The relationship between nightmares and PTSD: The possible role of

Image Rescripting in the treatment of PTSD

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Abstract

Post traumatic Stress Disorder (PTSD) is an anxiety disorder that may develop after a traumatic event. One of the most common and distressing symptoms are nightmares, which occur in 50 – 70% of PTSD patients. It is suggested that sleep problems are a core feature of PTSD, and that they form a risk factor in PTSD development. Despite the high prevalence of nightmares and the distress they cause, first-line treatment in PTSD does not focus on sleep. However, evidence suggests that sleep problems usually remain as residual symptoms after PTSD is treated. A successful cognitive-behavioral technique that is currently used in nightmare treatment is Imagery Rescripting (IR). In this literature review, first the relationship between nightmares and PTSD is investigated. Secondly, the possible role that IR can play in PTSD treatment is explored. Findings regarding the neurobiological mechanisms underlying nightmares and PTSD are speculative, but research shows an altered activity in the amygdala, hippocampus, medial prefrontal cortex and anterior cingulate cortex in both nightmares and PTSD. These structures are also implicated in the process of fear memory extinction. Findings suggest that IR improves sleep quality, nightmares and global PTSD symptoms in PTSD. However, clinical studies on IR in PTSD are difficult to compare because treatment protocols differ greatly between studies. Future research should include trauma-focused treatments in control conditions, so that comparisons in effectiveness can be made. Lastly, more research should be conducted on the neurobiology of nightmares.

Keywords: *Posttraumatic stress disorder (PTSD), nightmares, sleep disturbance, fear extinction, Image Rescripting (IR), treatment*

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Introduction

Posttraumatic stress disorder (PTSD) is a mental illness that affects a lot of people's lives in all age ranges. Estimates have indicated that 7 – 8% of the adult population in the United States at some point in their lifetime suffer from PTSD (Keane, Marshall & Taft, 2006). PTSD is an anxiety disorder that may develop after a person experienced a traumatic event (e.g., a car accident, violence or sexual abuse). PTSD impacts the patient's life, and the lives of the people close to him to great extend. There are a variety of consequences, including interpersonal, psychosocial and physical health problems. People with PTSD have higher divorce rates, have more trouble raising children, behave more aggressively towards their partner, report lower life satisfaction, have more trouble with the legal system, earn less, and change their job more frequently (Keane et al., 2006).

PTSD is defined by three symptom clusters, according to the DSM-IV (4th ed., text rev.; DSM–IV–TR; American Psychiatric Association, 2000).
The re-experiencing cluster includes flashbacks of the traumatic experience in which the patient (partially) relives the event, distress and physiological reactions when the patient is exposed to anything related to the trauma, and recurring nightmares of the event. The hyperarousal cluster includes a heightened startle response, hypervigilance, insomnia, trouble with concentrating, and anger control problems.
The third cluster encompasses avoidance behaviour, e.g., avoiding things that are reminding of the trauma, the inability to (partially) remember the event, feelings of apathy, and the inability to experience positive emotions (Keane et al., 2006).

A lot of problems experienced with PTSD are related to sleep. In 87% of war sufferers with PTSD sleep disturbances are prevalent (Lamarche & Koninck, 2007). Within this category of problems, there are a wide variety of symptoms that occur. For example, insomnia, which is the inability to initiate or maintain sleep, is reported in 40-50% of patients diagnosed with PTSD, and

nightmares are reported in 50-70% of PTSD patients (Spoormaker & Montgomery, 2008). Other sleep problems found in PTSD include Periodic Limb Movements (PLMs), Sleep Disordered Breathing (SDB) and disturbed Rapid Eye Movement (REM) sleep (Lamarche & Koninck, 2007).

While sleep disorders are among the most common problems of PTSD, they are usually viewed as secondary symptoms. In the DSM-IV there is no specific cluster of sleep related symptoms. Instead insomnia is viewed as a symptom of hyperarousal, while nightmares fall under the re-experiencing cluster, as described above. According to this view sleep problems do not require specific treatment, since they are expected to go away when PTSD is treated. However, studies have shown that most treatments for PTSD, such as trauma-focused cognitive behavioural therapy (CBT), do not resolve sleep disturbances (Zayfert & DeViva, 2004; Belleville, Guay, & Marchand, 2011). The relationship between sleep and PTSD, and it's underlying mechanisms might be more complex.

Indeed, an increasing number of researchers argue that sleep problems are not merely a symptom of PTSD. Instead they suggest that sleep problems form a basic foundation of the illness (Spoormaker & Montgomery, 2008). Disturbed sleep might not just be a consequence, but part of the cause of PTSD. For example, some studies found an association between the presence of sleep disturbances (i.e., insomnia and decrease in overall sleep quality) prior to the trauma and an increased risk of PTSD development (Bryant, Creamer, O'Donnell, Silove, & McFarlane, 2010). Others found the same results for nightmares, but not for insomnia (van Liempt, van Zuiden, Westenberg, Super, & Vermetten, 2013).

These insights might be of great importance for the treatment of PTSD, which currently does not focus on treating sleep problems. The effectiveness of standard PTSD treatments on sleep problems is minimal (Belleville et al., 2011). Instead, treatments specifically aimed at sleep disturbances could be more effective. Recent research, in which the effects of nightmare specific therapies on posttraumatic nightmares were tested, has yielded promising results. Studies using

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Imagery Rescripting were especially successful (Casement & Swanson, 2012). In IR the patient is instructed to 'rescript' the recurring nightmare by modifying its ending, and rehearsing this new dream by using imagination techniques. Even one behavioural intervention session using IR showed to significantly improve nightmares and overall sleep quality (Germain, Shear, Hall, & Buysse, 2007). These studies were not only successful in reducing posttraumatic nightmares, but they also improved daytime PTSD symptoms. The question that arises now is how patients suffering from PTSD could benefit from these findings.

This current literature study will try to investigate what possible role therapies that use IR techniques and that are specifically aimed at treating nightmares, can play in the overall treatment of PTSD. First, the relationship between PTSD and sleep problems, and in particular nightmares, will be explored. Secondly, the effectiveness of first-line PTSD treatment in resolving nightmares will be discussed. Finally, the possible role of IR in PTSD treatment will be explored by reviewing the effects of nightmare specific therapies that include IR techniques on both nightmares and other PTSD symptoms.

Nightmares

2.1 Definitions, prevalence and etiology of nightmares

According to the DSM-IV, nightmares are extremely frighting dreams that awake the sleeper (4th ed., text rev.; DSM–IV–TR; American Psychiatric Association, 2000). The assumption is that the sleeper will awake from his nightmare because of the intense fear that he experiences. A dream that does not cause awakening is therefore not considered distressing enough to be classified as a nightmare. Those are narrow criteria however, since nightmares frequently contain other negative emotions that cause distress as well, such as anger, disgust and guilt. Nightmare patients also do not

necessarily wake up from their nightmares (Zadra, Pilon, & Donderi, 2006). In general, disturbing dreams that do not awake the sleeper are defined as bad dreams, and are considered less invasive than nightmares. Both bad dreams and nightmares are vivid, visual and emotional and can usually be recalled after awakening from sleep (Spoormaker, Schredl, & van den Bout, 2006).

Nightmares are fairly common in the general population, with prevalence estimates varying between studies. Most estimates range between 2-4% for severe cases, and 7-10% for less severe cases depending on nightmare intensity and frequency (Spoormaker et al., 2006). Nightmares are more prevalent in females than males, although this might be because women have a higher dream recall, and therefore remember their nightmares more often than men. Furthermore, nightmares occur more frequently in childhood and adolescence, and less frequently in elderly populations. Children that have a lot of nightmares however, often continue to have them later in life (Nielsen & Levin, 2007).

In PTSD nightmares are highly prevalent, 50-70% of people diagnosed with PTSD also suffer from nightmares (Spoormaker & Montgomery, 2008). About 50% of the nightmares experienced are so called posttraumatic nightmares (Wittmann, Schredl, & Kramer, 2007). Those are recurrent nightmares in which the trauma itself is (partially) being relived. Different from posttraumatic nightmares are idiopathic nightmares, in which the dream content is unrelated to trauma. Both types of nightmares are being reported in PTSD patients (Wittmann et al., 2007). But while idiopathic nightmares are common in all nightmare patients, posttraumatic nightmares typically occur in PTSD.

Nightmares can occur in all stages of sleep, but happen mostly during REM sleep. REM sleep is one of the two types of sleep, and is characterized by high frequency (30–80 Hz) and low amplitude EEG activity (Walker & van der Helm, 2009). There is also an increase of activity in several brain areas such as the hypothalamus, amygdala and anterior cingulate cortex, which are part of the affect network (Dang-Vu et al., 2010). REM sleep is therefore associated with emotional

memory processing. Furthermore, REM sleep is characterized by frequent bursts of rapid eye movements that happen mostly during dreaming, paralysis of voluntary muscles and an increase in heart rate (HR) and respiratory activity (Walker & van der Helm, 2009).

Non-REM (NREM) sleep is the other type of sleep that can be further divided into four sleep stages. Stage 1 is a transitional stage between sleep and wakefulness that only lasts for a few minutes. Stage 3 and 4 are usually taken together and are known as Slow Wave Sleep (SWS), in which the sleep is deepest. EEG activity in SWS has a low frequency (0.5– 4 Hz) and high amplitude (Walker & van der Helm, 2009). Stage 2 sleep is lighter then SWS, and is characterized by K-complexes, which are sudden pikes in EEG activity that drastically descend and then return to normal (Walker & van der Helm, 2009). Sleep during the night consists of cycles of 90 minutes in which NREM and REM sleep alternate. The amount of time each sleep stage lasts varies between cycles, with more NREM (in particular SWS) earlier in the night, and more REM sleep in later cycles (Walker & van der Helm, 2009).

PTSD patients might also suffer from night terrors, which are often confused with nightmares. A night terror is an arousal disorder that occurs during NREM sleep, in particular in SWS. It is characterized by extreme terror and screaming, and increased autonomic activity (e.g., excessive sweating, rapid breathing, mydriasis etc.). The patient appears to be alert with wide open eyes, but doesn't react to his environment. This lasts for a few minutes before sleep returns to normal. Unlike nightmares, patients can't recall any mental images or details about the episode except for having feelings of primitive danger and fear (Provini, Tinuper, Bisulli, & Lugaresi, 2011).

In sum, PTSD patients suffer from bad dreams and both idiopathic- and posttraumatic nightmares that typically happen during REM sleep. In NREM sleep, night terrors are common.

2.2 Function of Nightmares

Although sleep has been studied intensively in the recent past years, the actual function of sleep is still to be understood. The same applies to the function of nightmares and its underlying neurobiological mechanisms. Despite the lack of conclusive evidence, several theories have been proposed regarding the function and the working mechanisms in nightmares (Revonsuo, 2000; Hartmann,1998; Kramer, 1993; Walker & van der Helm, 2009). In overall, these theories share the notion that REM sleep is associated with emotional processing and memory consolidation. These models will be summarized here.

Revonsuo (2000) proposed the Threat Simulation Theory (TST) of dreams. In this model, dreams and nightmares have the biological function of simulating threatening events based on reality, and rehearsing threat perception- and avoidance. From an evolutionary perspective, the explanation is that life was more threatening in the past when humans had to survive by hunting and gathering. A mechanism for dreaming in which dangerous situations were rehearsed would have been a great way to safely develop threat avoiding skills, which would increase reproductive chances in the real world. In this model, nightmares are not considered dysfunctional dreams. Nightmares, more often than dreams, contain powerful simulations of dangerous threats. Nightmares occur when there is an increased need for these powerful simulations, which makes them more adaptive than dreams. Although there are several arguments in favour of TST, there is also conflicting evidence. In TST for example, one would expect the majority of dreams to be threatening. Malcolm-Smith, Solms, Turnbull, & Tredoux (2008) however found that only about 20% of dreams featured threatening content. Furthermore, participants living in highly dangerous areas reported fewer threatening dreams than those living in less dangerous areas. Also, PTSD, and nightmares in general are not considered beneficial or adaptive.

Hartmann (1998) suggested a theory of Image Contextualization. Nightmares have the

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function to create a context for the dreamer's emotional concerns. These contexts are presented as Central Images (CIs), which are powerful and emotional dream images whose associated emotions, but not necessarily its specific contents, correspond with one's emotional concerns. A person, who for example had a car accident, might dream about being hit by a tornado. The tornado dream is a CI that contextualizes the emotion of fear. In Image Contextualization, the content of dreams and nightmares are guided by the emotions of the dreamer. The more powerful the emotion, the more intense is the CI. Most evidence for Image Contextualization comes from studies that found CIs to be more frequent and intense among traumatized participants, and in dreams that participants considered personally significant (Nielsen & Levin, 2007).

The theories described above try to explain the function of nightmares, but they lack neurobiological evidence.

A theory by Kramer (1993) suggests that dreaming has a function of mood regulation. REM sleep is characterized by an increase of activity of the limbic system, which is an area associated with emotion. Dream content is responsible for decreasing the intensity of this emotional activity, which is achieved by a pattern of dreaming spread across all REM sleep periods in a night. The function of this pattern is emotional problem solving and to improve mood. In contrast, recurrent posttraumatic nightmares address an emotional conflict without solving it, thus repeating the same dream over and over. This model is supported by studies that found that one's dream content is influenced by pre-sleep emotions, and post-sleep mood is related to dream content (Nielsen & Levin, 2007). A similar notion was postulated by Walker & van der Helm (2009), who proposed the Sleep to Forget and Sleep to Remember (SFSR) hypothesis. Like Kramer's theory, REM sleep has a function of affective memory processing by decreasing emotional intensity, en thereby improving mood. Several studies support this theory, including those that found that highly emotional memories (that are accompanied by high amygdala activity) lose their emotional reactivity over time (i.e., reduced amygdala activity during recognition of those memories). Other studies found

that REM sleep deprivation leads to lower mood and more negative emotions. In contrast, after sleep (in particular REM sleep), mood is restored and emotions are more positive (Gujar, McDonald, Nishida, & Walker, 2010).

2.3 Fear conditioning and a neurobiological model

Hobson proposed a neurological theory of dreaming, namely the Activation-Synthesis theory (Hobson & Pace-Schott 2002). Contrary to the other theories, dreams do not have a function. REM-sleep is a state in which the brain is active, which causes the experience of consciousness. However, there are differences in neurochemistry and brain activity patterns compared to the wake state. The brain areas responsible for motor activity and executive function are relatively deactivated during REM-sleep, which is why orientation and analytical thought is absent during dreaming. Furthermore, the limbic structures are relatively active, which explains the emotional nature of dreams. REM-sleep may have a function of integrating memories that are consolidated during NREM, with other stored memories. Dreams are the subjective experiences of those hyperactive processes during REM-sleep.

Nielson & Levin (2007) proposed a nightmare model that incorporates several other models with neurobiological findings called the Affect Network Dysfunction (AND) model. This model uses well supported evidence from research on fear memory acquisition and extinction, and suggests that dreams have a function of fear extinction. Nightmares are a result of a dysfunction in this mechanism. This model is illustrated in Figure 1. In classical fear conditioning, a person is exposed to a harmful unconditioned stimulus (US) that is accompanied by a neutral conditioned stimulus (CS). The harmful US evokes a reflexive response of fear. This fear response consists of behaviours such as freezing, the increase of autonomic activity and the release of stress hormones (Ehrlich et al., 2009). After repeated exposure to this CS-US combination, the CS will acquire the

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negative properties of the US, thus evoking the fear response when presented alone. Fear memory extinction is not a simple process of forgetting, but requires the formation of new extinction memories by repeatedly presenting the CS in neutral contexts.

In the AND model, there are three processes at work that create and maintain fear extinction memories. The first process is element activation, which is the increased availability of memory elements during dreaming. The second process is element recombination, which is responsible for reorganization of these elements into coherent simulations of reality in which a CS is presented in a new and neutral context that is incompatible with the original harmful US, thus creating a new fear extinction memory. The third process is emotional expression, which is the experience of the modified emotional reactions to this new fear extinction memory during dreaming (Nielsen & Levin, 2007).

Furthermore, they hypothesized two factors that have an influence on how successful fear extinction is. Affect load (situational factor) is the total amount of stress and negative emotions that someone experiences on a day, while affect distress (personality factor) is the sensitivity to emotional distress. High affect load will increase the chance on having nightmares, while someone with a high affect distress will experience nightmares as more emotionally distressing.

An important brain structure responsible for fear memory acquisition and storage is the amygdala (AMG) (Ehrlich et al., 2009). The amygdala is connected to a large number of brain structures. Among these structures are the Medial Prefrontal Cortex (MPC), the hippocampus (HIP) and the Anterior Cingulate Cortex (ACC) which are all associated with fear extinction, and are highly active during REM sleep. Together with the AMG they form the limbic network (Heim & Nemeroff, 2009). During a dream, the anterior HIP produces a context for emotional activation from loose memory elements. The basal and central nucleus of the AMG then processes this context, and gives it emotional value. The dorsal and rostral ACC and the MPC stabilize this emotion by inhibiting and regulating the AMG process, and signal the appropriate affect distress.

The AMG then signals the brainstem and hypothalamus, which produces the autonomic fear responses. By introducing neutral memory elements that are incompatible with the fear memory, new fear extinction memories are created (Nielsen & Levin, 2007).

Nightmares occur when there is a high activation of fear memories due to a (sudden) increase of affect load. This could result in an overactive AMG, decrease of MPC control on the regulation of the AMG or in failure of the HIP to produce incompatible contexts for fear extinction memories. Trauma memories are more resistant to recombination and modification of memory content than normal fear memories, which makes posttraumatic nightmares more difficult to process (Nielsen & Levin, 2007).

Objective and subjective sleep measures in PTSD

Both objective and subjective measures are being used to assess various aspects of sleep. Objective sleep measures are methods mostly used to study the structure and architecture of sleep. The most commonly used method is polysomnography (PSG), which includes measures of HR, eye movement, muscle tension, respiration and electroencephalogram (EEG). EEG is used to measure electric activity in the brain, and can monitor transitions between sleep stages (Babson & Feldner, 2010). Other objective measures that can be used in studying sleep architecture are functional neuroimaging techniques, such as Positron Emission Tomography (PET), which can link sleep functions to specific brain regions by measuring brain activity through changes in glucose metabolism in the blood.

Subjective sleep measures are helpful in providing subjective data from sleep, such as time of awakening, nocturnal awakenings, sleep quality, depth of sleep and severity and frequency of sleep disturbances. Subjective methods include questionnaires, sleep diaries and clinical interviews. Although useful in a clinical setting, subjective sleep measures have limited usefulness in research

because there is a high variability in subjective evaluations of sleep, and because outcomes are difficult to validate against objective sleep measures (Zhang & Zhao, 2007).

In PTSD, while there is a high prevalence of subjective sleep complaints among patients, studies investigating sleep disturbance using PSG have found inconsistent results (Table 1). Klein, Koren, Arnon, & Lavie (2003) for example found a discrepancy between subjective and objective sleep disturbance. No difference between PTSD and non-PTSD patients in objective sleep disturbance was observed using actigraphy, while PTSD patients reported significantly poorer sleep on the subjective mini-sleep questionnaire. They concluded that sleep complaints might be a result of an altered sleep perception, rather than real sleep disturbances in PTSD.

Breslau et al. (2004) also found no significant objective evidence for sleep disturbance in PTSD patients. No differences in sleep initiation and maintenance compared to healthy controls were reported using standard PSG measures. They did however found that lifetime PTSD patients had more brief arousals from REM sleep.

In a meta-analysis by Kobayashi, Boarts, & Delahanty (2007), 20 PSG studies comparing sleep in PTSD and non-PTSD patients were selected. The purpose was to synthesize findings of previous studies, and to examine the overall pattern of objectively observed sleep disturbances in PTSD despite the inconsistencies in the results of those studies. They found that patients with PTSD had more stage 1 sleep, and less SWS. Furthermore, PTSD patients had more REM sleep density. These results support the findings of increased hyperarousel during sleep in PTSD. Lastly, they found that variables such as age, sex, depression and substance disorder comorbidity appeared to moderate the effects of PTSD on sleep, and suggested that those moderating variables may explain the inconsistencies found in previous studies.

In a more recent study, Kobayashi, Huntley, Lavela, & Mellman (2012) measured several sleep parameters in PTSD using PSG, actigraphy, and a subjective sleep diary.
 They found some discrepancies between subjective and objective sleep measures (participants

reported lower wake-time-after-sleep-onset in the diary relative to actigraphy, and overestimated the sleep-onset-latency in the diary relative to PSG), however these discrepancies existed regardless of PTSD or trauma exposure status. There were no differences between healthy controls and those with PTSD or trauma exposure, thus the discrepancies were not associated with PTSD.

Lastly, Germain et al. (2012) used PET to study REM sleep in combat veterans. Participants slept in a sleep laboratory for 3 nights, and during the second REM sleep period in the third night PET scans were acquired over a 20 minutes period. Although there was only a small number of participants (6 veterans diagnosed with PTSD, 6 veterans without PTSD), a pattern of hypermetabolism was observed in brain regions that are involved in arousal, fear response and reward processing during wakefulness and REM sleep in veterans with PTSD, compared to veterans without PTSD.

In conclusion, reported subjective sleep complaints are common in PTSD. However, PSG studies provide inconsistent results. Nonetheless, PTSD patients did have more stage 1 sleep, less SWS and more REM sleep density. The discrepancies between subjective and objective sleep disturbance may not be specifically related to PTSD, and may be influenced by other moderating variables like age, sex and the comorbidity of other disorders. PET could be a useful objective method for determining which brain structures are overly active during sleep in PTSD.

The relationship between nightmares and PTSD

In the DSM-IV nightmares are considered secondary symptoms of PTSD, falling under the re-experiencing symptom cluster. However, in the last decade or so researchers have shifted from this idea, suggesting the notion that nightmares are important in PTSD development. This started with a study by Ross, Ball, Sullivan, & Caroff (1989) in which they stated that sleep problems are a hallmark of PTSD. They speculated that dream disturbance is relatively specific to PTSD, and

hypothesized that a dysregulation of REM sleep mechanisms may be implicated in the pathogenesis of posttraumatic nightmares. At that time, however, no research on REM sleep function prior to PTSD development was conducted.

More recently, Spoormaker & Montgomery (2008) argued that disturbed sleep is a core feature of PTSD. They discussed three questions about the nature of sleep disturbance in PTSD using findings from sleep research. They asked whether disturbed sleep is a risk factor for PTSD, whether disturbed sleep is a residual symptom after PTSD is treated, and whether treatment for sleep problems alleviate other PTSD symptoms. If sleep disturbance is a secondary symptom of PTSD, one would expect a negative answer on those questions.

4.1 Nightmares as a risk factor for PTSD development

Several studies have identified nightmares and other sleep disturbances as predictors and possible risk factors for PTSD. In a prospective cohort study, Bryant et al. (2010) assessed 1033 patients who were hospitalized after traumatic injury. They were given the Sleep Impairment Index (SII) questionnaire to identify sleep disturbance 2 weeks prior to the traumatic event, and the Mini-International Neuropsychiatric Interview to account for current psychiatric disorders. In a 3-month follow-up, the patients were assessed for emerging psychiatric disorders, and for PTSD using the Clinician Administered PTSD Scale-IV (CAPS). Results indicated that sleep disturbance 2 weeks prior to the traumatic event predicted PTSD development within 3 months after the trauma, even when other psychiatric disorders and variables such as age, sex and characteristics of the traumatic injury were controlled for. However, the sleep reports were acquired retrospectively, which means that sleep disturbance was not officially diagnosed, and subjective bias might have influenced the results. Also, the SII doesn't measure nightmares, so no conclusions can be made regarding nightmares and the prediction of PTSD.

In an other prospective cohort study by Melmann, Bustamante, Fins, Pigeon, & Nolan (2002), 21 patients with traumatic injuries were assessed, plus 10 healthy control subjects in order to control for the effects of traumatic injury on sleep. Within 1 month after the injury REM sleep was measured using PSG. The participants were also given the CAPS to measure PTSD symptoms at that same time, and during a follow-up 6 weeks later. They found no differences in sleep duration and maintenance within 1 month after trauma between patients with and without PTSD symptoms at the follow-up, however they found that the patients who development PTSD symptoms had more fragmented REM sleep.

Lastly, van Liempt et al. (2013) studied the effects of sleep disturbance on the development of PTSD symptoms in combat veterans in a prospective cohort study. 453 Dutch servicemen were selected prior to deployment to Afghanistan, and were given a selection of items related to sleep from the Self-Rating Inventory for PTSD (SRIP) and the SCL-90 to assess insomnia and nightmare symptoms. Depression and anxiety symptoms were also controlled for. In a 6-month follow-up post deployment they were given the SRIP to measure PTSD symptoms. The results of this study indicated that the presence of nightmares prior to deployment was associated with the development of PTSD symptoms. However, pre-deployment insomnia did not predict PTSD symptoms.

In conclusion, there are several studies that found an association between sleep disturbance prior to trauma, and the development of PTSD symptoms. Nightmares seem to predict PTSD development, but the evidence regarding the predictive value of insomnia is inconsistent. A possible explanation is that studies that found a significant effect for insomnia didn't control for mood and anxiety symptoms prior to trauma, which means that these factors might be responsible for both insomnia and the development of PTSD. Another explanation is that these studies measured insomnia only post trauma, or both prior and post trauma, which means that perhaps only the presence of insomnia after the traumatic event might contribute to PTSD development (van Liempt et al., 2013). Finally, fragmented REM sleep was associated with PTSD development, although the

number of participants was low in this particular study.

Nightmares could well be a risk factor for PTSD, which means that nightmare specific treatment immediately after trauma might prevent or slow down the development of PTSD.

4.2 Neurobiological mechanisms of nightmares in PTSD

The exact relation between nightmares and PTSD is still unknown, and no integrative neurobiological model of the underlying mechanisms has yet been proposed. As suggested above, nightmares could be a risk factor or mediating factor in the development and maintenance of PTSD. Nonetheless, nightmares and PTSD are closely related, and both show altered activity in the same brain regions. PTSD is directly associated with changes in the AMG, HIP, ACC and the MPC (Heim & Nemeroff, 2009). The same areas are associated with REM sleep, dreaming and nightmares, and have functions of mediating stress adaptation and fear conditioning (Nielsen & Levin, 2007). See also Figure 2 for an illustration.

In PTSD, the Hypothalamic–pituitary–adrenal (HPA) axis is dysfunctional due to prolonged exposure to stress hormones, resulting in a strong increase of glucocorticoid (i.e., cortisol) secretion from the adrenal glands (Fries, Hesse, Hellhammer, & Hellhammer, 2005). High levels of glucocorticoids are associated with a decrease in volume of the HIP (Heim & Nemeroff, 2009). The HIP is implicated in the formation of contexts for emotional imagery, so when function of the HIP is reduced or disturbed, emotional (e.g., fear) memories are not properly processed (e.g., due to the inability of the HIP to differentiate between fear- and neutral contexts) which can result in nightmares.

Furthermore, the initiation and termination of REM sleep is regulated by respectively cholinergic and aminergic activity in the brainstem. Noradrenaline is an aminergic neurotransmitter, which means that increased noradrenergic activity will disrupt REM sleep. High noradrenalin levels

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have been reported in PTSD patients, and are associated with AMG overactivity (Spoormaker & Montgomery, 2008). This means that increased noradrenalin levels and AMG overactivity may cause REM sleep terminations, a hypotheses that is supported by reports of REM sleep fragmentation and increased REM sleep density in PTSD patients (Melmann et al. 2002; Kobayashi et al. 2007).

Functional neuroimaging shows glucose hypermetabolism in the AMG during REM sleep and wakefulness in PTSD (Germain et al., 2012) and during exposure to both traumatic and non-traumatic emotional cues. This is further supported by a meta-analysis (Etkin &Wager, 2012) in which studies were examined that used Functional Magnetic Resonance Imaging (FMRI) and PET to measure brain activity in PTSD, social anxiety disorder or specific phobias. As predicted, results showed overactivity of the AMG in PTSD compared to healthy controls.

Decrease in volume of the MPC and the ACC has also been found in PTSD patients, and decrease of MPC- and ACC activity Is correlated with PTSD symptom severity (Heim & Nemeroff, 2009; Etkin &Wager, 2012). As suggested in the AND model, an overactive AMG and an inability of the MPC and ACC to inhibit and regulate AMG activity can cause nightmares.

Decreased HIP volume and AMG overactivity are not only consequences of PTSD, but are also associated with an increased risk of its development (Heim & Nemeroff, 2009). A case-control study with 40 male monozygotic twin pairs for example, found that more severe PTSD was associated with a smaller HIP. They also found that small HIP volume in severe PTSD patients did not differ from their identical twin brothers that did not have PTSD. This suggests that a small HIP volume might be a genetic risk factor instead of a consequence of PTSD, (Gilbertson et al., 2002).

Dysfunction of the fear extinction network due to nightmares, e.g., reduced function of the HIP, could hypothetically contribute to the development of PTSD, which makes the presence of nightmares a potential risk factor in PTSD.

Besides these suggested neurobiological mechanisms, Cognitive-behavioral factors could

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also be implicated. Because posttraumatic nightmares are extremely distressing, patients might display avoidance behaviour before bedtime, such as staying up late, letting the lights on or making something to eat in the middle of the night. This behaviour might contribute to the development of insomnia, and indirectly to problems in daytime functioning (Spoormaker & Montgomery, 2008).

4.3 Effectiveness of first-line PTSD treatment on nightmare symptoms

If nightmares are secondary symptoms of PTSD, then they should vanish when PTSD is successfully treated. If they remain after treatment they have probably developed into separate disorders, and will require specific treatment (Spoormaker & Montgomery, 2008).

Galovski, Monson, Bruce, & Resick (2009) studied the effects of trauma-focused cognitive processing therapy (CPT) and prolonged exposure (PE) on health concerns and sleep disturbances by using data from 108 female adult rape survivors diagnosed with PTSD, who were selected from within a larger randomized controlled trial (RCT). Results indicated that CPT and PE were successful in reducing health concerns related to PTSD. Both treatments also reduced sleep disturbance, however sleep problems persisted at a clinically significant level in the entire sample. CPT or PE treatment alone does not seem to be effective enough for treating sleep disturbance in PTSD, and might need additional specific treatment. In this study however, there was no report on nightmares specifically, only on general sleep disturbance.

In an other study, Belleville et al., (2011) examined the effects of trauma-focused CBT on sleep disturbances in 55 PTSD patients. They measured general sleep disturbance, PTSD related sleep disturbance (e.g., posttraumatic nightmares, bad dreams and night terrors) and general PTSD symptoms. Results found significant improvements on sleep quality, efficiency, sleep-onset-latency and sleep disturbances. However, these changes were not fully preserved after 6 months posttreatment, since 70% of patients who had sleep problems still reported them after treatment.

Nightmares showed the same results, and remained a problem after 6 months posttreatment. PTSD patients who showed more persistent sleep problems also had more severe PTSD, anxiety, depression and poorer health. This study showed that CBT for PTSD did reduce sleep problems and nightmares, however they remained as residual symptoms in most participants after 6 months posttreatment. A limitation is that measurements consisted mainly of self-report questionnaires, which could have influenced the results.

Spoormaker & Montgomery (2008) analysed several studies that examined the effects of psychological and pharmacological therapies for PTSD on associated sleep disturbances, including a meta-analysis that consisted of 38 RCTs. They found that most studies only reported mild or non-significant results regarding the effects on sleep disturbance, and most studies did not use validated instruments to diagnose sleep disturbance and nightmares. There were also conflicting results regarding nightmares, as some studies found positive results, while others found none results. A pharmacotherapy using Cyproheptadine showed a small negative effect, although non-significant. In overall, there were significantly more improvements in general PTSD symptoms than in associated sleep disturbances, which usually remained at a clinically significant level.

In conclusion, first line PTSD treatments such as standard CBT are effective in treating global PTSD symptoms, but less effective in treating sleep disturbance. Nightmares and other sleep problems are reduced, but persisted as residual symptoms after treatment was completed. The inclusion of sleep specific components in first line PTSD treatment might be beneficial for PTSD patients.

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Imagery Rescripting

5.1 Imagery Rescripting in the treatment of nightmares

In the last decade, there has been an increase in the amount of research focusing on nightmare specific interventions. Considerable advantages have been made, both pharmacologically and psychologically. The drug Prazosin for example has shown promising results in reducing nightmares, with relatively little side effects (Schoenfeld, DeViva, & Manber, 2012).

Psychologically, CBT treatments using Imagery Rescripting (IR) have been successful so far. There are different nightmare specific therapies in which IR is being used, such as Imagery Rehearsal Therapy (IRT), Exposure, Relaxation, and Rescripting therapy (ERRT) and Imagery Rescripting and Exposure Therapy (IRET) that are all in some way variations of IR. In short, the patient chooses (a part of) a particular distressing and recurrent nightmare, and changes details in this nightmare. For example a negative dream outcome from which the patient usually awakes is changed into a positive, non-threatening outcome. This modified dream is then rehearsed on a daily basis, so that eventually this new version of the nightmare replaces the original nightmare, and thereby removing any associated negative thoughts and emotions. The working of IR is illustrated in Figure 3. Besides writing down and changing the original nightmare and daily rehearsal of this modified dream, sleep education in order to improve sleep hygiene is included in all IR treatments.

Some treatments have added an additional exposure component, in which traumatic imagery is activated in a safe setting. This can for example be done by discussing the distressing nightmare, or by writing it down and reading it out loud. This way the patient can learn to control and identify trauma images and its associated physiological arousal. While not all IR treatments use exposure as a separate component, the patient is initially exposed to traumatic imagery on some level due to the necessity of recall of the original nightmare before rescripting (Long & Quevillon, 2009).

The working mechanisms of IR in PTSD are still unknown, although there are several theories. The cognitive-behavioral view states that IR reduces the symptoms of PTSD by activating the fear network, and by exposure to traumatic imagery, habituation to the trauma and its emotional and physiological effects occurs (Long & Quevillon, 2009). Furthermore, identifying and modifying negative and dysfunctional thoughts could enable the patient to get control over the traumatic images (Long & Quevillon, 2009).

In PTSD, most patients only have a small number of traumatic memories, that mostly involve sensory imagery. These memories are poorly integrated into other long-term autobiographical information (Hackmann, 2011). Integration and processing of those memories is further blocked because patients actively try to avoid anything related to the trauma. Overall, traumatic memories have distorted meanings, they do not connect with other memories of the individual, and they are easily triggered (Hackmann, 2011). This, in turn, can lead to symptoms of reliving through flashbacks or recurrent nightmares. In IR, these memories are being integrated into a wider context of past, neutral experiences, and associated negative affect is separated from the memory. This can for example be accomplished by correcting a wrongly remembered traumatic image, by changing the perspective on the traumatic event, by seeing the trauma from someone else's perspective, e.g., a dead relative that committed suicide, by imagining other possible outcomes that could have happened if the patients had done something differently, etc. (Hackmann, 2011).

Functional neuroimaging studies that investigated the neural activity in PTSD patients during exposure to traumatic imagery showed an increase in AMG activity, and a decrease in MPC activity (Shin et al., 2004). This supports the theory that the fear network is accessed during exposure and rescripting treatments. This is also in line with the nightmare model proposed by Nielsen & Levin (2007), that states that nightmares are a dysfunction of the fear extinction processes during dreaming. With IR, the fear imagery of traumatic nightmares is manually

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modified, a function normally carried out by the fear extinction network.

IR, and especially IRT, have already been used successfully for some time in idiopathic nightmares. In treatment of posttraumatic nightmares in PTSD however, trauma focused CBT and pharmacotherapy are still the primary choice despite the potential effectiveness of IR. Recently there have been some studies that examined the effects of IRT and other IR related therapies on PTSD and posttraumatic nightmares. Here, the findings of these studies will be discussed. (See Table 2 for an overview)

5.2 Effectiveness of IR therapies on posttraumatic nightmares and PTSD

In a meta-analysis, Casement & Swanson (2012) evaluated 13 studies that examined the efficacy of IR treatments on disturbed sleep in PTSD.

Results of this meta-analysis indicated that nightmare frequency and general sleep quality improved after IR treatment. Surprisingly, IR did also greatly reduce general PTSD symptoms. The positive effects on both nightmares and PTSD symptoms were preserved over 6 and 12 months. However, improvements in general PTSD symptoms were still larger after trauma-focused CBT than IR, as comparisons in effect sizes between different meta-analyses showed (Casement & Swanson, 2012). Furthermore, there were no differences between studies that used IR with a treatment component of direct exposure, and those without. Studies that used both IR treatment and CBTI reported greater improvements in sleep quality than studies that only used IR, but not in nightmares or other PTSD symptoms. This meta-analysis showed promising results for IR, since sleep, nightmares and PTSD symptoms were all improved after treatment. However, if treatment of general PTSD symptoms is the main purpose, then trauma-focused CBT should be considered before IR.

There are some limitations in this meta-analysis. From the 13 selected studies in this meta-

analysis, only 5 were RCTs. There was also only one study that had a control condition in which patients received a competitive treatment, consisting of CBT that focused on PTSD. This means that with exception of this particular study, the relative improvements in nightmares and PTSD after IR found in the other studies could not be compared to regular PTSD treatments. There was also only one study that measured group vs individual treatment. The other studies were all group therapies, so no conclusions regarding the efficacy of group vs individual therapy can be made. Lastly, there were 8 different varieties of IR treatment, which makes comparing between studies difficult, and makes it impossible to ascribe treatment effects to specific treatment components.

Thünker & Pietrowsky (2012) examined the effectiveness of a manualized IRT on patients with nightmares with or without comorbidity of depression or PTSD. 69 participants were selected, from which 26 had PTSD and nightmares. Those 26 participants were split up into a treatment group (14) and a waiting list control group (12). Patients in the control group underwent a trauma focused psychotherapy.

Results indicated that IRT significantly reduced nightmare frequency, anxiety during the nightmare, frequency of nocturnal awakenings due to nightmares, and level of distraction the following day for all three patient groups, and those effects remained during the follow-up 10 weeks later. Younger patients had more improvement than older patients, possibly due to more chronic nightmares at older age. Treatment effects on the number of nightmares and on the anxiety experienced during nightmares were less pronounced in PTSD patients than in the nightmare-only and major depression group, possibly because nightmare frequency and anxiety was higher in PTSD patients pretreatment. Furthermore, IRT was not significantly more effective in reducing nightmare frequency and anxiety in PTSD than trauma focused psychotherapy in the control group. In sum**,** while IRT did reduce nightmare frequency and severity in PTSD, it is still unclear if this treatment is more beneficial than first-line PTSD treatment in reducing nightmares in PTSD. Limitations in this study are the relatively low number of PTSD participants, with only 14 in the IRT, and 12 in the

control condition.

In a randomized controlled study, Rhudy et al. (2010) examined the effectiveness of ERRT on both subjective sleep- and nightmare disturbance, and objective physiological fear reactions.

Results indicated significant improvements in nightmare**s** and sleep quality. Furthermore, physiological reactions to nightmare imagery were decreased in the treatment group after ERRT, relative to pretreatment and the control group. Decrease in objectively measured arousal via skin conductance was sustained during follow-up. Decrease in HR was not sustained during the 3 month follow-up compared to posttreatment, but HR at the 6 month follow-up was significantly lower than pretreatment HR. EMG effects were not sustained during follow-up, but EMG activity was already relatively low at pretreatment. In short, this RCT provided evidence that ERRT improves physiological fear reactions and subjective distress in nightmares. The study did not have a control condition that underwent regular trauma focused CBT, so no comparisons in efficacy can be made.

In a pilot study, Germain et al. (2007) examined the effects of a single 90-minutes brief intervention session combining IRT, stimulus control and sleep restriction on sleep disturbance and nightmares in PTSD patients. Anxiety and depression was also measured.

Preliminary findings indicated that sleep quality was modestly improved, that nightmare frequency was decreased and that daytime PTSD symptoms were decreased as well. No improvement in anxiety or depression was found. Since this was an open-labeled pilot study with 7 participants, no broad conclusions can be drawn. It is unclear which intervention component is responsible for the found effects, and what the long term effects are. Despite the limitations, the results of this pilot study indicate that a single session of IRT might improve sleep quality and nightmares in PTSD.

Discussion

In this literature review the relationship between nightmares and PTSD was explored, and the potential role of IR in PTSD treatment was investigated.

In order to explore the relationship between nightmares and PTSD, the mechanisms underlying nightmares had to be examined first. Findings indicated that these mechanisms are still poorly understood. Several models tried to explain the (dys)function of nightmares, including threat-simulation, Image Contextualization and mood regulation. However, these models lack neurobiological evidence and are mostly speculative.

The most comprehensive model of nightmare function that was found was the AND model, which tried to integrate neurobiological findings with the well supported theory of fear memory extinction (Nielsen & Levin, 2007). The notion of nightmares as a dysfunction of dream processes that regulate fear memory extinction is supported by findings that link fear extinction to the AMG, HIP, MPC and ACC; by brain image studies that found an increase of activity in these structures during REM sleep, and by an increase of nightmares in patients who had lesions in this network (Nielsen & Levin, 2007). Despite the plausibility of this model, more research should be conducted to establish the link between actual dream content and the process of fear conditioning. Measuring nightmares is difficult due to the high subjectivity and variability in nightmare content. There is currently no objective way to measure nightmare content, so subjective measures such as dream diaries and questionnaires have to be used although they are susceptible to subjective bias. While objective sleep measures could be helpful in assessing changes in REM sleep in nightmares, they might underestimate nightmare frequency and severity because patients generally feel safer during sleep in a laboratory setting.

In research on measurements of sleep in PTSD, reports of subjective sleep complaints are common. However, PSG studies provide inconsistent results (Klein et al., 2003; Breslau et al.,

2004). These discrepancies may not be unique to PTSD, and moderating variables may have influenced results (Kobayashi et al., 2007). Despite the found inconsistencies, PTSD patients did have more stage 1 sleep, less SWS and more REM sleep density. A possible explanation for the inconsistent PSG findings might be that differences in REM sleep between non-PSTSD and PTSD patients are too subtle for PSG to detect. Other objective measures, such as functional neuroimaging, might be more able to assess these differences (Germain et al., 2012). While this pilot study showed differences in brain activity between PTSD and non-PTSD in REM sleep, only 12 veterans participated which makes it impossible to generalize these findings. Future researchers should use functional neuroimaging more often in examining relations between sleep and PTSD, using larger patient samples.

Several researchers investigated the presence of sleep problems prior- or immediately post trauma, in order to shed light on the temporal relationship between sleep problems and PTSD.

Bryant et al. (2010) found that sleep disturbance 2 weeks prior to trauma predicted PTSD development 3 months after trauma. However, sleep disturbance was measured retrospectively via subjective questionnaires. This means that no official diagnoses of sleep disturbance were made. Also, memories about the subjective experience of sleep disturbance could have been forgotten or changed over time, and interpreted more positively or negatively than the actual sleep disturbance. The study had a large patient sample (1033) which increases the reliability of the findings. However, no specific data on nightmares were reported.

Melmann et al. (2002) found no differences between PTSD and non-PTSD patients in sleep initiation and maintenance short after trauma. However, fragmented REM sleep did predict PTSD development. Only 21 patients were assessed, which gives this study little power. Also, sleep was measured after trauma, which means that the trauma itself could have had an effect on sleep quality.

The study by Van Liempt et al. (2013) was the strongest, since they controlled for mood and anxiety, recruited a large sample (453) of veterans prior to deployment, and measured long term

PTSD development over 6 months post-deployment. They also made a distinction between nightmares and insomnia. They found that the presence of nightmares prior to deployment increased the risk of developing PTSD. A limitation is that all participants were veterans, so all trauma was war-related. different trauma-types (e.g., sexual assault or a car accident) might have other influences on PTSD development, or show a different pattern of PTSD symptoms.

Since the exact neurobiology of nightmares is unclear, the neurobiological relationship between nightmares and PTSD is speculative. If nightmares are considered a dysfunction of the fear extinction network like suggested in the AND model, then several possible mechanisms can been identified (Heim & Nemeroff, 2009). A dysfunctional HPA-axis due to stress can lead to reduction of HIP volume, while increased noradrenergic activity leads to AMG overactivity and REM-sleep termination. Reduction in HIP volume, AMG overactivity and reduced MPC and ACC function can cause nightmares. In turn, altered HIP and AMG activity are risk factors for PTSD, which is why nightmares could also contribute to PTSD development. Avoidance behaviour before sleep due to nightmares can contribute to insomnia development, and has a negative effect on daytime functioning, which could worsen daytime PTSD symptoms (Spoormaker & Montgomery, 2008). These proposed mechanisms explain the close relationship between nightmares and PTSD, and how nightmares might mediate in PTSD development. However, more fundamental research on the neurobiology of nightmares is needed, as mentioned above.

Findings further indicated that first-line PTSD treatments have a moderate or small effect on nightmares, and that nightmares typically remain as residual symptoms (Belleville et al., 2011). Notably, there were only a small number of studies that reported effects on nightmares specifically. Most studies analysed by Spoormaker & Montgomery (2008) didn't use validated sleep instruments. In future research, the effectiveness of first-line PTSD treatment on nightmares should be examined by using validated nightmare measurements, by making a distinction between different sleep disturbances and by investigating why nightmares remain after treatment. Again, more fundamental

research on nightmare mechanisms is needed. Insomnia and nightmares are related- but separate sleep problems that require specific assessment.

Sleep specific therapies that include IR techniques are found to improve nightmares in PTSD, and improve general sleep quality. Notably, daytime PTSD symptoms were reduced as well. Most studies to date that examined IR therapies such as IRT, ERRT, IRET etc. on nightmares in PTSD were included in the meta-analyse by Casement & Swanson (2012). These studies however varied greatly in design, patient groups and treatment protocols. Length of treatment, long or short term follow-ups, inclusion or exclusion of exposure- or CBTI components, individual or group therapy, veterans or civilians, etc. may all affect treatment outcomes. This makes comparisons between different IR therapies and first-line PTSD treatment such as trauma-focused CBT very difficult. 12 of 13 studies lacked adequate control conditions in which competitive treatments were given. In short, results were promising regarding the improvements in nightmares, sleep and daytime PTSD symptoms. However, due to variation in design and treatment protocols, the exact efficacy of IR is not clear.

Thünker & Pietrowsky (2012) did include a competitive treatment group (trauma-focused CBT), and also compared different patient groups (nightmares alone, nightmares + PTSD and nightmares + depression). They found improvements in all patient groups, however less improvements were found in PTSD patients compared to the other groups. Compared to trauma-focused treatment in the control group, IR treatment was not significantly more effective. Because the patient sample was small, no conclusions should be made regarding the relative efficacy of IR. It is possible that subtle treatment gains only show in larger patient groups.

One study also measured objective physiological treatment changes. Rhudy et al. (2010) found that ERRT reduced both physiological and emotional fear reactions, and improved nightmares and sleep quality. There was no standard treatment in the control condition, so it is unknown if, for example trauma-focused CBT, has the same physiological benefits as ERRT.

In the last study, it was found that a brief intervention with IR improved sleep, nightmares and PTSD symptoms. They do suggest that PTSD patients benefit from even 1 session, which is promising. However, the small patient group (7 patients), lack of control condition, lack of long term follow-up limit these findings.

In overall, this literature study found that neurobiological mechanisms in nightmares are still poorly understood. Since nightmares can be a risk factor in PTSD, and are usually persistent even after first-line PTSD treatment, they are possibly more than secondary symptoms of PTSD. More fundamental research on nightmares should be conducted. In theory, nightmares can contribute to daytime PTSD symptoms. This is supported by IR studies that found improvements in global PTSD symptoms after nightmare specific therapies. Furthermore, IR improves nightmares and general sleep quality. This means that first-line PTSD treatments might benefit from a nightmare focused IR component. However, it is unclear if IR is more beneficial than current first-line treatment. Standard trauma-focused CBT is generally successful in treating global PTSD, so in order to know which treatment is more effective, future research should include competitive PTSD treatment conditions.

Besides that, IR therapies themselves should be examined. IR therapies consist of combinations of several different treatment components, and it is unclear which component is responsible for the beneficial treatment effect. By conducting an experiment in which different groups get different combinations of treatment components, the relative effect of each component could be identified.

Lastly, despite the popularity of subjective measures in nightmare research, more objective measures should be used. For example, functional neuroimaging studies could be used to observe differences in brain activity between normal dreams and nightmares, in both non-REM and REM sleep. This could provide more information on the neurobiological mechanisms in nightmares.

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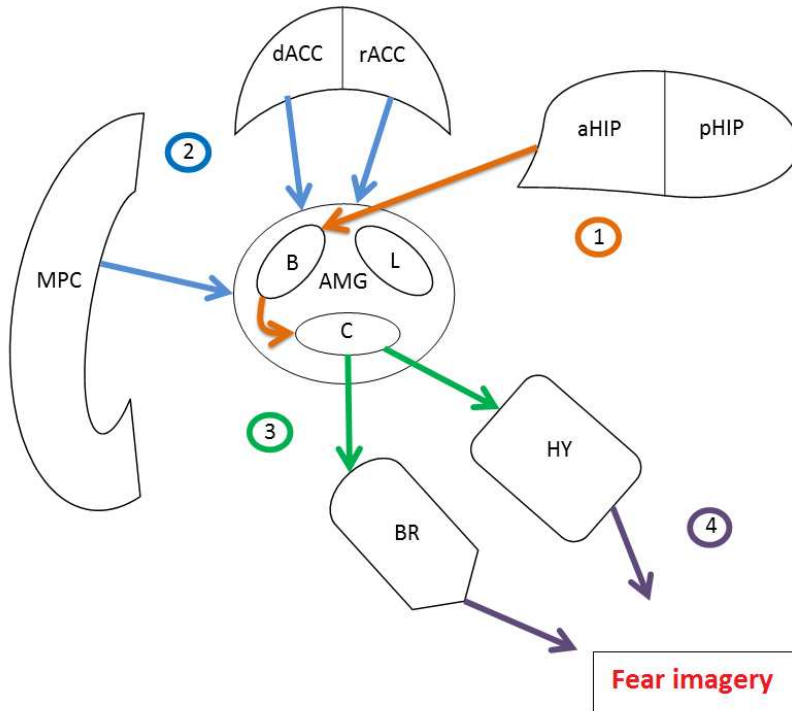Bull, 23*(4), 236-240.

Appendix

Figure 1. Dreaming according to the AND model (Nielsen & Levin, 2007). 1) the aHIP produces a dream context. This context is processed by the bAMG, and given emotional value by the cAMG. 2) The dACC, rACC and MPC regulate and inhibit this generated emotion and the AMG processes, and signal the appropriate affect distress. 3) The cAMG stimulates the BR and HY which 4) generate the associated autonomic fear responses. Nightmares occur when this network cannot create adequate fear extinction memories, due to high affect load or a dysfunction.
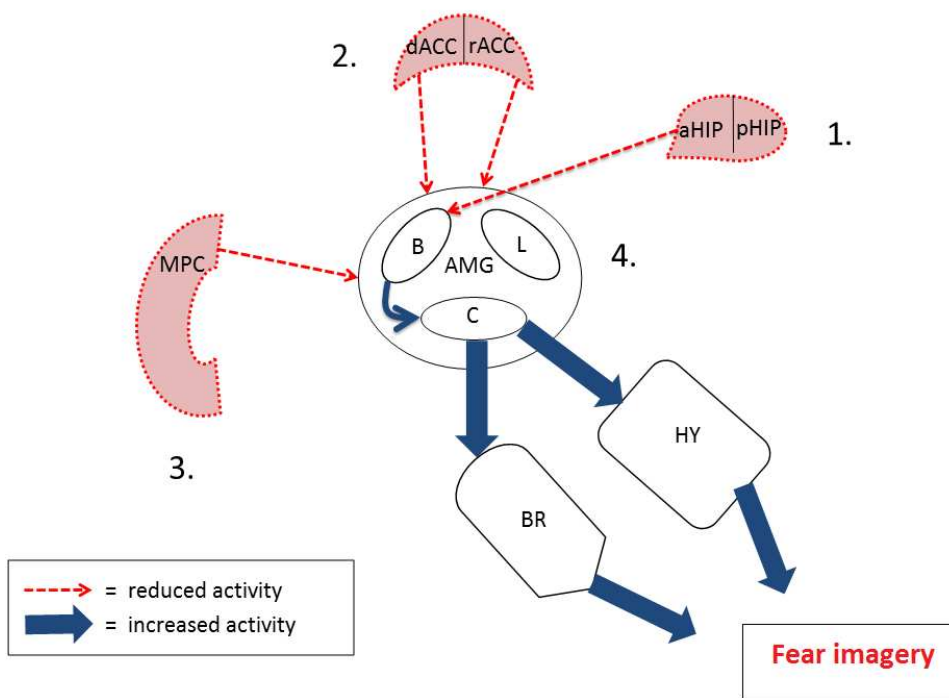
Figure 2. Neurobiology of PTSD in the AND model. 1) Reduced HIP volume is found in PTSD, possibly caused by increased glucocorticoid levels due to a dysregulated HPA-axis. HIP dysfunction can lead to nightmares. 2) Reduced ACC volume is associated with PTSD. A dysfunctional ACC cannot adequately inhibit the AMG or signal affect distress, which leads to nightmares. 3) Reduced MPC volume is associated with PTSD. A failure of the MPC to control the AMG can lead to nightmares. 4) ACC and MPC dysfunction, and increased noradrenalin levels can cause AMG overactivity, which can lead to nightmares. High noradrenalin levels and AMG overactivity also cause REM sleep disturbances.

Before IR

Traumatic event	→	Traumatic memory	→	Autonomic fear response	→	Avoidance behaviour

Traumatic memory ↕ Negative affect

After IR

Neutral context ↕ New memory →

Traumatic event ↗ New memory

~~Traumatic memory~~ → ~~Autonomic fear response~~ → ~~Avoidance behaviour~~

~~Traumatic memory~~ ↕ ~~Negative affect~~
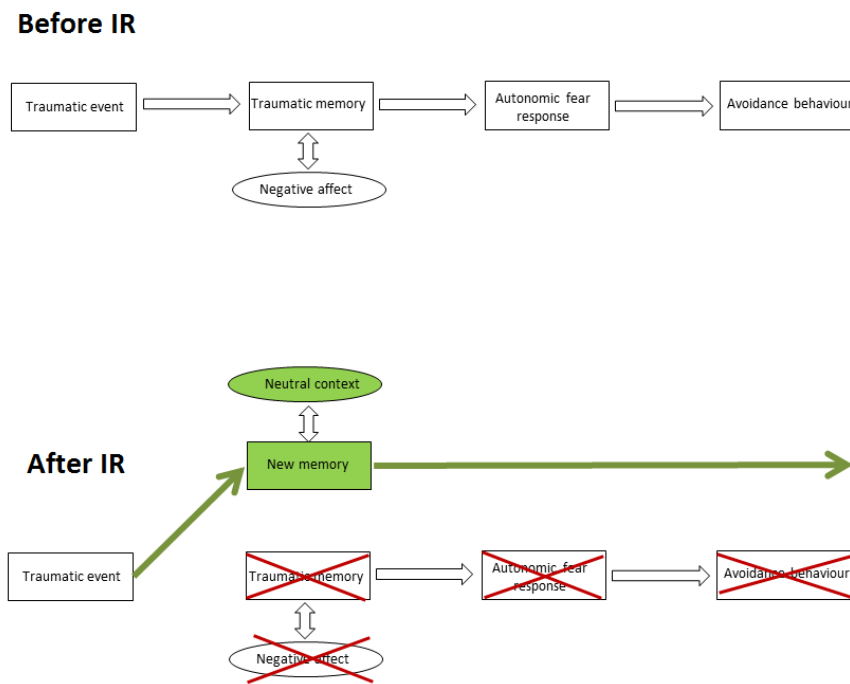
Figure 3. Illustration of image rescripting. The old traumatic memory is replaced with a new neutral memory.

Table 1. Characteristics of studies measuring subjective and objective sleep in PTSD

Author	Design / participants	Obj. measures	Subj. measures	Results	Limitations
Breslau et al., (2004)	• A selected Data sample was used from a large-scale longitudinal community study • N = 283 (71 PTSD; 212 non-PTSD)	• PSG • MSLT	• NIMH-DIS	• No differences in obj. sleep disturbance was measured between PTSD and non-PTSD • PTSD patients had more brief arousals in REM sleep	• The NIMH-DIS is a conservative measure in diagnosing PTSD, which means PTSD rates might have been underestimated
Germain et al., (2012)	• Cross-sectional pilot study • N = 12 veterans (6 PTSD; 6 non-PTSD)	• PET • EEG	• CAPS • SCID	• hypermetabolism was observed in brain regions that are involved in arousal, fear response and reward processing during wakefulness and REM sleep in veterans with PTSD	• Low number of participants • The causality of the hypermetabolism in PTSD patients is unclear, due to the cross-sectional study design
Klein et al.,(2003)	• Longitudinal prospective study • N = 102 motorvehicle accident survivors (26 PTSD; 76 non-PTSD; 19 hospitalized controls)	• ACT	• MSQ • SHQ • SCID	• Participants with PTSD reported poorer sleep on the MSQ compared to the other groups, but there were no differences in obj. Sleep as measured with ACT	• ACT does not assess important sleep parameters such as REM sleep density or depth of sleep
Kobayashi et al., (2007)	• Meta-analysis • 20 PSG studies examined • Total N = 772	• PSG	–	• Patients with PTSD had more stage 1 sleep, less SWS, and more REM sleep density than non-PTSD patients	•Many potential moderating variables have not been controlled for
Kobayashi et al., (2012)	• Cross-sectional study • N = 103 African-Americans with and without trauma exposure and PTSD	• ACT • PSG	• A modified sleep questionnaire • A sleep diary • CAPS	• Participants underestimated WASO, and overestimated SOL in the sleep diary • No differences between PTSD and non-PTSD participants	• No clinical population examined, and participants with PTSD only reported mild to moderate PTSD. More severe PTSD patients might experience subjective sleep disturbance differently

Obj. = objective; Subj. = subjective; MSLT = Multiple Sleep Latency Test; NIMH-DIS = National Institute of Mental Health Diagnostic Interview Schedule; CAPS = Clinician-Administered PTSD Scale; SCID = Structured Clinical Interview for DSM-IV; ACT = actigraphy; MSQ = Mini Sleep Questionnaire; SHQ = Sleep Habit Questionnaire

Table 2. Characteristics of studies measuring the effects of IR on nightmares and PTSD

Author	Design / participants	Intervention / Outcome Measures	Results	Limitations
Casement & Swanson (2012)	*Design* • Meta-analysis • 13 studies examined, inc. 5 RCTs • 6 studies included 6- and 12 month follow-ups *Participants* • Total N = 511 adults (287 civilians; 286 veterans; 11 active-duty military personnel) • Approx. 86% diagnosed with PTSD	*Intervention* • IR (4x), IRT (3x), ERRT (3x), IRET, SDT, SIP • 7 studies included CBTI • 3 studies included exposure therapy • 3 – 10 sessions x 60 – 200 min. *Outcome measures* • PTSD severity • Nightmare freq. • Sleep quality	• Nightmare frequency and PTSD symptoms were reduced, and sleep quality was improved • Effects were sustained for 6 and 12 months	• The large variety in design, treatment protocols and participant groups makes comparisons between studies difficult
Germain et al., (2007)	*Design* • Prospective open-label trial • Assessment at 6- and 8 weeks posttreatment *Participants* • N = 7 adult PTSD patients	*Intervention* • A single brief sleep intervention session using IR, stimulus control and sleep restriction • 1 x 90 min. *Outcome measures* • Sleep quality (PSQI) • PTSD related sleep disturbance (PSQI-A) • PTSD symptoms (CAPS)	• *Sleep* quality was modestly improved, while nightmares and daytime PTSD symptoms were reduced • Anxiety and depression were unchanged.	• Low number of participants • Lack of control condition • No long term follow-up
Rhudy et al., (2010)	*Design* • RCT • Follow-up at 6- and 12 months posttreatment *Participants* • N = 40 trauma exposed participants who reported posttraumatic nightmares • Treatment group n = 19 • Waitinglist control group n = 21	*Intervention* • ERRT • 3 x 120 min. *Outcome measures* • PTSD symptoms (CAPS) • Sleep quality (PSQI) • PTSD related sleep disturbance (PSQI-A) • Subjective arousal (SAM) • Physiological arousal i.e., negative affect (EMG), heart rate (ECG), skin conductance	• Physiological reactions to nightmare imagery were decreased, nightmares were reduced, and sleep quality was improved • Results were sustained during follow-up, except for EMG activity	• No active control condition means that no comparisons between different treatments can be made

Thünker & Pietrowsky (2012)	*Design* • Pre – post comparison study • Follow-up at 10 weeks posttreatment *Participants* • N = 69 (22 nightmare sufferers; 21 major depression sufferers; 26 PTSD + nightmare sufferers) • IRT group n = 57 • Control group n = 12 (PTSD + nightmare sufferers)	*Intervention* • Manualized IRT • 8 x 50 min. *Control group* • Trauma-focused psychotherapy *Outcome measures* • Self report questionnaires (inc. Nightmare freq., fear of recurrence, anxiety during nightmares, overall improvement) • Depression (BDI)	• Nightmare freq. and severity were sig. reduced in all patient groups, and effects were sustained during follow-up • Treatment effects were more pronounced in nightmare-only and depression compared to PTSD • IRT was not sig. More effective than trauma-focused psychotherapy in reducing nightmare freq. and severity	• Relatively low number of PTSD participants in IRT and control condition • No long-term follow-up

IR = imagery rehearsal; IRT = imagery rehearsal therapy; ERRT = Exposure, Relaxation, and Rescripting therapy; IRET = Imagery Rescripting and Exposure Therapy; SDT = Sleep Dynamic Therapy; SIP = Sleep Intervention for PTSD; freq. = frequency; PSQI = Pittsburgh Sleep Quality Index; PSQI-A = Pittsburgh Sleep Quality Index Addendum for PTSD; SAM = Self-Assessment Manikin; sig. = significant; BDI = Beck Depression Inventory