et al., 2013; Motomura et al., 2014), and one study involved 3 hours of partial sleep loss (Tamm et al., 2019). The single study that included REM sleep deprivation (Rosales-Lagarde et al., 2012), had sleep loss from REM stage in experimental group, and sleep loss from NREM stages in control group (Table 1).

Regarding study designs, a total of seven studies are within-subject designs (Chuah et al., 2010; Goldstein et al., 2013; Goldstein-Piekarski et al., 2015; Klumpers et al., 2015; Motomura et al., 2013; Motomura et al., 2014; Simon et al., 2015), and four studies are between-subject designs (Gujar et al., 2011; Rosales-Lagarde et al., 2012; Tamm et al., 2019; Yoo et al., 2007a) (Table 1). In all the within-subject studies, subjects performed tasks in both a sleep-deprived and sleep-rested condition. In three between-subject studies, a sleep-deprived group was compared to a sleep-control group, whereas one between-subject study (Tamm et al., 2019) compared two age-groups.

All the studies that were included in this review involved fMRI as the neuroimaging method (see Table 1). Only one study (Klumpers et al., 2015) also included PET neuroimaging. In terms of the type of behavioral tasks that were involved, 10 studies used emotional pictures as stimuli, whereas only one study (Klumpers et al., 2015) used emotional words as stimuli.

Table 1

Overview of Studies Included in the Systematic Review

Authors	Subjects	Design	Task	Stimuli	Measures	Results
Chuah et al. (2010)	24 healthy subjects (14 F; mean age: 22.33±1.34 years).	24 h of sleep deprivation. Within-subjects. Sleep-deprived session took place in laboratory. One week between sleep-rested and sleep-deprived session.	Delayed-match-to-sample working memory task involving faces, with distracters presented.	Negative, neutral, and scrambled distracters.	fMRI and behavioral task.	Sleep deprivation caused greater amygdala activation in response to negative distracters, together with decreased connectivity between amygdala and prefrontal regions.
Goldstein et al. (2013)	18 healthy subjects (9 F; mean age: 19.6±1.45 years).	24 h of total sleep deprivation. Within-subjects. Sleep-deprived session took place in laboratory. At least 6 days between sleep-rested and sleep-deprived session.	Emotional-anticipation task: trials consist of an anticipatory cue, followed by an emotional picture.	Neutral, negative, and ambiguous images.	fMRI and behavioral task.	Sleep deprivation increased activity in amygdala and anterior insula during the anticipation of potentially aversive stimuli.
Goldstein-Piekarski et al. (2015)	18 healthy subjects (9 F; mean age: 19.6±1.45 years).	24 h of total sleep deprivation. Within-subjects. Sleep-deprived session took place in laboratory. At least 6 days between sleep-rested and sleep-deprived session.	Viewing increasingly threatening faces while classifying their level of threat.	10 different Caucasian face identities. Each identity had 7 versions of threat, ranging from not threatening to increasingly threatening.	fMRI and behavioral task.	Sleep deprivation decreased activity in dorsal anterior cingulate cortex, insula, and amygdala in response to discrimination of threat.
Gujar et al. (2011)	27 healthy subjects (14 F; mean age:	One day of total sleep deprivation (mean: 31.9±1.31 h).	Viewing increasingly pleasant images.	Emotional images gradually changing from emotionally	fMRI and behavioral task.	Sleep-deprived group showed increased reactivity throughout

	23.6±1.4 years). 14 sleep-deprived and 13 controls.	Between-subjects. Sleep-deprived subjects were monitored in laboratory.		neutral to increasingly pleasant.		mesolimbic reward brain networks in response to positive stimuli. Additionally, it was associated with stronger connectivity in processing visual pathways and extended limbic regions, and weaker connectivity in medial and orbitofrontal cortex.
Klumpers et al. (2015)	12 healthy subjects. 6 female (mean age: 29.2±10.2 years) and 6 males (mean age: 28.5±4.8 years).	24 h of total sleep deprivation. Within-subjects. Sleep-deprived session took place in laboratory. One day between sleep-rested and sleep-deprived session.	Semantic emotional classification task: subjects responding as fast as possible to emotional targets and avoiding emotional distracters.	Positive, neutral, and negative targets and distracters (words).	fMRI, PET and behavioral task.	Sleep deprivation caused increased activity in insula in response to emotional words. Processing positive and negative words caused increased activity in (para)hippocampal region. Processing only positive words caused increased left dorsolateral prefrontal activation.
Motomura et al. (2013)	14 healthy male subjects (mean age: 24.1±3.32 years).	5-day session of sleep debt (4 h of sleep) and 5-day session of sleep control (8 h of sleep). Within-subjects. 3 days were spent at home	Viewing images of facial expressions under conscious and non-conscious conditions.	Happy, neutral and fearful facial expressions.	fMRI and button response.	Sleep deprivation caused increased activity in left amygdala in response to fearful facial expressions. Sleep deprivation

		and 2 days were spent at the laboratory per session. 2 weeks between the sessions.				also caused decreased connectivity between amygdala and ventral anterior cingulate cortex.
Motomura et al. (2014)	11 healthy male subjects (mean age: 24.5±3.67 years).	5-day session of sleep debt (4 h of sleep) and 5-day session of sleep control (8 h of sleep). Within-subjects. 3 days were spent at home and 2 days were spent at the laboratory per session. 2 weeks between the sessions.	Viewing images of facial expressions under conscious and non-conscious conditions.	Happy, neutral and fearful facial expressions.	fMRI and button response.	Sleep deprivation caused increased activation in amygdala, ventromedial prefrontal cortex, hippocampus, and insular cortex together with increased connectivity between amygdala and superior colliculus in response to fearful faces.
Rosales-Lagarde et al. (2012)	20 healthy male subjects (mean age: 24.2±4 years). 12 REM-sleep deprived and 8 NREM-controls.	REM-sleep deprived awakened in REM-stage. Controls awakened in NREM-stages. Between-subjects. Monitored in laboratory.	Viewing and imagining being part of an emotional scene. Button responding to defend oneself or not.	Pictures of positive and negative valence. Defending responses were labelled high emotional reactivity (HER) and non-defending responses as low emotional reactivity (LER).	fMRI and behavioral task.	Increased activity in emotional processing areas, in particular ventrolateral prefrontal cortex, was found in REM-sleep deprived group. Same brain areas showed an overall decrease in NREM-controls.
Simon et al. (2015)	18 healthy subjects (10 F; mean age: 26.8±3 years).	24 h of total sleep deprivation. Within-subjects. Sleep-deprived session took	Emotional N-back task: indicating by button response when presented number is the same as	Neutral and negative images (distractors) combined with low (1-back) and high (2-	fMRI and behavioral task.	Sleep deprivation showed increased activity in dorsolateral prefrontal cortex during

		place in laboratory. Sleep-rested and sleep-deprived sessions were separated by a mean of 13.8 days.	number of trials ago.	back) cognitive load.		neutral distractors. Increased left amygdala activity in response to all stimuli during sleep deprivation.
Tamm et al. (2019)	61 healthy subjects. 38 young (20-30 years) and 23 older (65-75 years).	Partial sleep deprivation (3 h of sleep). Between-subjects. Monitored in laboratory.	Cognitive reappraisal task: viewing emotional pictures and getting instructed how to emotionally respond.	Negative and neutral pictures.	fMRI and behavioral task.	Partial sleep deprivation showed no significant increase on amygdala activity in response to negative pictures.
Yoo et al. (2007a)	26 healthy subjects (13 F; mean age: 24.1±2.3 years). 14 sleep-deprived and 12 controls.	35 h of total sleep deprivation. Between-subjects. Monitored in laboratory.	Viewing increasingly aversive images while giving emotional classification responses to verify wakefulness.	Emotional images gradually changing from emotionally neutral to increasingly aversive.	fMRI and behavioral task.	Sleep-deprived group showed greater amygdala activation with weaker connectivity in medial-prefrontal cortex in response to increasingly aversive images.

Abbreviations: fMRI = functional magnetic resonance imaging; PET = position emission tomography; REM = rapid eye movement; NREM = non-rapid eye movement; F = females

The Neural Basis of the Effects of Total Sleep Deprivation on Emotional Reactivity

Seven studies were found that investigated the neural basis of the effects of total sleep deprivation on emotional reactivity. Six studies used tasks involving emotional pictures (Chuah et al., 2010; Goldstein et al., 2013; Goldstein-Piekarski et al., 2015; Gujar et al., 2011; Simon et al., 2015; Yoo et al., 2007a), whereas one study used a semantic task involving emotional words (Klumpers et al., 2015).

The first known study that investigated the neural basis of the effects of total sleep deprivation on emotional reactivity was conducted by Yoo and colleagues (2007a). In this study, the aim was to explore amygdala's involvement in processing aversive stimuli when the human brain is sleep-deprived. A total of 26 healthy young adults participated in this between-subject study that consisted of a sleep-deprived group and a sleep-control group (Table 1). Sleep-deprived subjects were awake for 35 hours: the first day, the first night, and the second day. Sleep-controls slept at home during the first night. On the second day, fMRI scanning took place when subjects performed a task involving a presentation of increasingly aversive images. Results indicated that the activity in the amygdala was similar between sleep-deprived group and sleep-control group during the presentation of the most neutral stimuli (i.e. lower quartile of stimulus set). Significant differences in amygdala activation between the groups only became apparent for the most aversive stimuli (i.e. upper quartile of stimulus set). However, both groups showed significantly increased amygdala activation in response to increasingly aversive stimuli. Sleep-deprived subjects had at least 60% greater amygdala activity compared to sleep-controls in response to increasingly aversive stimuli. Furthermore, the amplified response in the amygdala during sleep deprivation caused a significantly weaker functional connectivity with the MPFC. In contrast, significantly stronger connectivity was observed between the amygdala and autonomic brainstem regions (midbrain and locus coeruleus) following sleep deprivation.

In another study, conducted by Gujar and colleagues (2011), the authors investigated the reactivity in the brain reward networks in response to increasingly positive stimuli following one day of total sleep deprivation. This study consisted of a sleep-deprived group and a sleep-control group that performed an fMRI task with increasingly pleasant images (Table 1). Regions of interest (ROI) in this study were within mesolimbic reward areas, including ventral tegmental area (VTA), insula, putamen, and amygdala. Functional brain imaging data revealed that the sleep-deprived group, compared to the sleep-control group, displayed significantly increased activity in mesolimbic regions in response to increasingly pleasant stimuli. These brain regions included the VTA and the left putamen of the dorsal striatum. Significantly increased activity following sleep deprivation was also observed in emotion-related regions, including the amygdala and the left insula cortex, in response to increasingly pleasant stimuli. Additionally, sleep deprivation caused significantly greater activation to increasingly pleasant stimuli in other brain regions that were not of interest, including the visual processing pathway in the left fusiform gyrus. In contrast, sleep-deprivation caused significantly less activation in the left middle occipital gyrus, precuneus, and the right posterior hippocampus in response to increasingly pleasant stimuli. When investigating functional connectivity differences between sleep-deprived and sleep-control groups in response to increasingly pleasant stimuli, data demonstrated a significantly stronger connectivity between VTA and left amygdala as well as left anterior temporal pole following sleep deprivation. Additionally, significantly stronger connectivity was found between left posterior insula and several visual cortex regions in response to increasingly pleasant stimuli. In contrast, a significant loss of connectivity was observed during sleep deprivation between amygdala and MPFC as well as orbitofrontal cortex (OFC) in response to increasingly pleasant stimuli (Gujar et al., 2011).

In a study conducted by Goldstein and colleagues (2013), the authors wanted to test the impact of 24 hours of total sleep deprivation on the human brain’s anticipatory response to emotional events. The study was a within-subject design with healthy young adults (Table 1). The subjects performed an emotional-anticipation task in an fMRI, both in a sleep-deprived and sleep-rested condition. The authors used a ROI-analysis in this study focusing on the amygdala and the anterior insula. Results based on the effects of sleep deprivation on these targeted brain regions revealed a significantly increased activation in the entire amygdala, regardless of anticipatory cue (neutral, negative, or ambiguous). Right anterior insula showed significantly increased activity during sleep-deprived condition only towards certain (negative and neutral) anticipatory cues, and not towards uncertain (ambiguous) anticipatory cues. In contrast, during sleep-rested condition, increased activity in right anterior insula was only observed in response to uncertain anticipatory cues. Furthermore, left anterior insula showed no significant effects in sleep-deprived condition towards anticipatory cues (Goldstein et al., 2013).

A study by Goldstein-Piekarski and colleagues (2015) examined the impact of 24 hours of total sleep deprivation on the discrimination of social threat within and between the central nervous system (CNS) and peripheral nervous system (PNS). The presented results from this study will only focus on the findings concerning the impact of sleep deprivation on the discrimination of social threat within the CNS. Subjects that participated were healthy young adults who performed an fMRI emotional face discrimination task when being sleep-deprived and sleep-rested (Table 1). The analysed ROIs in this study were the amygdala, the anterior insula, and the dorsal anterior cingulate cortex. In the sleep-rested condition there was significantly greater activity in the dorsal anterior cingulate cortex (dACC) and the anterior insula when viewing threatening compared to nonthreatening faces. In comparison, no significant effects were found in the sleep-deprived condition. Despite no detected interaction effects in the amygdala concerning both sleep-rested and sleep-deprived condition, significantly greater left amygdala activation was found in sleep-rested condition in regards to the average activity to threatening faces subtracted from the average activity to nonthreatening faces (Goldstein-Piekarski et al., 2015).

Research conducted by Simon and colleagues (2015) explored the impact of 24 hours of total sleep deprivation on emotional processing using two different cognitive-emotional tasks. One task was used during fMRI session and the other task used during electroencephalography (EEG) session. Results from the fMRI task will only be presented in this paper. A total of 18 healthy subjects participated in this within-subject study, consisting of a sleep-deprived and a sleep-rested condition (Table 1). The fMRI task was used as a way of examining the effects of cognitive load on emotional processing. Therefore, the fMRI analysis focused on executive and limbic ROIs. The executive ROI was the DLPFC, whereas the limbic ROI was the amygdala. Findings from this study revealed that in the sleep-deprived condition there was significantly increased activity in the right DLPFC when comparing neutral to negative distractors with low cognitive load, whereas no significant effects were found in sleep-rested condition. In the sleep-deprived compared to sleep-rested condition there was also significantly greater left amygdala activity, regardless of distractor (negative or neutral) and cognitive load (high or low). Greater activity in left amygdala was observed when comparing low cognitive load to high cognitive load conditions across sleep-rested and sleep-deprived conditions. When investigating the effects of distractor type on the amygdala, significantly higher activity in the left amygdala was found in response to neutral distractors during the sleep-deprived compared to sleep-rested condition. Significantly higher amygdala activity was found in the sleep-rested condition when negative compared with neutral distractors were presented. In sleep rested condition, amygdala activity did not differ in response to negative compared with neutral distractors. In high cognitive load conditions, significantly increased left amygdala activity was found in response to both distractors during sleep-deprived compared with sleep-rested condition. When comparing high with low cognitive load, functional connectivity between the amygdala and anterior cingulate cortex (ACC) was only found during the sleep-rested condition. In comparing neutral to negative distracters (during low cognitive load conditions), similar results were observed, where connectivity between amygdala and ACC was only found during the sleep-rested condition. Weaker connectivity between amygdala and ACC was associated with sleep-deprived condition, as well as negatively correlated with accuracy scores and REM sleep (Simon et al., 2015).

The objective of the study by Chuah and colleagues (2010) was to determine if 24 hours of total sleep deprivation would increase the impact of negative emotional distracters on working memory. A total of 24 healthy subjects completed this within-subject study, involving a sleep-deprived and a sleep-rested condition (Table 1). Subjects performed a delayed-match-to-sample working memory task, with faces and distracters as stimuli. The objective of the task was to remember a set of three faces, and then view a pair of distracters, and finally view a face and indicate if it had been presented earlier. The amygdala was targeted as ROI in this study. According to functional neuroimaging data, increased activity was observed in the amygdala, ventrolateral prefrontal cortex (VLPFC), and occipital cortex following sleep deprivation when negative distracters were presented. Simultaneously, decreased activity below baseline was observed in the DLPFC and lateral occipital complex (LOC) following the presentation of negative distracters. Sleep-deprived compared to sleep-rested condition resulted in increased amygdala activity when negative distracters were presented. Moreover, an impairment in working memory was observed when negative distracters were presented during sleep deprivation. In terms of functional connectivity, a stronger connectivity was found between the amygdala and the DLPFC and the ventromedial prefrontal cortex (VMPFC) following the presentation of emotional distracters during sleep deprivation. No significant effect was observed in amygdala connectivity in response to neutral distracters following sleep deprivation (Chuah et al., 2010).

The study by Klumpers and colleagues (2015) aimed at investigating the neurophysiological effects of 24 hours of total sleep deprivation using a semantic emotional classification task. A total of 12 healthy subjects participated in this within-subject study that used fMRI and raclopride PET scanning in a sleep-deprived and sleep-rested condition (Table 1). During the semantic emotional classification task, subjects had to respond as fast as possible to emotional target stimuli and ignore distracter stimuli. Target and distracter stimuli could either be presented as neutral, negative, or positive words. The valence of each target was differed from the valence of the following distracter (e.g., neutral targets with negative distracters). In the sleep-deprived condition compared to sleep-rested condition there was significantly increased activity in the left DLPFC when processing positive and negative vs. neutral words. During sleep-deprived condition, a subthreshold increased activity was observed in the left parahippocampal/hippocampal area when processing only negative and positive words (both targets and distracters) compared to sleep-rested condition. Presenting any emotional stimulus (target and/or distracter) following sleep deprivation compared to sleep-rested condition resulted in increased activation in the left anterior insula. According to raclopride PET imaging data, sleep-deprived condition compared to sleep-rested condition showed a significantly decreased voxel-by-voxel based binding potential in the left caudate nucleus. Additionally, sleep deprivation resulted in a significant decrease in relative delivery (R1) in right caudate nucleus. The authors speculated that the decreased voxel-by-voxel based binding potential in the left caudate nucleus during sleep deprivation could relate to the increased difficulty in controlling word interference from task unrelated processing, which may explain the increased prefrontal activity (Klumpers et al., 2015).

The Neural Basis of the Effects of Partial Sleep Deprivation on Emotional Reactivity

The first known study investigating the neural basis of the effects of partial sleep deprivation on emotional reactivity was conducted by Motomura and colleagues (2013). The objective of this study was to measure emotional reactivity in the human brain when subjects have gotten accumulated sleep debt over a 5-day period. All subjects that participated in the study were right-handed men (Table 1). The subjects underwent a within-subject crossover study that consisted of a 5-day session of sleep debt (4 hours of daily sleep) and a 5-day session of sleep control (8 hours of daily sleep). In both the sleep debt and sleep control session, subjects stayed at home for the first three days and then stayed at the sleep-lab for the remaining two days. On the last day of each session, subjects performed an fMRI emotional face viewing task. During fMRI scanning, subjects viewed images of emotional faces under conscious and non-conscious conditions. The ROI that was analysed in this study was the amygdala, and functional connectivity between amygdala and ventral anterior cingulate cortex (vACC) was analysed as well. In the conscious condition, subjects had enough time for supraliminal visual perception when viewing emotional faces. During the non-conscious condition, subjects had a short time for subliminal perception when viewing emotional faces followed by a neutral face to mask an emotional face. When subjects had undergone a sleep debt session compared to sleep control session, they showed significantly greater activity in the left amygdala when comparing fearful against neutral faces for the conscious condition. Sleep debt session also resulted in higher activation of the right amygdala, although not significantly higher. When comparing happy against neutral faces, there were no significant differences in amygdala activity between the sessions. Moreover, no significant differences in amygdala activity were found between the sessions when comparing fearful against neutral faces, as well as happy against neutral faces for the non-conscious condition. Functional connectivity between amygdala and vACC significantly decreased when comparing fearful against neutral faces for the conscious condition in the sleep debt session compared to the sleep control session. Based on all the task results from both sessions, left amygdala activation caused impaired functional connectivity between amygdala and vACC (Motomura et al., 2013).

The objective of a follow-up study conducted by Motomura and colleagues (2014) was to investigate the neural effects of partial sleep deprivation on subliminal emotional processing. The same sleep restriction protocol and fMRI task as in Motomura and colleagues (2013) was used (Table 1). The difference between this study and the previous one (Motomura et al., 2013) was that the impact of subjective sleepiness on emotional reactivity was investigated, rather than the impact of five days of partial sleep deprivation on emotional reactivity. Subjects reported subjective sleepiness after having completed the fMRI task during the last day of both the sleep debt and sleep-rested session. A total of 11 healthy right-handed men participated in this within-subject crossover study. The analysed ROI in this study was the super colliculus, as this is a region known for transmitting visual information directly to the amygdala. Results showed that when viewing nonconscious fearful faces there was a significantly positive correlation between subjective sleepiness and activity in the VMPFC, amygdala, insular cortex, and hippocampus. Viewing nonconscious fearful faces also showed a significantly negative correlation between subjective sleepiness and activity in the secondary and tertiary visual cortices, and the fusiform face area (FFA). When viewing nonconscious neutral faces, a significantly negative correlation was found between subjective sleepiness and activity in the FFA, and the secondary and tertiary visual cortices. Viewing nonconscious neutral faces contrasted with nonconscious fearful faces showed a significantly positive correlation between subjective sleepiness and activity in the VMPFC, posterior cingulate cortex, and precuneus. In contrasting nonconscious fearful faces with nonconscious neutral faces, a significantly positive correlation was found between subjective sleepiness and activity in the amygdala, whereas a significantly negative correlation was found between subjective sleepiness and activity in the posterior cingulate cortex. Significantly stronger functional connectivity was observed between the amygdala and superior colliculus during the presentation of fearful faces. In contrasting nonconscious fearful faces with nonconscious neutral faces, significantly stronger connectivity was found between the amygdala and superior colliculus (Motomura et al., 2014).

In the study conducted by Tamm and colleagues (2019), the authors aimed at investigating the effects of partial sleep deprivation on emotional regulation via cognitive reappraisal. One group of young adults and another group of older adults performed a fMRI cognitive reappraisal task after one night of sleep and after three hours of sleep (Table 1). In the cognitive reappraisal task, subjects were instructed to upregulate, downregulate, or maintain their emotional response to stimuli. Presented stimuli could either be negative or neutral, with neutral stimuli having only the instruction to maintain emotional response. After stimuli had been presented, subjects were asked to rate how well they succeeded in regulating their emotions. The targeted ROIs in this study were the amygdala, the left OFC, and the DLPFC. Only results regarding the emotional reactivity (and not the emotional regulation) task will be presented here. Results based on subjects passively viewing the stimuli revealed that negative stimuli were associated with increased activity in the amygdala, regardless of age group and sleep condition. Functional connectivity was stronger between amygdala and occipital and extrastriate cortex during passive viewing of negative stimuli, in all age groups and sleep conditions. No significant effects of sleep deprivation on amygdala activity nor connectivity was found in regards to passive viewing of negative stimuli. These results differed from the study by Yoo and colleagues (2007a), where the authors found increased amygdala activity in response to negative stimuli during sleep deprivation. The authors of this study speculated that a possible explanation for the lack of amygdala activity could be that subjects had enough REM sleep, considering that subjects were partially sleep deprived. They also argued that another possible explanation could be that some subjects were partially sleep deprived during the sleep-rested condition, which caused both sleep conditions to not have enough difference for a significant change in amygdala activity or connectivity.

The Neural Basis of the Effects of REM Sleep Deprivation on Emotional Reactivity

This subsection will present results from the one and only study that has investigated the neural effects of REM sleep deprivation on emotional reactivity. This study, conducted by Rosales-Lagarde and colleagues (2012), aimed at exploring how all phases of sleep affects the human brain's emotional reactivity to threatening visual stimuli. One group was only sleep-deprived during the REM phase, and the other group was only sleep-deprived during the NREM phases (Table 1). Subjects performed an fMRI emotional reactivity task that presented different emotional scenes displayed on pictures. The instructions of the task were to imagine being part of the presented scene and react to the scene as quickly as possible by pressing one of two buttons to either defend oneself or not. Trials with defending responses were labeled as high emotional reactivity (HER) and trials with non-defending responses were labeled as low emotional reactivity (LER) (Rosales-Lagarde et al., 2012).

In both HER and LER trials, NREM sleep deprivation compared to baseline-sleep showed significantly decreased activation in right inferior and middle frontal gyri, right fusiform gyrus, superior frontal gyrus, inferior parietal lobe, parahippocampal gyrus and posterior middle temporal gyrus. REM-sleep deprivation compared to baseline-sleep in both HER and LER trials showed significantly decreased activation in left anterior and posterior cingulate gyrus. HER trials in contrast to LER trials caused significantly greater activation in left middle occipital gyrus during REM sleep deprivation compared to baseline-sleep. In comparing REM sleep deprivation to NREM sleep deprivation, activity in left middle occipital gyrus decreased significantly during NREM sleep deprivation in HER trials. The contrast between HER and LER trials during NREM sleep deprivation did not differ significantly in left middle occipital gyrus compared to baseline-sleep. A particular finding in this study was the level of activity in the VLPFC, which remained the same between baseline-sleep and REM deprivation, whereas activity in this brain region significantly decreased between baseline-sleep and NREM deprivation (Rosales-Lagarde et al., 2012).

Discussion

The aim of this thesis was to conduct a systematic review on the neural basis of the effects of sleep deprivation on emotional reactivity in the human brain. Studies that were selected in this review had to involve experimental tasks with emotional stimuli. Only neuroimaging studies were included in this review, in which all included tasks with fMRI scanning, and only one study included PET scanning. The presented results from the studies were divided into three categories, based on the condition of sleep deprivation. The categories of sleep deprivation that were summarized in this review include total sleep deprivation, partial sleep deprivation, and

REM sleep deprivation. This section discusses the findings from the included studies, as well as the implications of these findings, and the limitations and future directions.

Total Sleep Deprivation and Emotional Reactivity

A total of seven studies have investigated the impact of total sleep deprivation on reactivity to emotional stimuli. These studies had all been designed to involve only one night of total sleep deprivation.

It is well established that the human amygdala has an important role in processing emotional stimuli, especially negative stimuli (Costafreda et al., 2007). Neuroimaging studies have revealed that the amygdala responds to both positively and negatively valenced stimuli (Garavan et al., 2001), as well as neutral stimuli (Somerville et al., 2004). Additionally, studies suggest that the amygdala acts as a relevance detector, which means that the amygdala is involved in processing relevant stimuli (e.g., stimuli that is directed toward the observer) (Sander, Grafman, & Zalla, 2003). Moreover, it has also been demonstrated in various studies that the amygdala responds to emotional stimuli without awareness and focused attention (Diano et al., 2017).

Three of the selected studies (Yoo et al., 2007a; Simon et al., 2015; Chuah et al., 2010) showed significantly increased amygdala activation in response to negative emotional images during sleep-deprived condition compared to sleep-rested condition. Additionally, the study by Goldstein and colleagues (2013) showed significantly increased amygdala activity in response to negative anticipatory cues. These findings indicate that total sleep deprivation is associated with hyperreactivity in response to negatively valenced emotional stimuli. However, in another study (Goldstein-Piekarski et al., 2015), no significant effects were found in amygdala activity in response to increasingly threatening faces during sleep-deprived condition compared to sleep-rested condition. This may instead indicate that the amygdala does not display hyperreactivity to negatively valenced complex social emotions.

Sleep deprivation has been shown to increase amygdala reactivity not only to negatively but also to positively valenced stimuli. Gujar and colleagues (2011) found increased amygdala activity in response to increasingly positive stimuli after total sleep deprivation. Moreover, the authors found increased mesolimbic activity in response to pleasant stimuli. These findings suggest that total sleep deprivation is associated with emotional hyperreactivity to both increasingly negative and increasingly positive stimuli.

Increased amygdala activity following total sleep deprivation was also found in response to neutral stimuli. In the study conducted by Goldstein and colleagues (2013), significantly increased activation in the amygdala was found in response to neutral anticipatory cues following sleep deprivation. Additionally, Simon and colleagues (2015) found during sleep deprivation significantly increased amygdala activity in response to neutral distractors. These findings suggest that alterations in amygdala reactivity occur in response to all types of stimuli (neutral, negative, and positive), which may indicate that emotional processing is altered in general.

In terms of functional connectivity, a significantly weaker connectivity between amygdala and prefrontal regions was observed in three studies (Chuah et al., 2010; Yoo et al., 2007a; Simon et al., 2015) in response to negative emotional stimuli during total sleep deprivation. In addition, a significantly weaker connectivity between amygdala and prefrontal regions was also found in response to positive emotional stimuli after total sleep deprivation (Gujar et al., 2011). Furthermore, these mentioned studies (Chuah et al., 2010; Yoo et al., 2007a; Simon et al., 2015; Gujar et al., 2011) showed a correlation between increased amygdala activation and reduced connectivity between amygdala and prefrontal regions. These findings therefore suggest that increased amygdala activation results in a disconnection between the amygdala and prefrontal cortex during total sleep deprivation when processing visual emotional stimuli.

Although most findings revolve around the amygdala in the studies about total sleep deprivation, the insula is another brain region which has commonly been involved in processing emotional stimuli. The insula is known for playing an important role in interoception (the sense of the physiological state of the body) as well as in experiencing emotions (Craig, 2002, 2009). Sleep deprivation has resulted in increased activity in the insula response to positive stimuli (Gujar et al., 2011), negative stimuli (Goldstein et al., 2013; Klumpers et al., 2015), and neutral stimuli (Goldstein et al., 2013). These findings indicate that both the insula and amygdala are involved in the processing of all types of valenced stimuli and that total sleep deprivation affects this processing.

Partial Sleep Deprivation and Emotional Reactivity

Included studies that have examined the neural basis of the effects of partial sleep deprivation on emotional reactivity to visual emotional stimuli have been designed to either include three hours or four hours of sleep. Two studies (Motomura et al., 2013; Motomura et al., 2014) are identical in design, in which subjects were partially sleep-deprived (4 hours daily sleep) for five consecutive days. The study by Tamm and colleagues (2015) distinguishes from these studies, where subjects slept for three hours for only one night before performing the experimental task.

The study by Motomura and colleagues (2013) showed increased amygdala activity in response to negative stimuli (i.e., fearful faces) following sleep deprivation, whereas the study by

Motomura and colleagues (2014) observed increased activity in amygdala in response to negative stimuli following increased subjective sleepiness. The similarities in brain activity in these two studies are the significant increases in amygdala activity in response to negative stimuli during the sleep-deprived session compared to the sleep-rested session. In comparison, no significant increase in amygdala activity was found in the study by Tamm and colleagues (2019), when subjects passively viewed negative stimuli (i.e., negative pictures) after partial sleep deprivation. This might mean that the amygdala displays a lack of response to passively viewing negative pictures compared to viewing negative facial expressions during partial sleep deprivation.

Significantly weaker functional connectivity between amygdala and prefrontal regions in response to negative stimuli was also related with partial sleep deprivation. In the study by Motomura and colleagues, significantly reduced functional connectivity was found between the amygdala and vACC (including the MPFC) in response to negative stimuli after partial sleep deprivation (Motomura et al., 2013). This finding showed similar results to the study by Yoo and colleagues (2007a), where weaker functional connectivity between amygdala and MPFC was observed in response to negative emotional stimuli after total sleep deprivation. This indicate that there is no distinction between partial and total sleep deprivation regarding the disconnection between the amygdala and MPFC in response to negative stimuli.

REM Sleep Deprivation and Emotional Reactivity

Only one study (Rosales-Lagarde et al., 2012) investigated the neural basis of the effects of REM sleep deprivation on emotional reactivity toward visual emotional stimuli. A particular finding in this study was that the activity in the VLPFC remained the same when comparing baseline-sleep to REM deprivation. In contrast, the activity in VLPFC significantly decreased when comparing baseline-sleep to NREM deprivation. Since the VLPFC is known for being involved in processing and regulating emotions (Mitchell, 2011), the results suggest that lack of REM sleep leads to increased emotional reactivity by way of reduced emotion regulation.

During REM sleep deprivation (compared to baseline sleep), when contrasting HER trials to LER trials, a significantly increased activation in the left middle occipital gyrus was observed. This result can be comparable with findings from other studies regarding the neural response to negative visual stimuli (Chuah et al., 2010; Tamm et al., 2019), where increased connectivity between the amygdala and middle occipital gyrus has been found in response to negative stimuli following partial sleep deprivation (Tamm et al., 2019), as well as increased activity in the occipital cortex in response to negative stimuli after total sleep deprivation (Chuah et al., 2010). Additionally, in the study by Gujar and colleagues (2011), significantly less activation was found in the left middle occipital gyrus in response to positive stimuli after total sleep deprivation. These findings indicate that the occipital cortex is increasingly involved in processing negative visual stimuli during total, partial, and REM deprivation. In contrast, these findings might also suggest that the occipital cortex is significantly less involved in processing positive visual stimuli during different conditions of sleep deprivation.

A Summary of the Effects of Sleep Deprivation on Emotional Reactivity

A number of similarities are shared between the results from all the included studies that have investigated the effects of different types of sleep deprivation on emotional reactivity. Most prominent is emotional reactivity toward negative stimuli during sleep deprivation, where enhanced amygdala activity was found in both total sleep deprivation (Yoo et al., 2007a; Simon et al., 2015; Chuah et al., 2010) and partial sleep deprivation (Motomura et al., 2013, 2014). This indicate that the amygdala displays hyperreactivity to negative emotions during sleep deprivation, even when having slept half of a night (approximately 4 hours). These results are also comparable with behavioral studies that have reported an increased subjective feeling of negative emotions in response to negative situations (Zohar et al., 2005; Minkel et al., 2012).

Two studies also shared similarities in decreased functional connectivity between the amygdala and the MPFC in response to negative stimuli following total sleep deprivation (Yoo et al., 2007a) and partial sleep deprivation (Motomura et al., 2013). This suggest that sleep deprivation results in a dysfunction between the amygdala and the MPFC in response to negative stimuli. Considering that the MPFC is involved in cognitive control (Koechlin, Ody, & Kouneiher, 2003) and emotion regulation (Quirk & Beer, 2006), this means that sleep deprivation negatively affects regulation or control of emotional reactivity.

Increased activity in the insula was found in both total sleep deprivation (Goldstein et al., 2013; Klumpers et al., 2015) and partial sleep deprivation (Motomura et al., 2014) in response to negative stimuli. Furthermore, increased activity in the insula was also observed in response to neutral (Goldstein et al., 2013) and positive stimuli (Gujar et al., 2011) during total sleep deprivation. These results might indicate that the insula only is significantly more activated in response to negative stimuli compared to neutral and positive stimuli during partial sleep deprivation.

Nevertheless, it remains to be determined whether the amygdala would display similar expressions of hyperreactivity to emotional stimuli when it concerns the absence of REM and NREM sleep. Furthermore, it is not known whether the absence of REM and NREM sleep would result in a dysfunction between the amygdala and the MPFC in response to negative stimuli.

Limitations and Future Directions

This section will discuss the limitations of the included studies in this systematic review as well as suggest what remains to be explored in the future of research. Out of the studies included in this systematic review, whereas four studies included an equal distribution of males and females (Goldstein et al., 2013; Goldstein-Piekarski et al., 2015; Klumpers et al., 2015; Yoo et al., 2007a), three studies only included a male sample (Rosales-Lagarde et al., 2012; Motomura et al., 2013; Motomura et al., 2014), and four studies included an unequal distribution of males and females (Chuah et al., 2010; Gujar et al., 2011; Simon et al., 2015; Tamm et al., 2019). Noticeable is the study by Rosales-Lagarde and colleagues (2012), which is the only study investigating REM and NREM deprivation. This implies that it is impossible to determine the effects of REM and NREM deprivation on emotional reactivity among a female population. Furthermore, regarding the other two studies (Motomura et al., 2013, 2014), these were the only studies that experimented with partial sleep deprivation for a longer period than one night. This means that it is not possible to conclude about the effects of several nights of partial sleep deprivation on emotional reactivity among females. Altogether, studies reveal that potential sex differences are generally not considered to be crucial when investigating the effects of sleep deprivation on emotional reactivity. Thus, it would be of interest in future studies to explore whether potential sex differences actually matter on this subject.

In general, the studies include only young adults as participants, usually not older than 30 years of age. Only two studies included participants older than 30 years (Tamm et al., 2019; Klumpers et al., 2015), whereas one of these studies also included older adults (65-75 years old) (Tamm et al., 2019). This makes it difficult to determine the effects of sleep deprivation on emotional reactivity among a general population.

In this review, only one study (Gujar et al., 2011) involved increasingly positive stimuli after total sleep deprivation. There were no studies that investigated the neural effects of increasingly positive stimuli during other conditions of sleep deprivation. Thus, it is not possible to confirm if similar effects toward positive stimuli would be found following partial and REM deprivation. The same issue concerns increasingly negative stimuli, where research only exists regarding total sleep deprivation (Yoo et al., 2007a). Therefore, research dedicated to investigating the reactivity to increasingly positive and negative stimuli in all possible conditions of sleep deprivation is needed.

Analysis of functional connectivity between brain areas was conducted in only a few studies, which limits the possibilities of comparing studies and generalizing the findings. This suggest that more research dedicated to analyze the functional connectivity between brain areas is needed in order to draw more conclusions about the neural mechanisms underlying sleep deprivation.

No investigation of the amygdala was included in the study by Rosales-Lagarde and colleagues (2012). This made it impossible to conclude about the involvement of the amygdala in processing emotional stimuli during REM deprivation. Since the amygdala has frequently shown to be involved in processing emotions, the focus of future research should be dedicated to explore the activity of the amygdala in response to emotional stimuli during REM deprivation.

In the study conducted by Goldstein-Piekarski and colleagues (2015), no amygdala activity was found in response to threatening faces after sleep deprivation. The type of emotional stimuli that was presented in this study was regarded as more complex compared to basic emotions. Thus, it would be of interest to explore further if amygdala shows a lack of response to other kinds of complex emotions during sleep deprivation.

Finally, only a total of 11 studies were included in this systematic review, which suggests that more research concerning the neural basis of the effects of sleep deprivation is needed. In addition, more focus regarding partial and REM deprivation is needed to provide a greater consensus about the neural mechanisms underlying these conditions of sleep deprivation.

Conclusion

This systematic review investigated the neural basis of the effects of sleep deprivation on emotional reactivity. A total of 11 studies were included in this review, where all studies concerned tasks that included visual emotional stimuli. Results showed significantly enhanced amygdala activity in response to negative emotional stimuli as a result of total and partial sleep deprivation. Hyperreactivity in the amygdala was also observed after sleep deprivation in response to positive and neutral emotional stimuli. Additionally, findings showed that total and partial sleep deprivation result in weaker functional connectivity between the amygdala and prefrontal regions (specifically the MPFC) in response to negative stimuli. However, it is unknown whether similar alterations would occur in the deprivation of particular sleep stages (i.e., as a result of REM or NREM sleep deprivation). The insula was another brain region that displayed enhanced activity toward all types of valenced emotional stimuli during sleep deprivation. Together, these results suggest that sleep deprivation induces hyperreactivity toward emotional stimuli and disrupts top-down regulation of emotional reactivity.

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Appendix A

Searches in PubMed, Scopus, and Web of Science:

#1 "sleep deprivation" AND "emotion*" AND neural

#2 "sleep loss" AND "emotion*" AND neural

#3 "sleep deprivation" AND "emotion*" AND "magnetic resonance imaging"

#4 "sleep deprivation" AND "emotion*" AND "positron emission tomography"

#5 "sleep loss" AND "emotion*" AND "magnetic resonance imaging"

#6 "sleep loss" AND "emotion*" AND "positron emission tomography"

#7 "sleep disruption" AND "emotion*" AND neural

#8 "sleep disruption" AND "emotion*" AND "magnetic resonance imaging"

#9 "sleep disruption" AND "emotion*" AND "positron emission tomography"

#10 "sleep restriction" AND "emotion*" AND neural

#11 "sleep restriction" AND "emotion*" AND "magnetic resonance imaging"

#12 "sleep restriction" AND "emotion*" AND "positron emission tomography"

#13 "sleep deprivation" AND "emotion*" AND brain

#14 "sleep loss" AND "emotion*" AND brain

#15 "sleep disruption" AND "emotion*" AND brain

#16 "sleep restriction" AND "emotion*" AND brain

#17 "sleep deprivation" AND "emotion*" AND "near infrared spectroscopy"

#18 "sleep loss" AND "emotion*" AND "near infrared spectroscopy"

#19 "sleep disruption" AND "emotion*" AND "near infrared spectroscopy"

#20 "sleep restriction" AND "emotion*" AND "near infrared spectroscopy"