Sleep Disturbances in Posttraumatic Stress Disorder



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Abstract

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Sleep disturbances are common in posttraumatic stress disorder (PTSD), and often persist following PTSD treatment (e.g., Zayfert & Deviva, 2004). However, it is unclear why sleep disturbances are residual, and there are also concerns that poor sleep may interfere with PTSD treatment. Furthermore, it has not been directly investigated whether factors known to maintain insomnia may also contribute to sleep disturbances in PTSD. This thesis presents five studies, designed to investigate five key research questions: 1) Does Cognitive Therapy for PTSD improve sleep disturbances? 2) Do sleep disturbances interfere with the efficacy of psychotherapy for PTSD? 3) How might sleep improvements occur with PTSD therapy? 4) Do factors known to perpetuate insomnia also contribute to sleep problems in PTSD? 5) What may account for persistent sleep problems after otherwise effective PTSD therapy? Study 1 showed that sleep improved more with trauma-focused compared to non-trauma-focused psychotherapy. Updating and reprocessing the trauma memory promoted sleep duration improvements, and sleep improvements were associated with improvements in nightmares and hyperarousal. Pre-treatment sleep did not predict PTSD treatment outcome. Insomnia was residual for over a third of patients after treatment. Study 2 found that sleep improved with CT-PTSD in routine clinical care, but remained residual for nearly half of patients. Further, the results showed that modification of trauma appraisals and reduction in the flashback-quality of intrusions predicted improvements in sleep duration during CT-PTSD. Study 3 presented the development of a new scale to measure pre-sleep cognitive activity in PTSD. Pre-sleep cognitive activity was associated with disturbed sleep in PTSD. The PTSD group reported pre-sleep cognitions with content similar to those with insomnia, but also cognitions that are specific to PTSD. Study 4 showed that pre-sleep cognitive activity mediated the relationship between PTSD symptoms and disturbed sleep. People with PTSD had higher physiological arousal, and more pre-sleep cognitive activity, which was associated with worse subjective sleep. Finally, Study 5, showed that subjective and objective sleep was improved with CT-PTSD, but sleep problems remained residual for half of patients. Residual sleep problems were associated with sub-clinical PTSD and depression symptoms, pre-sleep cognitive activity and physiological arousal. In sum, theses studies showed that sleep improves but remains a residual problem after PTSD therapy. Processing and updating trauma memories, modifying trauma appraisals and reducing re-experiencing symptoms may promote sleep improvements in PTSD therapy. Pre-sleep cognitive activity contributed to disturbed sleep in PTSD, and was associated with residual sleep problems. The results have implications for understanding sleep problems in PTSD and after PTSD treatment, and may have clinical relevance for the treatment of sleep problems in PTSD therapy.

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Chapter 1: Introduction

Overview

Sleep disturbances, such as nightmares and insomnia, are common and distressing features of posttraumatic stress disorder (PTSD) (Ohayon & Shapiro, 2000). Research suggests that they are involved in the development and the maintenance of PTSD (Spoormaker & Montgomery, 2008). Few studies have investigated the effects of first-line treatments for PTSD on sleep disturbances and have consistently found that sleep problems are persistent for many patients after therapy (Belleville, Guay, & Marchand, 2011), including those whose other PTSD symptoms have remitted (Zayfert & DeViva, 2004). However it is unclear why sleep disturbances persist when other PTSD symptoms have resolved. While the nature of primary insomnia and its contributing factors has been well researched and models have been developed (e.g., Espie, Broomfield, MacMahon, Macphee, & Taylor, 2006; Harvey, 2002), there are as yet no empirically tested models of sleep disturbances in PTSD. Studies have examined a number of factors that may contribute to maintaining sleep problems in PTSD, such as fear of sleep and nightmares (DeViva, Zayfert, & Mellman, 2004; Pruiksma et al., 2016). Furthermore, models have been proposed that link hyperarousal and sleep problems in PTSD (Sinha, 2016). However, it has not been investigated whether other factors known to maintain primary insomnia, such as pre-sleep cognitions, may also contribute to sleep problems in PTSD. An investigation such as this would be particularly relevant to understanding why sleep problems, such as insomnia, persist after otherwise effective PTSD therapy. The overall aim of this thesis was to advance understanding of the effects of PTSD therapy on sleep disturbances, and to examine possible reasons for residual sleep problems after otherwise effective PTSD therapy.

The thesis further aimed to add to the understanding of factors that may contribute to maintaining sleep disturbances, such as insomnia, in PTSD. A better understanding the nature of insomnia in PTSD may help to inform targeted treatment of sleep disturbances in PTSD.

The following chapter will review literature relevant to the studies conducted in the thesis. It will first describe an overview of PTSD, sleep, and insomnia, and then review sleep abnormalities evidenced in PTSD. Then the relationship between PTSD and sleep, and preliminary theories of sleep and PTSD will be described, followed by a review of studies investigating the effects of PTSD therapy on sleep disturbances. Finally, literature on the role of pre-sleep cognitions, sleep hygiene, and hyperarousal in insomnia, and the potential role of these factors in insomnia comorbid with PTSD will be reviewed.

Posttraumatic Stress Disorder

Defining Trauma

Posttraumatic stress disorder (PTSD) is mental disorder that may develop following exposure to a traumatic event. A traumatic event is strictly defined in the diagnostic and statistical manual of mental disorders (5th edition; DSM-5, American Psychiatric Association, 2013). It defines trauma as 'exposure to actual or threatened death, serious injury, or sexual violence' and specifies that this may occur through direct experience, witnessing it happening to another, learning about it happening to another person (for death it specifies that the cause must have been violent and accidental), or by experiencing repeated exposure to details of traumatic events, for example through work (but not through television exposure) (APA, 2013). Trauma under the DSM-5 definition is referred to as a Criterion A event. Examples of traumatic events include,

rape/sexual assault, road traffic accidents, and natural disasters. In a recent survey of 2,953 US adults, 90% were estimated to have been exposed to at least one traumatic event in their lifetime, and most had experienced more than one event, with three events estimated as the most common number of traumatic events experienced (Kilpatrick et al., 2013). A recent survey conducted in the UK in 2014 has yielded lower estimates, where a third (31%) of UK adults reported having experienced at least one Criterion A traumatic event in their lifetime, and prevalence was similar for women (31%) and men (32%) (Fear, Bridges, Hatch, Hawkins, Wessely, 2016).

Posttraumatic stress disorder: definition and epidemiology

Following a traumatic event, a minority of people may go on to develop PTSD. PTSD is characterised by four clusters of symptoms; re-experiencing symptoms associated with the trauma (Criterion B); avoidance of stimuli associated with the trauma (Criterion C); negative alterations in cognitions and mood (Criterion D); and alterations in arousal (Criterion E). To qualify for a diagnosis of PTSD, the trauma must meet the definition for a Criterion A event, symptom(s) in each cluster must be endorsed, and must have persisted for more than one month since the traumatic event, and must be associated with clinically significant distress and impairment.

Specifically, the symptom clusters specified in the DSM-5 (APA, 2013) include the following symptoms:

Criterion B: Re-experiencing (endorsement of at least one symptom, occurring at least twice a month):

- B1. Recurrent, involuntary distressing memories
- B2. Recurrent, distressing dreams with content/affect related to the trauma

- B3. Dissociative reactions or flashbacks where the trauma feels like it is happening again
- B4. Intense and prolonged distress in response to external of internal cues associated with the traumatic event
- B5. Physiological reactions to cues associated with the traumatic event

Criterion C: Avoidance (endorsement of at least one symptom):

- C1. Avoidance of distressing memories, thoughts or feelings associated with the trauma, at least twice a month.
- C2. Avoidance of people or places or things associated with the trauma, at least twice a month.

Criterion D: Negative alterations in cognition and mood (endorsement of at least two symptoms, beginning or getting worse with the trauma)

- D1. Inability to remember important aspects of the trauma (not due to drugs, alcohol, medication or injury)
- D2. Persistent, exaggerated negative beliefs about oneself, the world or others
- D3. Persistent, distorted cognitions about the cause of the traumatic event, leading to misplaced blame (self/others)
- D4. Negative emotional state (fear, horror, anger, guilt, or shame)
- D5. Diminished interest in significant activities
- D6. Feeling detached from others
- D7. Difficulty experiencing positive emotions, like love or happiness

Criterion E: Altered arousal (endorsement of at least 2 symptoms, beginning or getting worse with the trauma)

- E1. Irritable behaviour, including anger, without much provocation
- E2. Reckless or destructive risk taking behaviour, with risk of being harmed
- E3. Hypervigilance, i.e alert, watchful, or on guard
- E4. Exaggerated startle response
- E5. Difficulty concentrating
- E6. Problems falling or staying asleep, at least twice a month with at least 30 minutes sleep loss

A recent epidemiological study of American adults found that following a traumatic event 8% developed PTSD within their lifetime (related to that event). PTSD prevalence was higher in women (11%) than in men (5%). The type of traumatic event affected the likelihood of developing PTSD, which was most likely after interpersonal violence, and combat. Likelihood of developing PTSD increased with the number of traumatic events (Kilpatrick et al., 2013). The development of other psychiatric conditions was also found to be associated with the experience of a traumatic event, such as major depression, anxiety disorders and substance abuse (Ehring, Ehlers, & Glucksman, 2008a; Kessler, Chiu, Demler, & Walters, 2005).

Cognitive model of PTSD

Ehlers and Clark (2000) proposed a cognitive model to account for the development and persistence of PTSD. They proposed that unhelpful appraisals (e.g., 'I have to be on guard all the time' or 'The trauma showed that I am inadequate') induce a sense of current threat that maintains PTSD symptomatology such as hyperarousal and hypervigilance, and motivates maladaptive coping strategies (cognitive and

behavioural) that in turn prevents a change in appraisals and nature of the trauma memory (Ehlers & Clark, 2000; Ehlers, Clark, Hackmann, McManus, & Fennell, 2005). A second source of the current threat is thought to be the disjointed nature of trauma memories that leads to easy triggering of intrusive memories with a flashback-quality, i.e. the experience that the memories are happening in the present rather than the past (Ehlers & Clark, 2000). Other models of PTSD have been proposed (e.g., Brewin, Dalgleish, & Joseph, 1996), however Ehler's and Clark's (2000) cognitive model of PTSD and the treatment derived from it is most relevant to the thesis, and so other models will not be reviewed here.

Cognitive Therapy for PTSD

Cognitive Therapy for PTSD (CT-PTSD; Ehlers & Clark, 2000; Ehlers et al., 2005) was developed from Ehlers and Clark's (2000) model of PTSD. The treatment aims to reduce an individual's sense of current threat by elaborating the trauma memory and modifying negative appraisals about the trauma and its consequences. A core procedure involves updating the worst moments of trauma memories with less threatening information, such as 'I did not die' or 'it was not my fault' (see Ehlers et al., 2005). This contributes to modifications of problematic negative appraisals of the trauma, and a decrease in intrusive re-experiencing symptoms, and reduction in problematic behaviours (such as avoidance), and cognitive strategies (such as rumination), that also inadvertently maintain the appraisals and memory features. CT-PTSD has been found to be a highly effective treatment for PTSD (Ehlers et al., 2005). Evidence from randomised controlled trials has shown that CT-PTSD has specific treatment effects, as it is superior to alternative active treatments (Ehlers, Hackmann, Grey, Wild, & Liness, 2014). Furthermore, it is effective in children and adolescents (Smith et al., 2007) and for a wide range of traumas (e.g., Duffy, Gillespie & Clark 2007). In sum, CT-PTSD

has been found to be an effective treatment for PTSD. It is the effects of CT-PTSD on sleep that were investigated in this thesis.

Defining insomnia

As insomnia will be referred to throughout this thesis, it is also important to define insomnia. According to the DSM-5 (APA, 2013), insomnia is defined as dissatisfaction in sleep quantity or quality, and associated with difficulty falling or staying asleep, or early morning awakening, at least 3 times a week for 3 months, with associated distress and interference. In a recent review of 50 epidemiological studies, insomnia prevalence (warranting diagnosis) was estimated as occurring in between 6-15% of the general population (Ohayon, 2011). The DSM-4 (APA, 2000) previously distinguished between primary insomnia, and insomnia related to a mental or physical health problem. This distinction was removed in the DSM-5 (APA, 2013), which means that insomnia disorder can now be diagnosed as comorbid to mental health problems, such as PTSD. The DSM-5 specifies that insomnia may warrant independent clinical attention, regardless of other mental or medical problems (APA, 2013). It should be noted that the International Classification of Sleep Disorders, third edition (ICSD-3; American Academy of Sleep Medicine, 2005) discriminates a number of different sub-types of insomnia, including psychophysiologic insomnia (objectively verifiable sleep disruptions, and arises from arousal and learned sleep-preventing associations), and paradoxical insomnia (complaint of insomnia without objective evidence of sleep impairment).

Sleep

As abnormalities in sleep will be described throughout this thesis, this section provides a brief overview of healthy sleep, and the measures typically used to assess sleep.

Measuring sleep

Sleep assessment can be grouped into objective assessment and self-report measures, both of which provide useful information. This section will describe measures of sleep that will be referred to throughout the literature review.

Self-report or subjective measures can provide valuable information about the subjective experience of sleep and sleep disturbances, can capture information such as perceived sleep quality, and enable long-term home-based assessment of sleep. Subjective measures are required for the diagnosis of insomnia (Buysse, 2008), particularly as insomnia does not require objectively disturbed sleep, but rather dissatisfaction with sleep duration or quality (DSM-5, APA, 2013). Objective measures can provide unbiased estimates of sleep parameters, such as sleep duration, and wake after sleep. Recommendations for the standard assessment of sleep propose the use of a combination of subjective (sleep diary, questionnaire measures), and objective measures (polysomnography, actigraphy), and measures of the wake time correlates of poor sleep (e.g., daytime dysfunction and sleepiness) (Buysse, Ancoli-Israel, Edinger, Lichstein, & Morin, 2006). Sleep parameters typically assessed with both objective and subjective measures include: sleep onset latency (SOL; time taken to fall asleep); total sleep time (TST; duration of actual sleep); wake after sleep (WASO; duration of time spent awake after sleep); and sleep efficiency (SE; percentage of time in bed spent sleeping).

Objective sleep measures

Polysomnography is the gold standard of objective sleep measurement. It includes the assessment of (1) electroencephalogram recording (EEG) which assesses electrical brain activity, (2) electromyographic recording (EMG) which assesses muscle activity, and

(3) electrooculographic recording (EOG) which assesses eye movements. The sleep parameters described previously, as well as information about sleep stage (this is the only measure which can assess this), are derived from these recordings (Bastien, 2011). Polysomnography (PSG) is limited in that it is expensive, cumbersome for participants (Ancoli-Israel, Cole, Alessi, & Chambers, 2003), and has low ecological validity, as assessments are typically laboratory-based (Buysse et al., 2006). Actigraphy measures movement of the wrist via an accelerometer, from which sleep and wake can be calculated automatically or by hand (Buysse et al., 2006). It is less cumbersome than PSG, less expensive, and enables the collection of multiple nights of data in a participant's natural sleeping environment (Ancoli-Israel et al., 2003), and is therefore thought to have higher ecological validity. Actigraphy estimates of sleep duration have been found to correlate well with PSG measures (Cellini, Buman, McDevitt, Ricker & Mednick, 2013). However it does not directly measure sleep, and is not accurate in detecting wake after sleep (as times of stillness can be misinterpreted as sleep), compared to PSG (Paquet, Kawinska, & Carrier, 2007). Therefore sleep diaries should be used to interpret actigraphy data, and to distinguish still periods from sleep (Buysse et al., 2006).

Subjective sleep measures

The sleep diary is recommended as the gold standard of subjective prospective sleep monitoring (Carney et al., 2012) . Sleep diaries are typically completed over one week, and participants self-report each sleep parameter listed previously (e.g., SOL). There are standardized recommendations for what a sleep diary should contain, including: at what time you went to bed; started tying to sleep; how long it took to fall asleep; number of awakenings; length of awakenings; final awakening time; and sleep quality (among others) (see Carney et al., 2012). Sleep diaries are limited by relying on an individual's

ability to estimate their own sleep times (Buysse et al., 2006). Questionnaires can also provide insight into a person's perception of sleep. A number of sleep questionnaires have been developed to assess sleep parameters and disturbances retrospectively; for example, the Pittsburgh Sleep Quality Index (PSQI) (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) is one of the most common and widely used questionnaires recommended for assessing the global severity of sleep disturbances, and overall sleep quality, over the previous month (Buysse et al., 2006). The PSQI also has an addendum for PTSD, which measures the frequency of PTSD-related sleep disturbances, such as nightmares and nocturnal panic (Germain, Hall, Krakow, Katherine Shear, & Buysse, 2005).

Sleep in healthy subjects

Sleep consists of a number of stages, which occur in cycles throughout the night. The stages can be grouped into non-rapid eye movement (NREM) sleep, and rapid eye movement (REM) sleep. First, sleep begins with NREM sleep (stages 1-4), which is characterized by decreased arousal and neural activity compared to wakefulness. NREM includes two stages of lighter sleep (stages 1 and 2), followed by slow wave sleep (SWS) or 'deep sleep' (stages 3 and 4), comprised of increasing delta waves, and which is considered to be a restorative neural state (Borberly & Achermann, 2000). REM sleep then follows, which is characterized by rapid eye movements, and fast-frequency, low amplitude EEG activity, similar to wakefulness, but with muscle atonia. There is greater physiological arousal during REM sleep, including increased sympathetic dominance (Seiegel, 2005). In healthy subjects, nightmares most commonly occur during REM sleep. The average length of the first sleep cycle (stage 1-REM) is between 70 and 100 minutes.

Sleep Disturbances in PTSD: Nature and Relationship

Summary

Wide-ranging sleep problems can develop both after exposure to a traumatic event, in the absence of PTSD (e.g., Galea et al., 2002), and after the development of PTSD (see Babson & Feldner, 2010 for review). Sleep disturbances are common in PTSD, and have been termed the 'hallmark' of the disorder (Ross & Ball, 1989). They often have a chronic course, and are among the most distressing PTSD symptoms (see Nappi, Drummond, & Hall, 2012), and among others they include difficulties falling and staying asleep (Ohyaon & Shapiro, 2000), reduced sleep duration (Straus, Drummond, Nappi, Jenkins, & Norman, 2015), reduced sleep quality (Leskin, Woodward, & Young, 2002), comorbid insomnia (Ohyaon & Shapiro, 2000), and nightmares (Leskin et al., 2002). Sleep abnormalities are evidenced in PTSD with both objective and subjective measures (see Cox & Olatunji, 2016 for review). Difficulty falling and staying asleep, and nightmares are two of the diagnostic symptoms of PTSD, according to the DSM-5 (APA, 2013).

This section will review the role of sleep problems in the development and maintenance of PTSD, evidence of sleep disturbances in PTSD, and preliminary theories of sleep disturbances in PTSD.

Sleep as a core symptom in PTSD: maintenance and development

Until recently, sleep problems were considered secondary to PTSD, and the re-experiencing and hyperarousal symptoms that characterize the disorder. For example, unprocessed trauma memories may disturb sleep through nightmares and high arousal, both of which have been associated with worse sleep in people with PTSD (Nightmares: e.g., Davis, Byrd, Rhudy, & Wright, (2007); Arousal: e.g., Sinha, (2016)). However, in

recent years, sleep problems have been conceptualized as a core symptom of PTSD (Spoormaker & Montgomery, 2008), which is a now widely accepted view. This is supported by studies showing that sleep may play a role in the development and maintenance of PTSD. For example, reported difficulties sleeping before and after a traumatic event have been consistently shown to predict the onset and severity of PTSD (Gehrman, Seelig, Jacobson, & Boyko, 2013; Koffel, Polusny, Arbisi, & Erbes, 2013; Koren, Arnon, Lavie, & Klein, 2002; Mellman, Bustamante, Fins, Pigeon, & Nolan, 2002; Wright et al., 2011). Different processes have been suggested to account for the role that sleep disturbances may play in PTSD development, including the beneficial effects of sleep on fear extinction learning and generalization (Kleim, Wilhelm, et al., 2013b; Pace-Schott, Germain, & Milad, 2015a; Pace-Schott, Milad, Orr, & Rauch, 2009; Pace-Schott, Verga, Bennett, & Spencer, 2012), emotional memory consolidation (Holland & Lewis, 2007; Wagner, Hallschmid, Rasch, & Born, 2006; Yoo, Hu, Gujar, Jolesz, & Walker, 2007) and sleep-dependent emotional processing (see Goldstein & Walker, 2014 for review; Walker & van der Helm, 2009), and the negative effects of sleep deprivation on neurobiological alterations (Germain, 2013; Germain, Buysse, & Nofzinger, 2008) such as hyperarousal (Sinha, 2016), which could theoretically facilitate PTSD development, and compromise PTSD recovery. Overall, there is consistent evidence that disturbed sleep is a risk factor for the later development of PTSD.

There is also evidence that sleep may contribute to the maintenance of PTSD symptoms. Sleep disturbances have been suggested to independently worsen the daytime symptoms of PTSD (Germain et al., 2008), and poorer sleep is associated with more severe PTSD symptoms (Belleville, Guay, & Marchand, 2009; van

Liempt, 2012). However, PTSD is also related to the later development of subjective sleep problems (Babson & Feldner, 2010).

Taken together, these studies indicate a potentially vicious maintenance cycle between sleep disturbances and PTSD symptoms (van Liempt, 2012), and highlight the importance of investigating sleep disturbances in PTSD.

Subjective sleep abnormalities

Sleep disturbances in PTSD have been evidenced using both objective and subjective measures (see Cox & Olatunji, 2016 for review). There is consistent evidence of subjective sleep complaints in PTSD. Studies show that up to 90% of people with PTSD report difficulty in falling and staying asleep, 70% report clinically significant sleep impairment, 60% meet criteria for clinical insomnia (Ohyaon & Shapiro, 2000), and approximately 50-70% report nightmares (Leskin et al., 2002). Compared to healthy controls who have not experienced a trauma, people with PTSD report longer sleep onset latencies, lower sleep efficiency (Calhoun et al., 2007; Straus et al., 2015), reduced sleep duration (Calhoun et al., 2007; Hurwitz, Mahowald, Kuskowski, & Engdahl, 1998; Straus et al., 2015), lower sleep quality (Calhoun et al., 2007), longer time spent awake after sleep (Straus et al., 2015; van Liempt, Arends, Cluitmans, Westenberg, Kahn, & Vermetten, 2013a), and more severe global sleep disturbances as measured by the PSQI (Calhoun et al., 2007; Germain, Hall, Shear, Nofzinger, & Buysse, 2006; Klein, Koren, Arnon, & Lavie, 2003; Straus et al., 2015; van der Kloet, 2014; van Liempt, Arends, Cluitmans, Westenberg, Kahn, & Vermetten, 2013a; Woodward et al., 2009). Studies comparing people with PTSD to trauma-exposed controls without PTSD, have similarly found increased subjective sleep complaints in PTSD. People with PTSD report more sleep complaints (Babson, Badour, Feldner, &

Bunaciu, 2012; Klein et al., 2003; Mellman, Pigeon, Nowell, & Nolan, 2007), including lower sleep quality and shorter sleep duration (Lewis, Creamer, & Failla, 2009; Pietrzak, Morgan, & Southwick, 2010), longer sleep onset latency (Pietrzak et al., 2010; van Liempt, Arends, Cluitmans, Westenberg, Kahn, & Vermetten, 2013a), more time spent awake after sleep (van Liempt, Arends, Cluitmans, Westenberg, Kahn, & Vermetten, 2013a), and more clinician-assessed trauma nightmares and insomnia symptoms (Mellman et al., 2007), compared to trauma controls. One study did not find differences in reported sleep between trauma survivors with and without PTSD (Klein, Koren, Arnon, Lavie, 2002).

Overall, the majority of studies have found subjective sleep differences between people with PTSD and trauma exposed and non-exposed controls, and provide strong evidence of subjective sleep disturbances in PTSD.

Objective sleep abnormalities

Sleep disturbances in PTSD have also been evidenced using objective measures such as PSG and actigraphy, although the findings are more mixed, compared to findings from subjective sleep measures. Studies using PSG have shown that, compared to non-trauma exposed controls, people with PTSD had shorter sleep duration (Germain et al., 2006; Straus et al., 2015), longer sleep onset latencies (Germain et al., 2006; van Liempt, Arends, Cluitmans, Westenberg, Kahn, & Vermetten, 2013a), reduced sleep efficiency (Glaubman, Mikulincer, Porat, Wasserman, & Birger, 1990; Habukawa, Uchimura, Maeda, Kotorii, & Maeda, 2007; Lipinska, Timol, Kaminer, & Thomas, 2014), increased number of awakenings (Germain & Nielsen, 2003; Glaubman et al., 1990; Lipinska et al., 2014), and longer duration of waking after sleep onset (Germain & Nielsen, 2003; Glaubman et al., 1990; Mellman et al., 2002).

Similar results have also been found using actigraphy: In comparison to non-trauma exposed controls, actigraphic studies have found that people with PTSD exhibited shorter sleep duration (Straus et al., 2015), lower sleep efficiency (Calhoun et al., 2007; Straus et al., 2015), longer sleep onset times (Calhoun et al., 2007), and more awakenings and time awake after sleep onset (Ulmer, Calhoun, Edinger, Wagner, & Beckham, 2009). Studies comparing trauma survivors with and without PTSD have yielded mixed findings. Some PSG studies have found evidence that people with PTSD have lower sleep efficiency (Lipinska et al., 2014; Mellman & Kulick-Bell, 1995) and increased awakenings (Lipinska et al., 2014; van Liempt, Arends, Cluitmans, Westenberg, Kahn, & Vermetten, 2013a) compared to trauma-exposed controls. One actigraphy study found decreased sleep duration in PTSD compared to trauma controls (Klein et al., 2003). However, a number of studies found no evidence of objective sleep differences between trauma survivors with and without PTSD, when using PSG (Cohen et al., 2013; Mellman, Knorr, Pigeon, & Leiter, 2004; Mellman, Kobayashi, Lavela, Wilson, & Hall Brown, 2014) and three have found no differences using actigraphy (Dagan, Zinger, & Lavie, 1997; Engdahl, Eberly, Hurwitz, & Mahowald, 2000; Kobayashi, Lavela, & Mellman, 2014). It has been noted that some of the differences between studies may be accounted for by sample differences, such as different trauma types (Cox & Olatunji, 2016). Studies using PSG have also found REM sleep alterations in PTSD (see Kobayashi et al., 2014 for meta-analysis; Germain, Buysse, Katherine Shear, fayyad, & Austin, 2004; Glaubman et al., 1990; Habukawa et al., 2007; Mellman, Kumar, Kulick-Bell, Kumar, & Nolan, 1995), such as lower percentage of REM sleep (Lipinska et al., 2014), shorter REM sleep durations (Mellman et al., 2002), and lower percentage of slow wave sleep (Glaubman et al., 1990). There is evidence that REM sleep is important for emotional processing (Nishida, Pearsall, Buckner, & Walker, 2009).

REM sleep alterations in PTSD may therefore explain some of the exacerbation of PTSD symptoms by sleep, by disrupting sleep-dependent emotional and memory processing (see Germain, 2013 for a review).

In sum, there is evidence of objective sleep abnormalities and altered sleep architecture in PTSD compared to trauma exposed and non-exposed controls, using both actigraphy and PSG. Not all studies have found differences, particularly between PTSD and trauma controls, which could be in part accounted for by differences in PTSD samples. More research which compares objective and subjective sleep between trauma survivors with and without PTSD is needed.

Insomnia in PTSD

Up to 60% of people with PTSD meet criteria for clinical insomnia, compared to 20% of trauma survivors without PTSD (Ohayon & Shapiro, 2000). Insomnia has been found to be the most commonly reported symptom after trauma exposure, and predicts other PTSD symptoms (McLay, Klam, & Volkert, 2010). A study investigating the prevalence of insomnia symptoms in PTSD found that 61% of PTSD patients reported severe insomnia symptoms (Gellis, Gehrman, & Mavandadi, 2010), and 88% of PTSD treatment-seeking patients report insomnia at pre-treatment (Zayfert & DeViva, 2004). A recent study of 246 treatment-seeking PTSD patients found that 72% reporting sleep-onset problems, 92% mid-sleep awakening, and 56% early morning awakenings (Lommen et al., 2015). Models of insomnia development, such as the 3P model of insomnia (Spielman, Caruso, & Glovinsky, 1987) can be applied to the development of insomnia in PTSD. The 3P model is a diathesis-stress model, which proposes that predisposing biopsychosocial factors can increase risk for insomnia, and that a precipitating factor, or trigger (such as a stressful life event, or trauma) can lead to acute

insomnia, and perpetuating factors can lead to chronic insomnia in the absence of the precipitating event, in this case trauma.

Nightmares in PTSD

Nightmares are also common in PTSD (Ohayon & Shapiro, 2000; Wittmann, Schredl, & Kramer, 2007). They are classified as one of the re-experiencing symptoms, defined in the Clinician-administered PTSD Scale for DSM-5 (Weathers et al., 2013) as 'Recurrent distressing dreams in which the content and/or affect of the dream are related to the event(s)' (page 6). Studies have shown that up to 75% of PTSD patients report nightmares (Leskin et al., 2002; van Liempt, van Zuiden, Westenberg, Super, & Vermetten, 2013b), compared to 2-5% of the general population (van Liempt, van Zuiden, Westenberg, Super, & Vermetten, 2013b). Nightmares in trauma survivors with PTSD are thought to differ compared to those in people without PTSD (Mellman & Kulick-Bell, 1995). They often occur more frequently, and earlier in the night than idiopathic nightmares. Although nightmares are typically a REM sleep phenomenon, they have also been found to occur in NREM sleep in PTSD (van der Kolk, Blitz, Burr, Sherry, & Hartmann, 1984). In PTSD, nightmare content is often related to the trauma or thematically linked events (Davis et al., 2007; 2011). Compared to trauma survivors without PTSD, people with PTSD have reported more frequent and distressing nightmares, and were more likely to report replicative nightmares, and less likely to report trauma-dissimilar nightmares (Davis et al., 2007). It has also been found that nightmares are more distressing when they resemble the traumatic event (Davis et al., 2007). Trauma-replicative nightmares have been associated with worse sleep quality, shorter sleep duration, more severe PTSD symptoms, greater panic upon waking (Davis et al., 2007), and more objective awakenings after sleep (Germain & Nielsen, 2003; Woodward, Arsenault, Murray, & Bliwise, 2000),

suggesting that nightmares contribute to sleep disturbances. However, it is unclear whether nightmares caused awakenings or if awakenings resulted in increased memory of nightmares (Woodward et al., 2000). Finally, trauma-related nightmares have been associated with fear of sleep (Davis et al., 2007; 2011) due to fear of nightmares (Davis et al., 2007; 2011; Davis & Wright, 2007; Krakow, Tandberg, Scriggins, & Barey, 1995), and fear of sleep in turn has been associated with more severe sleep disturbances in trauma survivors (Pruiksma et al., 2016), highlighting another way in which nightmares may disturb sleep in PTSD.

Other sleep disturbances in PTSD

A number of other sleep disturbances have also been associated with PTSD; these include violent or dangerous behaviours during sleep (punching, running), typically during the first half of the night; parasomnias such as sleep paralysis and sleep talking; hypnagogic (during sleep-onset) and hypnopompic (during waking) hallucinations (Ohayon & Shapiro, 2000); and nocturnal panic attacks and sleep terrors, typically during NREM sleep (Fisher et al., 1973, Freed, Craske & Greer, 1999, Germain et al., 2005). These 'disruptive nocturnal behaviours' (including trauma nightmares), are suggested to represent more PTSD-specific sleep disturbances, less commonly found in other psychiatric disorders (Germain et al., 2005).

Preliminary theories of sleep disturbances in PTSD

There is as yet no empirically tested theory of sleep disturbances in PTSD. However, a number of suggestions have been made about how sleep disturbances may arise in PTSD. For instance, (Galovski et al., 2016) outlined the possibility that hypervigilance during sleep after trauma may initially be a biologically adaptive response, which becomes maladaptive when it persists in the absence of the initial

threat (trauma). Individuals with PTSD therefore may deliberately remain awake due to worry about perceived danger. Further they note that nightmares and night-time trauma cues (such as darkness) may interfere with sleep through fear of sleep (DeViva et al., 2004), and that sleep difficulties may evolve to become an independent problem, which can exacerbate the daytime symptoms by decreasing the ability to cope with trauma cues (Krakow, Germain, et al., 2001a). Similarly, Desjardins and Germain (2006) propose that a traumatic event may precipitate insomnia and nightmares in PTSD. Daytime PTSD symptoms such as hypervigilance may further impact sleep quality, and nightmares disrupting sleep may lead to compensatory behaviours such as avoidance of sleep and napping during the daytime (when chance of nightmares is lower). Avoidance and compensatory behaviours may then further perpetuate sleep problems. Other theories propose a key role for REM sleep disturbances in the development and maintenance of PTSD (see Germain 2013). REM sleep disturbances, have been proposed as a hallmark of PTSD (Ross et al., 1989). In addition, a recent review supported this proposition that disturbed REM (and NREM) sleep in PTSD may be a contributing risk factor for maladaptive response to trauma, such as the development and maintenance of PTSD (Germain, 2013). Evidence of the role of REM sleep in fear responses (Silvestri, 2005), and of sleep in affective and emotional processing (Nishida et al., 2009), and of REM sleep alterations in PTSD and predicting PTSD after a trauma (Mellman et al., 2002), support the role of disturbed sleep in PTSD-relevant processes, perhaps by compromising adaptive recovery after a trauma (see Germain, 2013). Furthermore, results of animal models of PTSD have shown that acute, inescapable stress can cause alterations in sleep that are long-lasting, which could be applied to the development of sleep disturbances after a trauma in humans (Philbert et al., 2011). Finally, Sinha (2016) proposed a model of trauma-induced insomnia. In this model, Sinha outlined

evidence of hyperarousal in insomnia, and evidence that a traumatic event can lead to sustained neurobiological disruptions and autonomic arousal that could then disrupt sleep and wake (see Hyperarousal section). Sinha suggested that hyperarousal may be a commonality that links trauma-exposure and the development of insomnia, including, but not limited to, when PTSD has also developed. In sum, there are promising but untested theories for the development and maintenance of sleep disturbances in PTSD, which point to the role of compensatory behaviours, fear of sleep, and hyperarousal in sleep disturbances in PTSD.

Treatment of Sleep Disturbances in PTSD

This section will outline the effectiveness of PTSD therapies for treating sleep problems, of sleep therapies for treating sleep problems in PTSD, and will discuss whether sleep may interfere with PTSD therapy.

The effects of PTSD therapy on sleep

Trauma-focused psychological therapy, such as Cognitive Therapy for PTSD (CT-PTSD; Ehlers & Clark, 2000, Ehlers et al., 2005) in the UK, and Cognitive Processing Therapy (CPT) (Reisick & Schnicke, 1993) or Prolonged Exposure Therapy (PE) (Foa, Hearst, Dancu, Hembree & Jaycox, 1994) in the USA, are the first-line recommended treatments for individuals suffering from PTSD, including when comorbid insomnia is present. It is therefore important to understand the effects of PTSD treatments on sleep outcomes in order to maximize treatment efficacy. Despite a good body of evidence for the prevalence of sleep disturbances in PTSD, only a handful of studies have investigated the effects of these first-line PTSD therapies on sleep outcomes (Belleville et al., 2011; Galovski et al., 2016; Galovski,

Monson, Bruce, & Resick, 2009; Gutner, Casement, Gilbert, & Resick, 2013; Levrier, Marchand, Belleville, Dominic, & Guay, 2016; Lommen et al., 2015; Nishith et al., 2003; Raboni, 2006; Zayfert & DeViva, 2004). The majority showed that despite improvements in sleep parameters, such as sleep duration and quality (Belleville et al., 2011; Galovski et al., 2009; Gutner et al., 2013; Lommen et al., 2015; Raboni, 2006; Zayfert & DeViva, 2004), sleep difficulties are commonly residual (i.e. fail to reach clinical remission) after PTSD therapy (Belleville et al., 2011; Galovski et al., 2009; 2016; Gutner et al., 2013; Lommen et al., 2015), including in those who have recovered from PTSD (Nishith et al., 2003; Zayfert & DeViva, 2004). The majority of studies measured subjective sleep disturbances as assessed by the insomnia and nightmare items on the Clinician-Administered PTSD scale (CAPS; Blake et al., 1995), and/or the Pittsburgh Sleep Quality Index (PSQI: (Buysse et al., 1989). Two studies included objective measures of sleep, which were laboratory-based PSG (Nishith et al., 2003; Raboni, 2006). Studies assessing the effects of first-line PTSD treatments on sleep are described in detail below.

Gutner et al., (2013) found that in female rape survivors, subjective sleep disturbances were significantly improved with either CPT or PE therapy for PTSD, and maintained at long-term follow-up, five to ten years later. Specifically, subjective sleep efficiency, sleep onset latency, total sleep time, sleep quality and overall sleep disturbances (PSQI) were significantly improved, and nightmares and insomnia symptoms (assessed by the CAPS; Blake et al., 1995) significantly decreased. However, sleep disturbances (PSQI) and insomnia symptoms remained clinically significant at post-treatment (Gutner et al., 2013). Similarly, in a sample of female rape survivors, Galovski et al., (2009) found that both CPT and PE improved subjective sleep; however, sleep disturbances (PSQI) were residual for all patients after treatment. Results of a recent study with female assault

survivors were comparable, showing improvements in subjective sleep disturbances (PSQI) and insomnia with CPT for PTSD; however, sleep disturbance (PSQI) remained clinically significant at post-treatment, although nightmare severity (CAPS) remitted below clinical cut-offs (Galovski et al., 2016). Levrier et al., (2016) investigated the effects of Cognitive Behavioural Therapy (CBT) for PTSD on CAPS assessed nightmares, and found that both nightmare frequency and distress were significantly reduced with treatment, but that 23% of patients still reported nightmares (more than twice a week) at post-treatment. Belleville et al. (2011) assessed PTSD patients, from a variety of traumas, before and after CBT for PTSD, and found that despite improvements in sleep parameters (apart from sleep duration and bad dreams not related to the trauma), 70% of those who had sleep problems at pre-treatment, continued to report clinically significant sleep disturbances (PSQI) at post-treatment. Lommen et al., (2015) examined the effects of CT-PTSD on subjective, retrospectively reported sleep duration and quality. While sleep duration and quality were significantly improved at post-treatment, sleep duration remained below current recommendations of seven to nine hours of sleep (Hirshkowitz et al., 2015) suggesting persistent sleep difficulties after treatment. Importantly, the study also showed that subjective sleep (duration and quality) and PTSD symptoms changed simultaneously over treatment, suggesting that improvements in both were related. These studies did not discriminate between those that did and did not recover from PTSD at post-treatment. One study investigated sleep problems after effective CBT for PTSD; of PTSD patients who no longer met criteria for PTSD, residual insomnia was reported by 48% on the CAPS at post-treatment, and 41% met criteria for clinically significant insomnia (Zayfert & DeViva, 2004). Insomnia was the second most common residual symptom after anger, also a hyperarousal symptom. Furthermore, 77% of those with post-treatment insomnia did not report nightmares and hypervigilance. The authors concluded that residual insomnia may

persist in the absence of PTSD, nightmares and hypervigilance, and could be accounted for by continuing hyperarousal symptoms, or perpetuating factors related to the maintenance of insomnia, but unrelated to PTSD symptoms, such as maladaptive learned behaviour patterns (Zayfert & DeViva, 2004). Two treatment studies combined subjective measures of sleep with objective (PSG) measures. The first study analysed sleep in five treatment responders (female assault survivors) before and after CBT for PTSD, and found significant improvements in both subjective sleep (PSQI), and objective sleep onset latency. Consistent with the other studies, sleep problems remained clinically significant after treatment (Nishith et al., 2003). The second study assessed seven PTSD patients (assault and kidnap survivors) before and after eye-movement desensitization and reprocessing therapy (EMDR). They found significant improvements in subjective sleep quality and objective sleep efficiency and wake after sleep duration (Raboni, 2006), providing some preliminary evidence that objective sleep improves with psychotherapy for PTSD, although it is unknown whether these results would generalise to other PTSD populations. It is also unknown whether objective sleep improvements with PTSD therapy would be found if patients were assessed at home rather than in a lab setting. In sum, these studies show that sleep improves with first-line treatments for PTSD, but sleep problems were found to persist in every study which included a measure of the clinical significance of sleep problems.

A number of studies have also investigated the effects of specific therapeutic interventions from PTSD therapies, and reported improvements in subjective sleep (Şalcıoğlu, Başoğlu, & Livanou, 2007). For example, a recent study investigated the effects of four sessions of written narrative exposure on PTSD symptoms and objective (PSG measured) sleep, in a non-clinical PTSD population. They found that both PTSD symptoms and objective sleep duration improved, providing some

evidence that processing trauma memories (a key procedure in most psychotherapies for PTSD) may improve objective sleep (Kobayashi, Mellman, Altaee, Howell, & Lavela, 2016b).

In sum, these studies show that when PTSD is treated, sleep symptoms improve, and that targeting trauma memories may be associated with sleep improvements. However, sleep problems such as insomnia and nightmares typically remained residual, and may require additional sleep interventions, or more specific focus during PTSD therapy. This supports suggestions that sleep is more than just a secondary symptom of PTSD, as a secondary symptom would be expected to remit with effective PTSD treatment (Spoormaker & Montgomery, 2008). Further research is required to better understand the relationship between PTSD and sleep, and to understand the effects of PTSD treatment on comorbid sleep complaints, and to identify components in PTSD therapy that may best promote sleep improvements.

The effects of sleep-focused therapy on PTSD

Sleep difficulties in PTSD can also be targeted with sleep-focused treatments. The effects of sleep-focused treatments on disturbed sleep in PTSD will be briefly reviewed here as it has relevance for understanding suggestions that sleep disturbances may be more than just a secondary symptom of PTSD (Spoormaker & Montgomery, 2008). It is also important to know what options exist for improving residual sleep problems after PTSD therapy.

CBT for insomnia (CBT-I) is a highly effective treatment (see Mitchell, Gehrman, Perlis, & Umscheid, 2012; Riemann & Perlis, 2009 for review), which has been shown to be effective for treating insomnia and comorbid insomnia (Edinger,

Wohlgemuth, Radtke, Marsh, & Quillian, 2001; Morin, Bootzin, Espie, Edinger, & Buysse, 2006). There is a growing body of evidence that CBT-I may also be effective for treating insomnia comorbid with PTSD, and that sleep-focused treatments such as CBT-I with nightmare therapy may also result in some daytime PTSD symptom improvements (for reviews see Casement & Swanson, 2012; Ho, Chan, & Tang, 2016; Nappi et al., 2012). A recent study found that, in patients with PTSD, CBT-I improved sleep on measures such as objective (PSG) total sleep duration, subjective sleep parameters, sleep disturbances (PSQI; large effect size, Cohen's d = 1.43), nightmares, and PTSD-related sleep disturbances (PSQIA). However, there were no differences in improvements in PTSD symptoms between CBT-I and the waitlist, with both groups showing a reduction in PTSD symptoms (Talbot, 2014). Other studies have also shown objective (actigraphy) (Margolies, Rybarczyk, Vrana, Leszczyszyn, & Lynch, 2013) and subjective sleep improvements, and daytime PTSD symptom improvements with CBT-I when nightmare treatment, such as Imagery Rehearsal Therapy (IRT), was also included (Germain, Shear, Hall, & Buysse, 2007; Margolies et al., 2013). The largest effects on both PTSD symptoms and sleep disturbances (PSQI) have been found when some aspects of CBT-based PTSD treatment are also included with CBT-I and IRT (Ulmer, Edinger, & Calhoun, 2011) (Casement & Swanson, 2012). IRT is a sleep-focused treatment which has been used to target posttraumatic nightmares (Kellner, Singh, & Irigoyen-Rascon, 1991). IRT is one of the most well supported nightmare treatments, and includes writing a dream narrative of a recurring nightmare, which includes a change to that nightmare, followed by daily imaginal rehearsal of the new dream narrative. As previously noted, people with PTSD report nightmares that are replicative of the trauma. In these cases, the dream narrative may be very similar to the trauma memory, and so may involve some exposure to the trauma memory. A recent meta-analysis found that IRT was

effective for improving both sleep and daytime PTSD symptoms, with large effect sizes (Casement & Swanson, 2012). Similar results have been found with Exposure, Rescripting and Relaxation Therapy (ERRT; Davis & Wright, 2007), a variant of IRT which includes some components of CBT for PTSD (Davis & Wright, 2007). Both IRT and ERRT include some treatment of insomnia as well as a focus on nightmares. A recent meta-analysis (Ho et al., 2016) evaluated the efficacy of sleep-focused CBT for treating sleep disturbances in PTSD, by analysing data from eleven RCTs which compared sleep-focused CBT (including studies using nightmare therapy) with a waitlist. Sleep treatments led to subjective sleep improvements (sleep onset latency, wake after sleep, sleep efficiency) with a large effect size (Hedges' g = 1.15), as well as daytime PTSD symptom improvements with a medium effect size (g = .58) (see Ho et al., 2016).

These studies show that both sleep and PTSD symptoms are improved with sleep-focused treatments, such as CBT-I, when nightmare treatment is included. These studies also show that PTSD symptoms improve to a greater extent, with large effect sizes (Cohen's d = 1.76) when aspects of CBT for PTSD are also incorporated (Ulmer et al., 2011), suggesting that some trauma-focus is necessary for PTSD symptom improvements. As previously described, PTSD treatments such as CT-PTSD have been shown to have large effects on PTSD symptoms (d = 2.53; Ehlers et al., 2014), and one study has found preliminary evidence of small effects of CT-PTSD on subjective sleep duration (d = .49; Lommen et al., 2015). Other studies have found similar effect sizes (d = .48) for CBT for PTSD on sleep disturbances (PSQI) (e.g., Belleville et al., 2011). However, it remains unclear what effects CT-PTSD has on other aspects of sleep, such as insomnia symptoms, and so further research is required.

Does poor sleep interfere with PTSD treatment?

As trauma-focused interventions are recommended as the first-line treatment for PTSD, it is important to consider whether sleep disturbances may impact PTSD treatment efficacy. This section will review literature on the possible impact of disturbed sleep on PTSD treatment outcomes.

Concerns have been raised regarding the detrimental effects of comorbid sleep problems on PTSD treatment efficacy, partly due to evidence of the negative effects of sleep deprivation on processes important in psychotherapies for PTSD, such as memory (Yoo et al., 2007), and the beneficial effects of sleep on emotional memory consolidation (Holland & Lewis, 2007; Silvestri, 2005; Wagner et al., 2006) and fear extinction learning (Kleim, et al., 2013b; Pace-Schott et al., 2009; 2012; Pace-Schott, Germain, & Milad, 2015a; Spoormaker et al., 2011; 2010). Experimental studies demonstrating the beneficial impact of good sleep on therapeutic procedures, such as exposure (Kleim, et al., 2013b) also support these concerns. Many of the trauma-focused treatments for PTSD involve some form of exposure to trauma memories and reminders (Schnyder et al., 2017). It is possible that reduced sleep duration may interfere with the effects of exposure through impairing retention of fear extinction learning (Kleim, et al., 2013b; Pace-Schott, Germain, & Milad, 2015a). Poor sleep may also interfere by having an impact on an individual's ability to retain learning from the treatment session through reducing concentration and attention in therapy, or interfering with consolidation of new information from the session, such as updated information and meanings in the trauma memory. In addition to support from experimental studies (Kleim, et al., 2013b), results from PTSD treatment studies have shown that PTSD patients with poor sleep at the end of treatment, showed less improvement in PTSD and depression symptoms from pre to post treatment (Belleville et al., 2011). These findings may support the important role of

sleep in PTSD treatment response, but could also indicate a worse general response to treatment. Another treatment study by Lommen et al. (2015) found that poor sleep quality at baseline predicted a slower response to PTSD treatment (although similar overall outcomes) in those with comorbid major depression (Lommen et al., 2015). In contrast, a recent study by Levrier et al., (2016) showed that nightmare severity (distress and frequency) did not have an impact on response to CBT for PTSD (Levrier et al., 2016). Furthermore, authors have noted that the efficacy of PTSD therapy and long-term maintenance of treatment gains in the presence of sleep disturbances do not support suggestions that sleep interferes with PTSD therapy (Gutner et al., 2013). A recent study by Galovksi and colleagues (2016) investigated whether PTSD treatment gains could be augmented when sleep-directed hypnosis was delivered before PTSD therapy (CPT) (Galovski et al., 2016). They found that sleep-directed hypnosis improved sleep and depression symptoms, but did not lead to greater gains in PTSD symptom reduction over PTSD therapy, compared to those who did not receive the sleep intervention before therapy. This lends support to suggestions that sleep does not interfere with PTSD therapy, as prior sleep improvements did not augment PTSD treatment gains with trauma-focused therapy (which would be expected if sleep interfered). Another recent study by Kobayashi and colleagues (2016) investigated whether the timing of sleep had an influence on the effectiveness of a Written Narrative Exposure (WNE) intervention with people with PTSD or sub-clinical PTSD (Kobayashi et al., 2016b). They found that proximity of sleep to WNE had no effect on the effectiveness of the intervention, suggesting that sleep after therapy did not enhance PTSD symptom reductions.

Overall, despite support from experimental studies of the role of sleep in processes important in therapy, there is as yet no strong evidence that sleep interferes with the

efficacy of PTSD treatment. Therefore, further research is needed to better understand the impact of sleep problems on PTSD treatment efficacy, in order to maximize PTSD treatment outcomes.

Possible maintenance factors of insomnia in PTSD

Overview

As previously described, clinically significant insomnia is highly prevalent in PTSD (Ohayon & Shapiro, 2000). Due to the common persistence of insomnia after PTSD treatment, researchers have suggested that factors unrelated to PTSD symptomatology may perpetuate persistent insomnia after PTSD treatment (Zayfert & DeViva, 2004). To better understand the maintenance of sleep difficulties in PTSD, it would therefore be important to consider the role of factors that are known to maintain insomnia. This would help to most effectively target PTSD-related sleep problems in treatment.

In this section, factors proposed to play a role in maintaining insomnia, and theories of sleep disturbances and perpetuating factors in PTSD will be described. Evidence for the contributing role of these factors in sleep problems in PTSD will then be reviewed. Three specific factors are reviewed; 1) Pre-sleep cognitive activity, 2) Sleep hygiene, 3) Hyperarousal.

Similar mechanisms underlying insomnia with and without PTSD

It is likely that insomnia comorbid with PTSD may have share overlapping maintenance factors with insomnia without comorbid PTSD. This would be consistent with a study showing that people with insomnia, and insomnia associated with depression, were not discriminated by insomnia measures (Kohn & Espie, 2005). However, researchers have

noted that insomnia alone may differ from insomnia comorbid with PTSD in a number of ways. For example, Ulmer et al., (2011) note that while people with insomnia view sleep favourably, people with trauma-related insomnia may view sleep as threatening or aversive due to fear of nightmares and loss of vigilance. Therefore, PTSD related sleep disturbances might have both similarities and differences to insomnia without PTSD. This has been suggested to account for findings that CBT for insomnia, without a trauma or nightmare focus, often fails to produce remission of sleep difficulties, demonstrating a need for treatment of sleep-specific concerns relevant to PTSD populations (Ulmer et al., 2011). There is a lack of empirically derived theories for the relationship between PTSD and sleep problems and so further investigation into the maintenance of sleep problems in PTSD is warranted.

Pre-sleep cognitive activity, sleep-incompatible behaviours (sleep hygiene), and hyperarousal are included (to some extent) as perpetuating factors in many models of insomnia (Espie et al., 2006; Harvey, 2002; Morin et al., 2006). Evidence for this will be outlined in the following sections. Furthermore, there are promising but untested theories for the development and maintenance of sleep disturbances in PTSD, which point to the role of compensatory behaviours, fear of sleep, and hyperarousal in sleep disturbances in PTSD (see, 'Preliminary theories of sleep disturbance in PTSD', p.23). For example, hyperarousal (Sinha, 2016), and fear of sleep (DeViva et al., 2004; Pruiksma et al., 2016) may contribute to poor sleep in PTSD, and the role of compensatory behaviours in contributing to sleep disturbances in PTSD has been proposed (Desjardins & Germain, 2006).

Evidence for the role of pre-sleep cognitive activity, sleep hygiene, and hyperarousal role in maintaining insomnia and their contribution to sleep problems in PTSD will be outlined below.

Pre-sleep cognitions

Pre-sleep cognitions in insomnia

The role of pre-sleep cognitions in insomnia will be reviewed to highlight how cognitive activity and content in the pre-sleep period may contribute to disturbed sleep.

Cognitive activity and arousal have long been implicated in the maintenance of insomnia. Insomniacs are ten times more likely to select cognitive over somatic arousal as the cause of their insomnia (Lichstein & Rosenthal, 1980), and 'having an over-active mind' has been found to be the most common reason given by insomniacs to account for poor sleep (Espie, Lindsay, Brooks, Hood, & Turvey, 1989). Accordingly, most models of insomnia include the role of cognitive processes in maintaining insomnia such as cognitive arousal, worry, maladaptive beliefs about sleep and its consequences (Espie et al., 1989; Lundh & Broman, 2000) as well as cortical arousal (Giles, Bootzin, & Wyatt, 1997). The latter theory is supported by findings of high frequency EEG in insomniacs at or around sleep-onset (Lamarche & Ogilvie, 1997; Perlis et al., 1997; Perlis, Smith, Andrews, Orff, & Giles, 2001), which is suggested to be a neural correlate of pre-sleep intrusions and worry (Perlis et al., 2001).

Models proposed to account for persistent insomnia include the role of cognitive processes to a greater or lesser extent. For example, Morin (1993) proposed an integrative model of insomnia, suggesting that dysfunctional beliefs and appraisals

about sleep (e.g., how much sleep is needed to function, and not being able to cope) interact with maladaptive habits and arousal (cognitive, emotional, physical) (Morin, 1993). Espie et al. (2006) proposed a psychobiological inhibition model called the "attention–intention–effort (AIE) pathway', which links cognitive processes and hyperarousal. The model conceptualizes persistent insomnia as due a failure in normal inhibition of pre-sleep arousal, due to attentional bias towards sleep, and high intention and effort to sleep (Espie et al., 2006). These cognitive processes are proposed to interfere with the usual automatic process characterising good sleep (Espie, 2002; 2007; Espie et al., 2006). Finally, and most relevant for the following review, Harvey (2002) proposed a cognitive model of insomnia. This model suggests that cognitive processes such as excessive (racing mind) and negatively toned (worries about the future, worries about sleep and its consequences) cognitive activity are causal in the maintenance of insomnia, by leading to selective attention toward sleep-related threats (internal and external signs of not sleeping, such as arousal and clock-watching), counterproductive coping strategies (staying in bed too long), elevated arousal and distress (physical and emotional), and a distorted perception of the sleep deficit and its impact. Together these processes may combine to interfere with sleep and produce an actual sleep deficit, as elevated cognitive and physiological arousal, and attention and effort to sleep are not conducive to the automatic, effortless sleep-onset process associated with good sleep (Espie, 2002; 2007; Espie et al., 2006). The cognitive model proposed by Harvey (2002) is well supported by a range of clinical and experimental studies (see Harvey, 2002; Harvey, Tang, & Browning, 2005 for reviews of supporting evidence).

First, there is good evidence that excessive cognitive activity interferes with poor sleep in insomnia (Harvey, 2002). As noted previously, insomniacs are most likely to attribute their sleep problems to cognitive factors such as a 'racing mind' (Espie et al., 1989;

Lichstein & Rosenthal, 1980) and measures of cognitive activity are highly correlated with sleep onset latency (Nicassio, Mendlowitz, & Fussell, 1985). Experimental studies have confirmed the link between excessive pre-sleep cognitive activity and poor sleep, demonstrating that inducing cognitive stress before sleep in good sleepers extends both objective and subjective sleep onset latencies, reduces sleep duration (Gross & Borkovec, 1982), and correlates with cortical arousal (high frequency EEG activity) in the first and second deep sleep periods (Wuyts et al., 2012). Furthermore, experimental studies have shown that interfering with pre-sleep cognitive activity in insomnia (Haynes et al., 1981; Harvey & Payne, 2002), for example with imagery distraction (Harvey & Payne, 2002), shortens sleep-onset by occupying sufficient cognitive space to prevent the typical cognitive activity that usually disrupts sleep-onset in this group (Harvey & Payne, 2002).

Second, there is also good evidence that pre-sleep thought content is negative and sleep-focused in insomnia. Studies have shown that both the pre-sleep (Kuisk, Bertelson, & Walsh, 1989) and wake after sleep (Borkovec, Lane, & VanOot, 1981) thoughts of people with insomnia are more negative (Borkovec et al., 1981; Kuisk et al., 1989), and worried (Borkovec et al., 1981) than those of good sleepers. There is evidence that while trying to sleep, insomniacs are preoccupied with thoughts about getting to sleep and the consequences of poor sleep, as opposed to the 'nothing in particular' more commonly reported by good sleepers (Harvey, 2010). Experimental studies have shown that when instructed to fall asleep as quickly as possible, good sleepers showed longer sleep onset latencies, particularly when this was combined with a high cognitive load (Ansfield, Wegner, & Bowser, 1996). This suggests that focusing on falling asleep may interfere with the automatic process of sleep-onset (Espie, 2002; 2007; Espie et al., 2006). Watts, Coyle, & East (1994) examined pre-sleep cognitions of insomniacs retrospectively. They

found that worrying about sleep and getting to sleep were commonly reported, as well as thoughts about trivial topics, long-term and recent concerns (including work and family matters), and preoccupation with bodily sensations (e.g., feeling tense). Using voice-activated audio recordings to measure pre-sleep thought content in insomnia, (Wicklow & Espie, 2000) similarly found that the most common thoughts reported by insomniacs while trying to get to sleep were thoughts about sleep, the consequences of poor sleep, active problem solving, and arousal status, which predicted longer sleep onset latencies. Using the content of live pre-sleep audio-recordings, (Harvey & Espie, 2004) developed a scale to measure the content of pre-sleep cognitive activity. Insomniacs scored significantly higher on the scale compared to controls, indicating greater pre-sleep cognitive activity of this content, which was associated with self-reported cognitive arousal, and longer sleep onset latency (Harvey & Espie, 2004).

Finally, CBT-I has been shown to reduce the frequency of pre-sleep cognitions (Espie et al., 2014) and modify maladaptive beliefs about sleep and its consequences (Edinger et al., 2001; Morin, Blais, & Savard, 2002). Changes in pre-sleep cognitive activity (GCTI scores) have been found to partially mediate sleep improvements with CBT-I, suggesting an important role for changing cognitions in treating insomnia (Espie et al., 2014).

In sum, there is good evidence for the role of pre-sleep cognitive activity in the maintenance of insomnia. In contrast to this, relatively little is known about pre-sleep cognitive activity in trauma survivors and PTSD patients, as it has not yet been directly investigated.

Pre-sleep cognitions in PTSD

Given the high rates of insomnia comorbidity in PTSD (Ohayon & Shapiro, 2000) and after a trauma (Galea et al., 2002; McMillen, North, & Smith, 2000; Varela, Koustouki, Davos, & Eleni, 2008), it seems worthwhile to consider the role of pre-sleep cognitions in the maintenance of sleep problems in PTSD. There are several ways in which cognitions relevant for sleep in PTSD may have been indirectly examined.

First, fear of sleep (DeViva et al., 2004) has been found to be elevated in trauma survivors experiencing regular nightmares (Pruiksma et al., 2016). Pruiksma and colleagues (2016) therefore suggested that fear of sleep may result from fear of experiencing nightmares (Krakow et al., 1995), particularly if the nightmare content was a replica of the trauma (Davis:2007cs; Davis:2007gi; Davis et al., 2011). Greater fear of sleep has been associated with higher PTSD symptom severity, nightmare frequency and insomnia symptoms, and suggested to account for some variance in the relationship between trauma and sleep disturbances (Pruiksma et al., 2016). Fear of sleep was also suggested to be related to the fear of a loss of vigilance (i.e. the inability to respond optimally to potential threats; Tsao & Craske, 2003), which predicted more severe self-reported sleep difficulties in veteran trauma survivors (Pietrzak et al., 2010). Furthermore, adaptive cognitive distraction strategies (e.g., 'When I experience an unpleasant/unwanted thought, I call to mind positive images instead' p.443, Pietrzak et al., 2010) have been associated with less severe sleep problems in veterans with PTSD (Pietrzak et al., 2010). This is consistent with the findings from insomnia research that cognitive distraction is adaptive and associated with reduced sleep onset latency (Harvey & Payne, 2002; Ree, Harvey, Blake, Tang, & Shawe-Taylor, 2005). These findings provided some evidence that similar cognitive mechanisms may underlie sleep problems in PTSD.

Second, additional evidence for the role of pre-sleep cognitive activity in sleep problems in PTSD is the effectiveness of CBT-I for improving sleep in PTSD (e.g., Talbot et al., 2014). CBT-I includes a cognitive component, which involves identification and restructuring of maladaptive thoughts and beliefs about sleep and its consequences, and has been shown to reduce pre-sleep cognitive activity (Espie et al., 2014). Studies investigating the effects of pure CBT-I for treating sleep disturbances in PTSD found significant improvements in subjective and objective sleep (Talbot, 2014). However, insomnia remitted for 41% of patients, suggesting additional intervention, or focus on PTSD specific factors may be required to enhance the efficacy of this treatment in a PTSD population (Ulmer et al., 2011).

Figure 1.1 illustrates some possible relationships, including associations found between poor sleep in PTSD and fear of sleep (DeViva et al., 2004; Pruiksma et al., 2016) and loss of vigilance (Pietrzak et al., 2010). It also illustrates proposed but untested relationships, such as between avoidance of the bed and poor sleep in PTSD, due to nightmares or hypervigilance (e.g., Desjardins and Germain, 2006). Finally it includes relationships proposed in the cognitive model of PTSD between trauma-related appraisals, such as 'If I go to sleep I will not notice intruders' (p. 330, Ehlers & Clark, 2000), which could lead to emotional responses such as fear, and use of dysfunctional strategies such as staying up late (see Ehlers & Clark, 2000).

The studies above suggest that trauma-related cognitions may play a role in maintaining sleep problems in PTSD. However, appraisals and cognitions in the pre-sleep period in PTSD, and their relation to subsequent sleep have yet to be investigated. More research is needed to build an empirical basis for the maintenance of insomnia in PTSD.

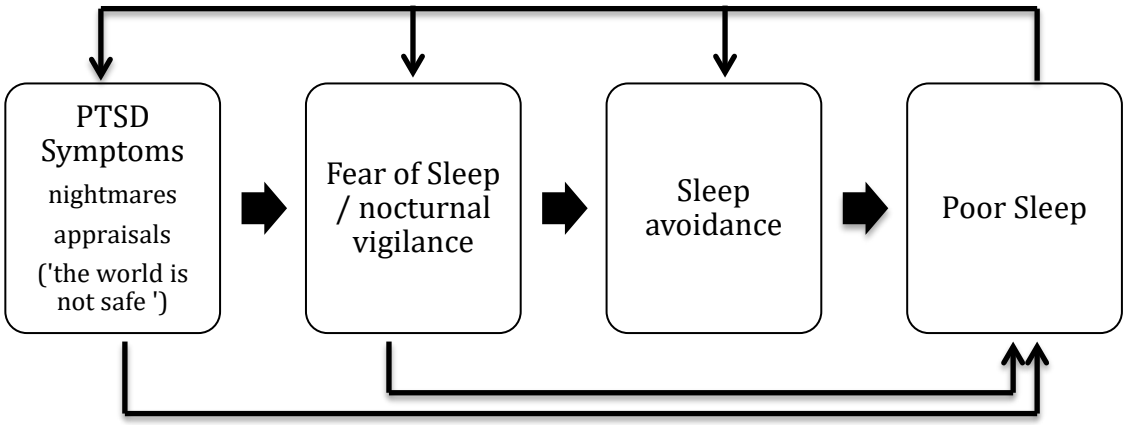


Figure 1.1. Summary illustration of some possible relationships between PTSD symptoms, including those proposed in the literature between fear of sleep (and lost vigilance) and poor sleep (e.g., Pietrzak et al., 2010; Pruiksma et al., 2016). Arrows indicate possible directional pathways, and the arrow from poor sleep to PTSD illustrates potential reciprocal exacerbation of PTSD symptoms by poor sleep. Poor sleep refers to prolonged sleep-onset, mid-sleep awakening, shorter duration and worse sleep quality, evidenced in PTSD.

Sleep hygiene and pre-sleep behaviours

Sleep hygiene in insomnia

Poor sleep hygiene is another factor that has been suggested to contribute to insomnia, although not as strongly as pre-sleep cognitions (Harvey, 2000). Sleep hygiene is targeted in CBT-I (Espie, 1999), although targeting it alone was not found to be an effective insomnia treatment (Lacks & Morin, 1992; Morin, Culbert, & Schwartz, 1994). Inadequate sleep hygiene has been classified as a diagnosis in the ICSD-3 (American Academy Of Sleep Medicine, 2005), and refers to a sleep disorder resulting from the practice of behaviours known to interfere with sleep, such as behaviours resulting in arousal (e.g., caffeine or alcohol use) and improper/irregular sleep scheduling. Studies examining the effects of poor sleep hygiene on sleep and insomnia have come to inconclusive results. Some studies found that sleep behaviours were related to insomnia. For example, a study by Mastin et al., 2006 found that elevated global sleep hygiene was related to poorer sleep quality (Mastin, Bryson, & Corwyn,

2006). Furthermore, several studies found that poor sleep habits were related to insomnia (Kazarian, Howe, Merskey, & Deinum, 1978), with up to 34% of individuals with a primary or secondary diagnosis of insomnia also qualifying for a diagnosis of inadequate sleep hygiene, according to the ICSD (Buysse et al., 1994). Studies have also shown that insomniacs engage in a higher frequency of poor sleep habits than good sleepers (Gellis & Lichstein, 2009; Jefferson et al., 2005; Kohn & Espie, 2005; McCrae et al., 2006) despite equivalent sleep knowledge (Lack & Rotert, 1986). However, not all studies have found sleep hygiene differences between insomniacs and good sleepers (Harvey, 2000), and one study found that individuals with insomnia may have better sleep hygiene than good sleepers (Cheek, Shaver, & Lentz, 2004), perhaps due to attempts to improve their sleep. Researchers have hypothesised that poor sleep habits may interfere with sleep onset by increasing pre-sleep arousal (Espie, 2002), supported by correlations between poor sleep hygiene and self-reported pre-sleep somatic arousal in insomnia, despite low correlations between sleep hygiene and sleep measures (Kohn & Espie, 2005). While there is some inconsistency between studies, overall the results tend to suggest that there is evidence of poor sleep hygiene in insomnia, compared to good sleepers. It is therefore possible that sleep hygiene may also be worse and associated with poor sleep in PTSD.

Sleep hygiene and pre-sleep behaviours in PTSD

Poor general sleep hygiene (as defined by the ICSD-3; American Academy Of Sleep Medicine, 2005) may also be found in PTSD; however, very few studies have directly investigated this. Correlations between PTSD symptoms and measures of sleep hygiene have often been low (Pruiksma et al., 2016). To date, little is known about pre-sleep behaviours that may be specific to PTSD and may interfere with sleep in this population. However, there have been several (untested) theories that nightmares and hypervigilance

may prompt compensatory behaviours that are incompatible with sleep, such as sleep-avoidance and sleeping during the day rather than at night (e.g., Belleville et al., 2011; Desjardins & Germain, 2006). For example, people with PTSD may put off going to bed or engage in behavioural strategies that may contribute to sleep difficulties, such as sleeping in a chair to feel safer, or repeatedly checking the security of the house. These pre-sleep behaviours may be related to maladaptive coping strategies that aim to control PTSD symptoms and a sense of threat (Ehlers & Clark, 2000). These coping strategies have been found to be correlated with PTSD symptom severity (Dunmore, Clark, & Ehlers, 2001), but have not yet been investigated in relation to sleep problems. As noted previously, researchers have theorised that symptoms such as chronic nightmares may lead to arousal, distress, and fear of sleep in trauma survivors. This, in turn, may lead to the subsequent development of poor sleep habits (such as staying up late and not sleeping) to avoid night-time trauma reminders (Davis & Wright, 2007; Krakow, Hollifield, et al., 2001b). Another poor sleep hygiene behaviour is the use of alcohol before bed (ICSD-3; American Academy Of Sleep Medicine, 2005). There is evidence that 'coping-related drinking' is associated with PTSD symptom severity, particularly with re-experiencing and hyperarousal symptoms (Stewart, Mitchell, Wright, & Loba, 2004). In female assault survivors with PTSD, sleep difficulties were found to be related to motives for alcohol use to control negative emotion (Nishith et al., 2001), suggesting that poor sleep may contribute to alcohol use, which could in turn exacerbate sleep problems. Therefore, alcohol use to control symptoms, and avoidance of the bed and sleep are two examples of maladaptive pre-sleep behaviours that people with PTSD may engage in, and that may interfere with sleep. Figure 1.2 illustrates some possible relationships between behaviours and poor sleep in PTSD, although these have yet to be investigated.

In sum, as with pre-sleep cognitions, very little is known about sleep hygiene practices in a PTSD population, or the role of these behaviours in sleep difficulties in PTSD, and so further investigation is warranted.

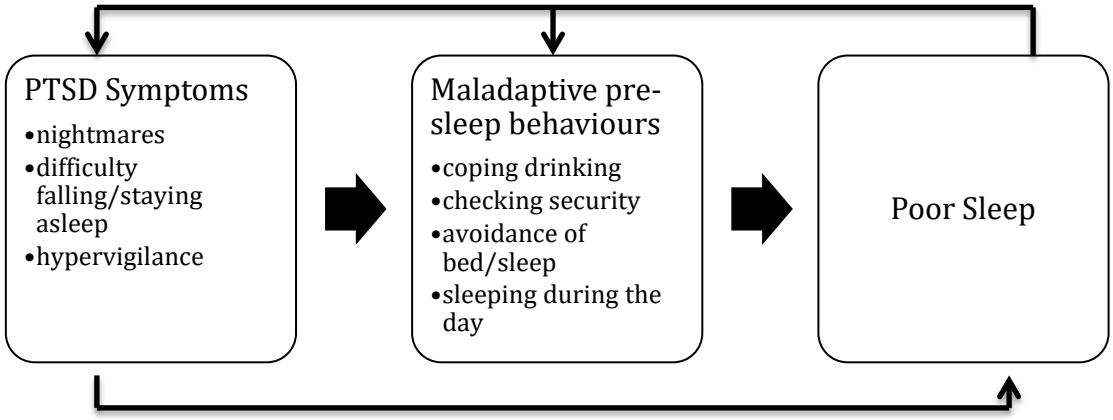


Figure 1.2. Illustration of some possible relationships between PTSD symptoms and maladaptive pre-sleep behaviours that may influence sleep disturbances in PTSD. Arrows indicate possible directional pathways. Poor sleep refers to prolonged sleep onset, mid-sleep awakening, shorter sleep duration and worse sleep quality, evidenced in PTSD.

Hyperarousal

A third factor that may play a role in the maintenance of sleep disturbances in PTSD is hyperarousal. Hyperarousal is central to many models of insomnia (Bonnet & Arand, 1997b; Espie et al., 2006; Riemann et al., 2010). It is also a symptom of PTSD (APA, 2013) and proposed to be a neurobiological underpinning of insomnia in PTSD (Germain, 2013). It is also seen as a pivotal mechanism linking trauma exposure and insomnia (Sinha, 2016) (see 'Preliminary Theories of Sleep disturbances in PTSD' p.23). In this section, two objective measures of hyperarousal (cortisol and heart-rate) and a brief overview of the hyperarousal concept of insomnia will be described. Evidence of objective alterations in cortisol and heart-rate in PTSD and their relationship to sleep will be given below.

Hyperarousal and insomnia

The hyperarousal perspective of insomnia (for comprehensive reviews of evidence see Bonnet & Arand, 2010; Riemann et al., 2010) proposes an interaction between psychological and physiological processes in perpetuating insomnia. It was developed from evidence that individuals with chronic insomnia have altered physiological arousal both at night and during the day, compared to healthy controls (Adam, Tomeny, & Oswald, 1986; Bonnet & Arand, 1997a; 1997b). This has led to propositions that insomnia is a disorder of physiological arousal, which disrupts sleep (Bonnet & Arand, 1997). Physiological arousal may arise from top-down processes such as dysfunctional cognitive processes leading to physiological hyperarousal, which can disrupt sleep (Perlis et al., 1997; Espie et al, 2006), or may reflect a predisposing risk factor for insomnia, or the result of learned sleep-preventing associations, such as conditioned arousal (see Riemann et al., 2010). A recent review described evidence of high arousal in people with insomnia from autonomous, neuroendocrine, neuroimmunological, electrophysiological and neuroimaging studies, and concluded that there is good support for physiological hyperarousal as a mechanism in the pathophysiology of insomnia, rather than just hyperarousal as a result of chronic sleep loss (Riemann et al., 2010).

Hyperarousal, sleep and PTSD: Cortisol and heart-rate

Measures of physiological hyperarousal can include neuroendocrine variables, such as basal cortisol, and indicators of autonomic nervous system activity such as heart-rate and heart-rate variability. Alterations have been found in PTSD and have been associated with sleep disturbances. The following section will review the basic literature on cortisol and heart-rate, and how they may be related to PTSD, and disturbed sleep in PTSD.

Cortisol

The hormone cortisol is involved in the stress response system, and has also been associated with sleep. Cortisol is often measured as an indicator of hypothalamic-pituitary-adrenal gland (HPA) axis functioning. The HPA-axis is a stress response system (see Tsigos & Chrousos, 2002), and cortisol is the final product released following HPA-axis activation; therefore cortisol is often used as a biological marker to measure stress and HPA-axis activity. The HPA-axis is activated in response to stress (physical or psychological) or perceived threat (Herman, Ostrander, Mueller, & Figueiredo, 2005). This, in turn, stimulates the hypothalamus, prompting the secretion of corticotrophin-releasing hormone (CRH). CRH prompts the secretion of adrenocorticotrophic hormone (ACTH) from the pituitary gland, which stimulates the release of glucocorticoids (cortisol) from the cortex of the adrenal gland. The HPA-axis functions via a self-regulating negative feedback inhibition loop, whereby circulating levels of cortisol act on glucocorticoid receptors in the hypothalamus, to inhibit the release of CRH and ACTH, reducing cortisol release, which terminates the stress response and restores the resting state (De Kloet et al., 1991), once the stressor has passed. Cortisol is secreted diurnally with a circadian rhythm (Buijs, van Eden, Goncharuk, & Kalsbeek, 2003), peaking 30-60 minutes after waking (Pruessner, Wolf, & Hellhammer, 1997) and then progressively decreasing over the course of the day to low levels in the evening (Keenan, Roelfsema, & Veldhuis, 2004). Basal cortisol secretion can be measured in urine, saliva or plasma (see Levine, Zagoory-Sharon, Feldman, Lewis, & Weller, 2007). The HPA-axis has also been associated with sleep regulation (Saper, Scammell, & Lu, 2005) in a bidirectional manner. In one direction, the hypothalamus inhibits arousal systems during sleep, and neurons in the lateral hypothalamic area are activated to promote wake (Saper et al., 2005). Cortisol is at its lowest point in the first half of the night, correlated with peaks in delta sleep activity,

and rises just before waking (Weitzman et al., 1971). Studies have also shown that sleep suppresses night-time cortisol (Weibel, Follenius, Spiegel, Ehrhart, & Brandenberger, 1995). In the other direction, sleep disturbances can also impact the stress response system. Sleep restriction and deprivation activate the HPA-axis, and chronic sleep deprivation may cause subsequent alterations in neuroendocrine responses, such as elevated cortisol after experimental sleep deprivation (Chapotot, Buguet, Gronfier, & Brandenberger, 2001). However, results of studies have been slightly mixed, with some showing no change, and some showing a reduction in cortisol (see Meerlo, Sgoifo, & Suchecki, 2008 for a review).

Due to the role of cortisol in response to stress and in regulating sleep and wake, researchers have been interested in alterations in the HPA-axis in PTSD, and the relationship between HPA-axis alterations and sleep disturbances in PTSD. Alterations in the HPA-axis are consistently evidenced in PTSD (Klassens, Giltay, Cuijpers, van Veen, & Zitman, 2012; Lehrner, Daskalakis, & Yehuda, 2016; for reviews see; Sherin & Nemeroff, 2011). Studies have found hypocortisolism in PTSD, proposed to result from evidenced increases in number and sensitivity of glucocorticoid receptors in the hypothalamus, resulting in an increased feedback sensitivity (Yehuda, 2006; Yehuda, Boisoneau, Mason, & Giller, 1993). Lower cortisol in PTSD (see Lehrner et al., 2016) has been found in the day (Yehuda, Teicher, Trestman, Levengood, & Siever, 1996), in the first half of the night (van Liempt, Arends, Cluitmans, Westenberg, Kahn, & Vermetten, 2013a), and at awakening (blunted response) (Rohleder, Nater, Wolf, Ehlert, & Kirschbaum, 2004; Wessa, Rohleder, Kirschbaum, & Flor, 2006; Yehuda et al., 1996). However, not all studies have found cortisol differences in PTSD compared to controls (see Klassens et al., 2012) and some studies have found higher cortisol in PTSD (Young & Breslau, 2004). Differences may in part be accounted for by differing

sample characteristics across studies (Yehuda, 2006). Differences are more commonly found between PTSD and non-traumatised controls (Meewisse, Reitsma, De Vries, Gersons, & Olff, 2007). This is in line with evidence showing HPA-axis alterations in trauma survivors without PTSD, suggesting trauma exposure itself can affect HPA-axis functioning (de Kloet et al., 2007; Klaassens, Giltay, van Veen, Veen, & Zitman, 2010). HPA-axis alterations may also indicate vulnerabilities to PTSD (van Zuiden, Kavelaars, Geuze, Olff, & Heijnen, 2013), as well as a response to trauma or PTSD. Lower cortisol was also found to be associated with more severe PTSD symptoms (Wessa et al., 2006), and administration of cortisol has been found to reduce re-experiencing and arousal symptoms in PTSD, perhaps due to the inhibiting effects of cortisol on memory retrieval (Aerni, Traber, & Hock, 2004). It has also been suggested that low cortisol may contribute to PTSD symptoms due to a reduced ability of the HPA-axis to contain sympathetic nervous system activation in response to trauma cues and memories (Yehuda, 2009). In sum, there is evidence of HPA-axis alterations in PTSD. The nature of these alterations is less clear, however research tends to suggest that cortisol is lower in PTSD.

Only a few studies have investigated relationships between the HPA-axis and sleep in PTSD. Nocturnal HPA-axis activity has been associated with fragmented sleep (awakenings) in PTSD (van Liempt, Arends, Cluitmans, Westenberg, Kahn, & Vermetten, 2013a), perhaps due to awakenings resulting in alterations in stress hormones (Steiger, 2007). One study found that higher 24-hour cortisol was associated with less delta sleep (Otte et al., 2005), consistent with previous studies which have found associations between high CRH and decreased delta sleep (see Neylan et al., 2003).

Heart-rate

The autonomic nervous system (ANS) contributes to physiological arousal. Heart-rate fluctuates around a mean value, influenced by the ANS, which regulates heart-rate via the sympathetic (SNS) and parasympathetic nervous systems (PSNS) (Cohen et al., 1999). Heart-rate variability (HRV) is a measure of the change in the interval between heart-rate beats, regulated by the ANS. HRV can therefore be used as non-invasive means of quantifying autonomic arousal, and relative input from the SNS and PSNS, reflecting sympathovagal balance. For example, in healthy individuals, at rest, the PSNS is dominant, and so HRV is high and resting heart-rate is low. The ANS has also been associated with sleep regulation (Saper et al., 2005), in a bidirectional manner, similar to the HPA-axis. SNS activity is increased in wakefulness, and sympathetic activity decreases during sleep, simultaneous with an increase in parasympathetic activity and dominance (Burgess, Trinder, Kim, & Luke, 1997). Sleep disruptions such as wake after sleep have been associated with higher heart-rate (Sforza et al., 2004), and fragmented sleep has been associated with sympathetic activation (Tiemeier, Pelzer, Jonck, Moller, & Rao, 2002). Insomnia has also been associated with HRV alterations during sleep (Bonnet & Arand, 1997b; Spiegelhalder et al., 2011). During experimental sleep deprivation, sympathetic activation has been found to be higher, compared to normal wake (without deprivation) (Zhong et al., 2005). This has led to concerns about the long-term effects of chronic sleep disruption on basal sympathetic activity (Meerlo et al., 2008). The relationship between PTSD, sleep and ANS activity has been investigated. In PTSD, elevated sympathetic activity during sleep has been found, reflected in higher nocturnal heart-rate compared to a mixed control group (Woodward et al., 2009) and compared to traumatised but not compared to healthy non-traumatised controls (van Liempt, Arends, Cluitmans, Westenberg, Kahn, & Vermetten, 2013a), and reflected in altered HRV during sleep in PTSD compared to traumatised controls

(Kobayashi et al., 2014; Mellman et al., 2004). These studies suggest that there is autonomic arousal during sleep in PTSD.

In sum, there is evidence of altered physiological arousal associated with disturbed sleep in PTSD. Models of insomnia propose that physiological arousal may directly contribute to sleep problems, such as difficulty initiating and maintaining sleep, and theories of sleep disturbances in PTSD have also proposed a key role for hyperarousal (e.g., Germain, 2013, Sinha, 2016).

Summary and aims of the thesis

In sum, sleep disturbances, such as insomnia, are common in PTSD, and evidenced in both subjective and objective sleep measures (see Cox & Olatunji, 2016 for review). Only a small number of studies have investigated the effects of first-line PTSD interventions on sleep disturbances (Belleville et al., 2011; Galovski et al., 2009; 2016; Gutner et al., 2013; Levrier et al., 2016; Lommen et al., 2015; Nishith et al., 2003; Raboni, 2006; Zayfert & DeViva, 2004). These studies have found that sleep disturbances show improvements with PTSD therapy. However it is unknown whether sleep improvements are also reflected in home-based objective sleep measures, as only laboratory PSG measures have been included so far (Nishith et al., 2003; Raboni, 2006). Only a small amount of research has been done to investigate which aspects of PTSD therapy best promote sleep improvements (e.g., Kobayashi et al., 2016) and what symptom changes may accompany sleep improvements with PTSD therapy (e.g., Lommen et al., 2015).

Furthermore, the role of sleep in processes important in psychotherapy and recovery from PTSD, such as memory, emotional processing (e.g., Wagner et al., 2006; Yoo et al., 2007), and fear extinction learning and generalisation (Kleim, et al., 2013b; Pace-Schott et al., 2009; 2012; Pace-Schott, Germain, & Milad, 2015a; Spoormaker et al., 2010; 2011), has raised concerns that sleep may interfere with the efficacy of psychotherapy for PTSD. However, few studies have examined this question.

Finally, clinically significant insomnia frequently persists after first-line, evidence-based psychotherapies for PTSD (e.g., Zayfert & Deviva, 2004), although reasons for this persistence remain relatively unknown. Researchers have posed a number of suggestions, including that insomnia develops into an independent problem, maintained by perpetuating factors unrelated to PTSD symptomatology (Zayfert & DeViva, 2004). There is evidence for the role of pre-sleep cognitive activity (Harvey, 2002), sleep incompatible behaviours (e.g., Bootzin et al., 1993), and hyperarousal (Bonnet & Arand, 2010; Espie et al., 2006; Riemann et al., 2010) in perpetuating insomnia; however, there is little research investigating whether these factors may also contribute to sleep problems in PTSD, and persistent sleep problems after PTSD therapy. The majority of research has focused on the relationship between hyperarousal and sleep disturbances in PTSD (see Germain, 2013, Sinha, 2016), although some research has investigated the role of fear of sleep (DeViva et al., 2004; Pruiksma et al., 2016) and loss of vigilance (Pietrzak et al., 2010) in maintaining sleep problems in PTSD.

The primary aim of this thesis was to investigate the effects of Cognitive Therapy for PTSD (CT-PTSD; Ehlers & Clark, 2000; Ehlers et al., 2005) on sleep disturbances, to identify aspects of therapy and associated symptom changes that may promote sleep improvements with PTSD therapy, and to explore reasons for residual sleep problems

after PTSD therapy. The studies presented in this thesis were designed to investigate five key research questions:

Research question 1) Does Cognitive Therapy for PTSD improve sleep disturbances?

Research question 2) Do sleep disturbances interfere with the efficacy of psychotherapy for PTSD?

Research question 3) How might sleep improvements occur with PTSD therapy?

Research question 4) Do factors known to perpetuate insomnia also contribute to sleep problems in PTSD?

Research question 5) What may account for persistent sleep problems after otherwise effective PTSD therapy?

These research questions were examined in five studies:

Study 1 (Chapter 2) addressed whether Cognitive Therapy for PTSD improves sleep disturbances (Question 1); whether sleep interferes with PTSD treatment efficacy (Question 2); and how sleep might improve with PTSD therapy (Question 3). The effects of Cognitive Therapy for PTSD on subjective sleep (duration, quality, nightmares, insomnia) were investigated in a randomized controlled trial (RCT) comparing trauma and non-trauma-focused psychotherapies for PTSD (Question 1). It was investigated whether the extent of sleep improvements was associated with the degree to which the intervention focused on processing trauma memories, by comparing the interventions. It further investigated whether memory-updating, a key procedure in CT-PTSD, facilitated sleep improvements, by comparing sleep before and after memory-updating (Question 2). Finally, the impact of sleep disturbances on PTSD treatment outcome was investigated (Question 3).

Study 2 (Chapter 3) also addressed whether CT-PTSD improves sleep disturbances (Question 1); whether sleep interferes with PTSD treatment efficacy (Question 2); and how sleep might improve with PTSD therapy (Question 3). It investigated the effects of Cognitive Therapy for PTSD on subjective sleep (duration, quality) in a large NHS outpatient sample (Question 1), and examined whether sleep severity was related to long-term PTSD treatment outcome (Question 2). It built on the findings of Chapter 2 by investigating temporal relationships between changes in PTSD symptoms, trauma appraisals and subjective sleep over treatment, to examine mechanisms of therapeutic change in sleep with PTSD therapy (Question 3).

Study 3 (Chapter 4) addressed whether factors known to perpetuate insomnia also contribute to sleep problems in PTSD (Question 4). This Chapter built on evidence for the role of pre-sleep cognitive activity in the maintenance of insomnia (Harvey, 2002), and evidence of poor sleep hygiene impacting sleep (e.g., Bootzin et al., 1993). The Chapter presents the development and validation of measures of pre-sleep cognitions and sleep-incompatible behaviours that include items from existing, validated measures (developed with insomnia populations), and new items which may relate specifically to PTSD (such as thinking about the trauma while in bed, or avoiding sleep). People with PTSD and insomnia were compared, to determine whether pre-sleep cognitions (such as concerns about sleep and its consequences) were present in both insomnia and PTSD, and whether there were PTSD-specific cognitions and behaviours that may also contribute to sleep problems in this population.

Study 4 (Chapter 5) also addressed whether factors known to perpetuate insomnia also contribute to sleep problems in PTSD (Question 4). People with PTSD, trauma-exposed

controls without PTSD, and non-trauma exposed controls were compared on subjective and objective measures of sleep, measures of pre-sleep cognitive activity (from Chapter 4), and objective measures of autonomic arousal (heart-rate), and HPA-axis functioning (cortisol). Associations between pre-sleep cognitive activity, arousal and sleep were examined to investigate the possible contribution of these factors to maintaining sleep problems in PTSD.

Study 5 (Chapter 6) addressed whether Cognitive Therapy for PTSD improve sleep disturbances (Question 1); whether sleep interferes with PTSD treatment efficacy (Question 2); how sleep might improve with PTSD therapy (Question 3); and examined what may account for persistent sleep problems after otherwise effective PTSD therapy (Question 5). It investigated the effects of CT-PTSD on self-reported and objectively (actigraphy) measured sleep problems (Question 1). It investigated whether objective and subjective pre-treatment sleep were associated with PTSD treatment outcome (Question 2). It examined variables associated with change in sleep problems over PTSD treatment, such as pre-sleep cognitive activity (Question 3). It also aimed to investigate possible reasons for the persistence of sleep problems after PTSD therapy, by investigating treatment effects on pre-sleep cognitive activity and arousal (heart-rate and cortisol), and the association between these measures and sleep problems at post-treatment (Question 5).

Chapter 2: The Effects of Psychotherapies for Posttraumatic Stress Disorder on Sleep Disturbances: Results from a Randomized Clinical Trial

Introduction

As described in Chapter 1, sleep disturbances, such as difficulty falling and staying asleep and nightmares are diagnostic symptoms of posttraumatic stress disorder (PTSD) (APA, 2013). Sleep problems in PTSD include reduced sleep duration (Straus et al., 2015), and sleep quality (Leskin et al., 2002). Only a small number of studies have investigated the effects of first-line PTSD therapies on sleep outcomes (Belleville et al., 2011; Galovski et al., 2009; 2016; Gutner et al., 2013; Levrier et al., 2016; Lommen et al., 2015; Nishith et al., 2003; Raboni, 2006; Zayfert & DeViva, 2004). These studies have found that despite sleep improvements, sleep difficulties, such as insomnia, are persistent after PTSD therapy for up to 70% of patients (Belleville et al., 2011; Galovski et al., 2009; Gutner et al., 2013; Nishith et al., 2003; Zayfert & DeViva, 2004).

Given the commonly residual nature of sleep problems after PTSD therapy it would be important to understand which aspects of PTSD therapy, and which PTSD therapies, best promote sleep improvements. Two studies have directly compared the effects of two evidence based, trauma-focused PTSD therapies (Cognitive Processing Therapy and Prolonged Exposure) on sleep outcomes, and found equivalent sleep improvements (Galovski et al., 2009; Gunter et al., 2013). One study has found that sleep duration improved the night after a written narrative exposure to the trauma

memory (Kobayashi et al., 2016), suggesting that processing trauma memories leads to sleep improvements. Processing and updating trauma memories is a key procedure in trauma-focused Cognitive Therapy for PTSD (CT-PTSD) (Ehlers et al., 2005). It involves elaborating and updating the worst moments of trauma memories with information that puts them into perspective, such as ‘I did not die’ or 'It was not my fault' (see Ehlers et al., 2005), which is thought to make the personal meanings of the trauma less threatening, and lead to a decrease in intrusive re-experiencing symptoms. If processing trauma memories plays a role in sleep improvements with trauma-focused therapy, then trauma-focused therapy such as CT-PTSD would be expected to lead to greater improvements than a psychotherapy that does not involve reprocessing trauma memories, such as supportive counselling. However, no known study has compared the effects of trauma-focused with non-trauma-focused PTSD therapy on sleep, thus it is unknown what role processing trauma memories may play in sleep improvements with PTSD therapies such as CT-PTSD. Comparing trauma and non-trauma-focused PTSD treatments would enable a more direct examination of the importance of memory-updating procedures for improving sleep with PTSD therapy.

Furthermore, as discussed in Chapter 1, research demonstrating the importance of sleep in learning and memory, emotional processing and reactivity (Yoo et al., 2007; Holland & Lewis, 2007; Wagner et al., 2006), and retention and generalization of fear extinction (Kleim, et al., 2013b; Pace-Schott et al., 2012; Spoormaker, 2008; Spoormaker et al., 2010; 2011) has led to concerns that reduced sleep duration may have a detrimental effect on response to psychological PTSD treatments. There is also some evidence that poor sleep quality predicts a slower response to PTSD treatment, in people with PTSD and comorbid depression (Lommen et al., 2015). However, a

recent study showed that nightmares did not impact the efficiency of CBT for PTSD (Levrier et al., 2016). In sum, despite concerns regarding the effects of sleep deprivation, there is currently no strong evidence that sleep impacts overall PTSD treatment outcome, and further research is needed into the effects of reduced sleep duration on PTSD treatment outcomes.

Overall, more research is needed to add to the small number of studies investigating PTSD treatment effects on sleep, and to determine which aspects of PTSD therapy best promote sleep improvements. Furthermore, research is needed to investigate whether reduced sleep duration may interfere with the overall outcome of PTSD therapy.

Study aims

The primary aim of this study was to investigate whether trauma or non-trauma-focused psychotherapy for PTSD was most effective for improving sleep, and whether processing and updating trauma memories is important for improving sleep with trauma-focused therapy. Specifically, the study investigated 1) the effectiveness of psychological therapies for PTSD for improving self-reported sleep, and 2) whether the degree of sleep change depends on the extent to which the therapy focuses on processing trauma memories, by comparing trauma and non-trauma-focused psychological interventions. If unprocessed trauma memories contribute to disturbed sleep in PTSD, then targeting and re-processing the trauma memories would be expected to lead to sleep improvements simultaneous with improvements in PTSD symptoms, such as re-experiencing symptoms and arousal. There is already some evidence in support of this hypothesis (Lommen et al., 2015).

The study further investigated 3) whether the memory-updating procedure facilitated sleep improvements in CT-PTSD. To do this, the study compared two versions of CT-PTSD, a standard weekly version and an intensive version, in which the interventions which promote memory-updating were delivered over five to seven working days, compared to three months for standard CT-PTSD. This enabled investigation of whether sleep improvements coincided with interventions that facilitate memory-updating: First, by comparing standard and intensive treatment at a time point when memory-updating had taken place for the intensive, but not the standard weekly CT-PTSD group; and second, by analysing daily sleep diaries completed by the intensive CT-PTSD group, to compare sleep directly before and after memory-updating. If processing trauma memories promote sleep improvements with CT-PTSD, then it would be expected that equivalent sleep improvements would have occurred by seven days with intensive CT-PTSD, and that sleep would significantly improve after memory-updating in therapy.

Next, 4) the relationship between baseline sleep duration and end of treatment PTSD treatment outcome (controlling for baseline PTSD symptoms) was also investigated. If reduced sleep duration interferes with treatment outcome, it would be expected that lower baseline sleep duration would predict more severe PTSD symptoms at post-treatment. Finally, 5) in patients who received CT-PTSD, associations between sleep duration improvements and symptoms hypothesised to be related to sleep improvements were explored. These were reductions in nightmares and hyperarousal and reduced anxiety about going to bed. CT-PTSD may affect sleep duration via reductions in nightmares, hyperarousal and anxiety about going to bed, resulting from re-processed trauma memories with therapy. If so, CT-PTSD would be expected to lead to greater reductions in nightmares, hyperarousal and pre-bed anxiety than

supportive therapy. Furthermore, sleep duration improvements with CT-PTSD would be expected to correlate with improvement in hyperarousal, nightmares and anxiety about going to bed.

Methods

Overview of the study design

Changes in self-reported sleep were analysed in patients treated during a 2014 randomised controlled trial by Ehlers and colleagues (2014). In the trial, CT-PTSD (Ehlers & Clark, 2000; Ehlers et al., 2005) was compared to an alternative, active, but non-trauma-focused treatment, emotion-focused supportive therapy, and a waitlist control condition. The results of the trial showed that both psychotherapies (cognitive and supportive therapy) led to greater changes in PTSD symptoms than the waitlist, and Cognitive Therapy lead to greater improvements in PTSD symptoms than supportive therapy (see Ehlers et al., 2014 for full results).

Participants

Participants were out-patients with PTSD (N = 121) who participated in a randomized controlled trial (RCT) comparing psychological treatments for PTSD and a waitlist condition (Ehlers et al., 2014), ISRCTN: 48524925. The sample comprised 71 women and 50 men (aged 18-65) who met diagnostic criteria for PTSD, as determined by the Structured Clinical Interview for DSM-IV (First, Gibbon, Spitzer, & Williams, 1996). Participants were included if PTSD was their primary diagnosis, and their current intrusive memories were linked to one or two traumas in adulthood. Details of trauma type and demographics are shown in Table 2.1 (see Ehlers et al., 2014, for further sample details). The sample size was determined by power analysis on the basis of effect sizes for cognitive therapy observed in previous trials. A group

size of 30 per condition yields 85% power for detecting an effect size of 0.8. For comparing therapy conditions (cognitive therapy, and supportive therapy) with the waitlist, at least 30 per group were required for p = .025 (waitlist is compared with two groups, hence .05/2) with a power of 80% and effect size of 0.8. For comparing cognitive therapy with supportive therapy, an effect size of about 0.6 was expected, and n = 98 needed for an allocation ratio of 2:1.

Treatment Conditions

Participants were randomly allocated to one of four conditions: (1) trauma-focused Cognitive Therapy for PTSD (CT-PTSD), delivered over 12 weeks (N = 31); (2) intensive CT-PTSD (N = 30) delivered over five to seven days; (3) emotion focused supportive therapy, delivered over 12 weeks (N = 30); or (4) a 14-week wait list (N = 30). By the 14-week assessment, patients in all treatment conditions had received equivalent therapist input of up to 20 hours of therapy. The therapy conditions are outlined below (see Ehlers et al., 2014, for full details).

Cognitive Therapy for PTSD (CT-PTSD; Ehlers et al., 2005): This is a trauma-focused therapy, which follows Ehlers and Clark's model of PTSD (Ehlers & Clark, 2000). The treatment aims to reduce the patient's sense of current threat by changing problematic meanings of the trauma and its consequences, elaborating and updating the memories of the trauma with information that gives them a less threatening meaning at present, discriminating triggers of intrusive memories, and changing behaviours and cognitive processes that maintain PTSD, such as rumination and safety behaviours. For details of procedures see: *http://oxcadat.psy.ox.ac.uk/downloads/CT-PTSD%20Treatment%20Procedures.pdf/view.* Sleep was not directly targeted. CT-PTSD was delivered in 12 weekly sessions over three months (standard CT) or as an

intensive therapy (intensive CT), which was delivered daily over five to seven working days and two shorter sessions one week and one month later.

Emotion-focused supportive therapy (EST): This non-directive treatment focuses on the patient's emotions rather than cognitions. After normalizing PTSD symptoms, the therapist gave the rationale that the trauma had left the patient with unprocessed emotions and that therapy would provide them with support and a safe context to address their unresolved emotions. Patients could freely choose what problems to discuss in the session, including any aspect of the trauma. Therapists helped patients clarify their emotions and solve problems. EST was delivered in 12 weekly sessions over 3 months.

14 Week waitlist: Patients waited for 14 weeks before random allocation to either weekly (n = 13) or intensive CT-PTSD (n = 11).

Measures

Self-reported PTSD symptom severity (excluding sleep) and sleep duration were assessed at baseline (pre-treatment/wait), 6 weeks and 14 weeks (post-treatment/wait). Treatment groups were also assessed at 3 weeks, and at the 27- and 40-week follow-ups. Clinician assessments were conducted at baseline (pre-treatment/wait), 14 weeks, 27 and 40 weeks.

Measures completed by all groups

PTSD symptoms. The main PTSD symptom measure for the purposes of the present study was the Posttraumatic Diagnostic Scale (PDS) (Foa, Cashman, Jaycox, & Perry, 1997), a self-report questionnaire measuring the overall severity of 17 PTSD

symptoms specified in DSM-IV. The PDS has shown good reliability and concurrent validity with other PTSD measures. Sum scores range from 0–51, and a clinical cut-off of 18 has been found to indicate PTSD (Ehring, Kleim, Clark, Foa, & Ehlers, 2007). In the present study, the results of independent assessments with the Clinician-administered PTSD Scale (CAPS) for DSM-IV (Blake et al., 1995) showed identical results to the PDS for outcome, but the CAPS was given less frequently than the PDS (see Ehlers et al., 2014), and so PDS-assessed PTSD symptom severity is reported. The PDS sleep item (‘*having trouble falling or staying asleep’*), was omitted for the purposes of the present analyses, and the PTSD severity score was based on the remaining 16 items.

Self-reported sleep duration (1 item on a questionnaire). Patients in each treatment group, at each assessment point (baseline, 3, 6, 14, 27 and 40 weeks), reported how many hours of sleep they had had on average per night over the past week. This was used as the primary outcome measure in this study, as this was available at every assessment point, and in the sleep diary (see below), whereas the other sleep measures were only available at initial assessment and 14-weeks.

Self-reported sleep quality (1 item on a questionnaire). Patients in each treatment group, at initial assessment and 14 weeks, rated their overall sleep quality over the past week (‘*overall, how well did you sleep*?’ rated on a scale from 0 *'not at all well*' to 100 *'very well*'). Two participants in each group had missing data because the measure was introduced with delay.

Insomnia symptoms (from PTSD measures). Severity of sleep problems was also assessed with the CAPS insomnia item (Blake et al., 1995) (*‘problems falling or*

staying asleep'; frequency plus intensity rating, each measured on a scale from 0 to 4), and the PDS insomnia item 13 (*'having trouble falling or staying asleep'*; frequency rated on a scale from 0 '*not at all*' to 3 '*5 or more times a week*'), at initial assessment and 14 weeks. The percentage of patients meeting the clinical cut-off for the CAPS insomnia item (frequency at least 1, and intensity at least 2 *'30 – 90 minutes loss of sleep'*) at initial assessment and 14 weeks, was also calculated.

Possible treatment mechanisms. Variables that may be indicators of possible mechanisms of treatment effects on sleep duration were analysed at 14 weeks. These were nightmares (CAPS and PDS item), hyperarousal symptoms, excluding difficulty falling and staying asleep (mean of CAPS hyperarousal items, and of PDS hyperarousal items: 14, 15, 16 and 17), and patient ratings of feeling anxious about going to bed (on a scale from 0 *'not at all*' to 100 *'very much'*).

Measures completed by intensive Cognitive Therapy group only

Sleep diary. Participants receiving intensive CT-PTSD (including some initially allocated to waitlist; N = 32) completed a sleep diary each morning for 6 weeks in total; two weeks pre-treatment, two weeks during the intensive treatment phase (one week) and the following week (one week), and two weeks before the 6-week assessment. Participants reported how many hours and minutes of actual sleep they had slept the previous night. Weekly self-reported sleep duration correlated with the mean sleep duration reported in the diary at pre-treatment (r = .85, N =32), and post-treatment (r = .78, n = 26).

Data Analysis

Analyses were conducted using SPSS version 22. To test whether psychological treatments lead to improvements in sleep (Question 1), an analysis of covariance (ANCOVA) compared reported sleep duration at 6 and 14 weeks, with the between-subject factor 'condition' (CT, EST, wait) and the within-subject factor 'time', and the covariate baseline hours of sleep. ANCOVA was used as the analysis strategy as missing data was minimal. Overall effects of condition are reported, as well as adjusted mean differences and 95% confidence intervals (CI) for differences between the treatment conditions and waitlist. Effect sizes (ES) are reported as partial $\eta 2$, with small ES $\geq$ 0.01; medium $\geq$ 0.06; and large $\geq$ 0.14. Group differences on sleep quality, and the CAPS and PDS insomnia items were also analysed. ANCOVAs compared sleep quality, CAPS, and PDS insomnia items at 14 weeks, with between factor 'condition' (CT, EST, wait), controlling for baseline severity. Overall effects of condition are reported, as well as adjusted mean differences and 95% confidence intervals (CI) for differences between the treatment conditions and waitlist. Changes in the proportion of patients meeting the clinical cut-off on the CAPS insomnia item before and after therapy were compared with related-samples McNemar tests.

To test whether cognitive therapy leads to greater improvement in sleep than supportive therapy (Question 2), an ANCOVA compared reported sleep duration at 6, 14, 27 and 40 weeks, with the between factor 'condition' (CT, EST) and the within-subject factor 'time', controlling for baseline hours of sleep. For comparison, parallel analyses are reported for PTSD severity excluding sleep (see Ehlers et al., 2014, for comprehensive analyses of PTSD and other outcome measures).

Question 3 was analysed in three steps. First, an ANCOVA compared intensive and standard CT at 3 weeks, controlling for baseline sleep duration. By the 3-week assessment, the intensive, but not the standard CT group, had completed the memory-updating interventions. This analysis included the patients randomly allocated after waiting for treatment (N = 44 standard CT, N = 41 intensive CT). Second, sleep diaries completed by the intensive CT group were analysed. A one-way repeated measures ANOVA, and planned contrasts compared mean reported sleep duration before, during and after intensive CT. Third, the impact of memory-updating procedure on sleep duration was examined by comparing sleep duration reported in the diary before and after the first discrete period of memory-updating in intensive CT, with sleep duration before and an equivalent amount of time after a randomly selected pre-treatment day (Mean day = 4.78, SD = 2.75). Memory-updating was most commonly done for the first time on the second day of intensive treatment (39.3% of patients). Updating was done between one and four times (M = 2.09, SD = 1.04), and on average concluded on day 4 of treatment (M = 4.12, SD = 1.54).

To address Question 4 (impact of reduced sleep duration on treatment outcome), correlation and regression analyses examined the relationship between sleep duration at initial assessment and end of treatment (14 weeks), and treatment outcome (PDS at 14 and 40 weeks), controlling for baseline PDS. This analysis included all 85 patients who received cognitive therapy, including post-wait allocations. An ANCOVA checked beforehand that there were no effects of type of CT (intensive versus standard) or allocation (immediate versus post-wait), nor an interaction, all p's > .32.

To investigate other measures that may be associated with improvement in sleep duration in therapy, symptoms that were hypothesised may be associated with sleep

improvements were explored (Question 5). ANCOVAs tested differences between conditions (CT, EST, wait) in nightmares, hyperarousal symptoms (CAPS, PDS), and patient rated anxiety about going to bed at 14 weeks, controlling for baseline severity. In patients treated with cognitive therapy, sleep duration change with treatment was correlated with change in nightmares and hyperarousal symptoms (CAPS, PDS), and anxiety about going to bed.

Results

Question 1: What is the effectiveness of psychological therapies for PTSD for improving self-reported sleep?

Sleep duration

Figure 2.1 illustrates the changes in reported sleep duration across the assessment points for cognitive therapy, supportive therapy and waitlist (see Table 2.2 for descriptive statistics). The ANCOVA showed a significant difference between the conditions, $F(2, 117) = 4.30$, $p = .016$, partial $\eta^2 = .07$. Cognitive therapy, but not supportive therapy, led to greater improvement in sleep duration than the waitlist control, baseline-adjusted differences (sleep duration) for CT = 0.73 (95% CI = .20 to 1.26), $p = .008$; and for EST = .21 (95% CI = -.41 to .82), $p = .51$. Patients receiving CT reported sleeping 55.2 minutes longer after treatment (14 weeks), compared to a change of 21.6 minutes with supportive therapy and 12.6 minutes on the wait-list (see Table 2.2).

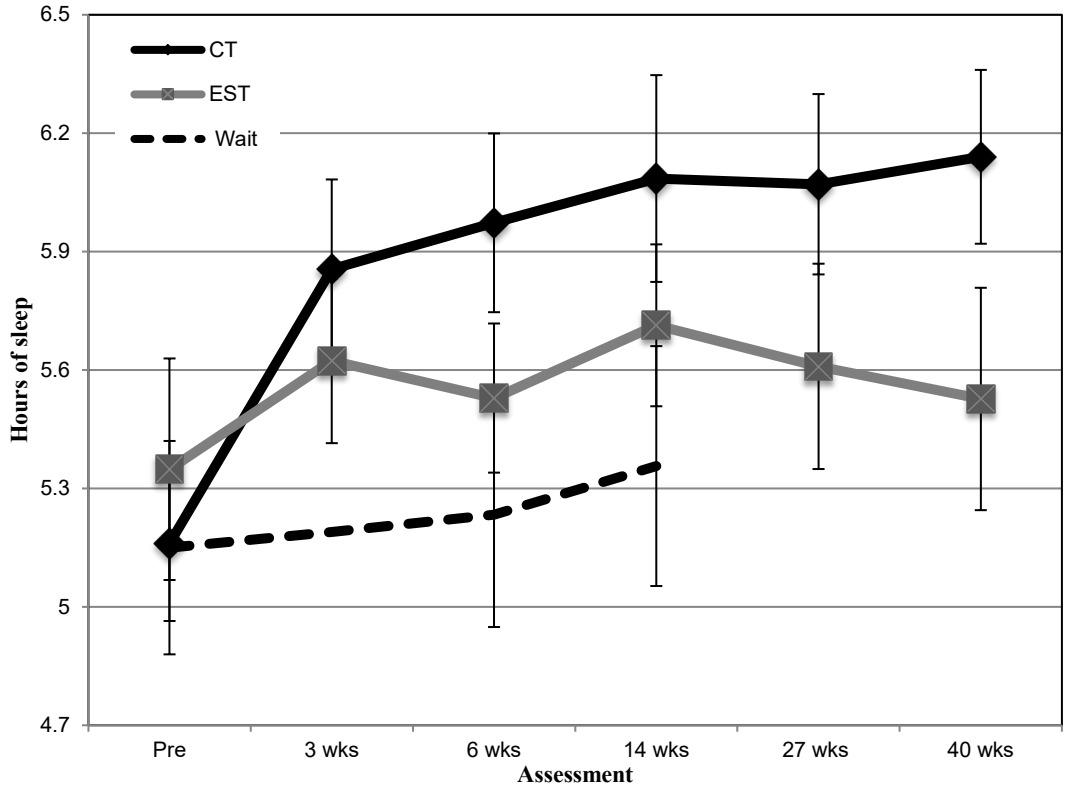


Figure 2.1. Mean hours of sleep (and standard error bars) reported by patients receiving cognitive therapy (CT, standard and intensive combined, immediate allocations only), emotion-focused supportive therapy (EST) and waitlist.

Table 2.1. Demographic information and trauma characteristics by treatment condition

		Intensive Cognitive Therapy (*N* = 30)				**Standard Cognitive Therapy (*N* = 31)**				**Supportive Therapy (*N* = 30)**				**Waitlist (*N* = 30)**			
Demographics		M	SD	N	%	M	SD	N	%	M	SD	N	%	M	SD	N	%
Sex	Female			18	60.0			18	58.1			17	56.7			18	60
	Male			12	40.0			13	43.9			13	43.4			12	40
Ethnic Group	Caucasian			22	73.3			20	64.5			22	73.3			21	70
	Ethnic Minority			8	26.7			11	35.5			8	26.7			9	30
Age	(Years)	39.7	12.4			41.5	11.7			37.8	9.9			36.8	10.5		
Traumas		M	SD	N	%	M	SD	N	%	M	SD	N	%	M	SD	N	%
Type of Main Traumatic Event	Interpersonal Violence[1]			12	40.0			12	38.7			11	36.7			10	33.3
	Accidents/ Disaster			11	36.7			11	22.6			14	10.0			10	33.3
	Death/ Harm to Others			2	6.7			1	3.2			2	6.7			4	13.3
	Other			5	16.7			7	22.6			3	10.0			6	20
Time since Main Traumatic Event	3 months - 1 year			10	33.3			14	45.2			8	27.8			14	46.7
	1 to 2 years			10	33.3			5	16.1			7	24.1			6	20
	2 to 4 years			7	23.3			11	35.5			8	27.6			3	10
	More than 4 years			3	10.0			1	3.2			6	20.7			7	23.3
History of Other Trauma	Yes			22	63.3			21	67.7			23	76.7			20	66.7
	No			8	26.7			10	32.3			7	23.3			10	33.3

Reported History of Childhood Abuse	Yes	5	16.7	2	6.5	4	13.3	3	10.0
	No	25	83.3	29	93.5	26	86.7	27	90.0
Comorbidity									
Anxiety Disorder	Yes	10	33.3	7	22.6	10	33.3	10	33.3
	No	20	66.7	24	77.4	20	66.7	20	66.7
Depressive Disorder	Yes	12	40.0	7	22.6	11	36.7	14	46.7
	No	18	60.0	24	77.4	19	63.3	16	53.3
Substance Abuse	Yes	6	20.1	6	19.5	6	20.1	2	6.7
	No	24	80.0	25	80.6	24	80.0	28	93.3
History of Substance Dependence	Yes	2	6.7	4	12.9	2	6.7	1	3.3
	No	28	93.3	27	87.1	28	93.3	29	96.7
Axis II disorder	Yes	7	23.3	5	16.1	4	13.3	8	26.7
	No	23	76.7	26	83.9	26	86.7	22	73.3

Table 2.2. Mean and standard deviations (SD) at each assessment point for the psychological treatment and waitlist conditions, and for intensive and standard cognitive therapy (including those initially allocated to the waitlist).

	Cognitive Therapy (CT) (N = 61)		**Supportive Therapy (N = 30)**		**Waitlist (N = 30)**		**Intensive CT, including post-wait (N = 41)**		**Standard CT, including post-wait (N = 44)**	
Hours of Sleep										
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Baseline	5.16	1.53	5.35	1.54	5.15	1.48	5.13	1.53	5.38	1.69
3 weeks	5.86	1.77	5.62	1.14	---	---	6.11	1.59	5.62	1.84
6 weeks	5.97	1.77	5.53	1.03	5.23	1.56	5.95	1.86	5.98	1.66
14 weeks	6.08	2.05	5.71	1.12	5.36	1.66	6.03	1.66	6.31	2.23
27 weeks	6.07	1.78	5.61	1.42	---	---	5.88	1.72	6.42	1.71
40 weeks	6.14	1.72	5.53	1.54	---	---	6.08	1.78	6.51	1.85
Sleep Diary Data: Hours of Sleep										
Pre-treat (*n* = 29)	---	---	---	---	---	---	5.43	1.44	---	---
During treat (*n* = *32)*	---	---	---	---	---	---	5.62	1.34	---	---
Post-treat (*n* = 24)	---	---	---	---	---	---	6.43	1.73	---	---
PTSD Severity (excluding sleep)										
Baseline	30.69	6.79	32.11	6.93	30.05	7.33	30.69	6.94	29.74	7.01
3 weeks	18.59	10.27	26.43	11.48	---	---	16.21	8.90	22.67	10.51
6 weeks	14.53	9.56	21.73	12.33	29.76	6.86	13.86	8.41	16.80	11.71
14 weeks	9.75	9.51	18.40	13.03	27.04	9.02	10.77	8.60	8.73	9.66
27 weeks	11.01	11.01	17.37	12.06	---	---	11.82	10.01	8.81	10.31
40 weeks	10.45	10.80	19.38	13.96	---	---	12.17	10.98	9.56	10.35

Further measures at Baseline and 14 Weeks										
Sleep Quality										
Baseline	34.82	21.30	31.07	20.61	36.07	19.69	35.85	20.25	33.08	20.64
14 weeks	58.95	27.33	46.61	26.81	33.04	16.74	57.56	31.03	56.79	23.60
Insomnia item (PDS)										
Baseline	1.98	1.01	2.15	0.88	2.40	0.72	1.98	0.98	2.17	0.92
14 weeks	0.89	1.05	1.57	0.97	2.20	0.85	0.80	1.18	0.99	0.99
Insomnia item (CAPS)										
Baseline	5.48	2.43	6.05	1.83	5.08	2.22	5.11	2.38	5.40	2.62
14 weeks	2.99	3.23	4.50	3.33	4.73	2.66	2.63	3.27	3.01	3.04
Insomnia item (CAPS, percent and N meeting clinical cut-off)										
Baseline	78.7%	48/61	90.0%	27/30	76.7%	23/30	78.0%	32/41	75.0%	33/44
14 weeks	44.3%	27/61	63.3%	19/30	70.0%	21/30	46.3%	19/41	36.4%	16/44
Bad dreams and nightmares (PDS)										
Baseline	1.57	0.96	1.53	0.86	1.53	0.94	1.43	0.93	1.51	1.05
14 weeks	0.43	0.67	0.90	0.99	1.17	0.96	0.42	0.72	0.46	0.74
Bad dreams and nightmares (CAPS)										
Baseline	3.75	2.60	3.42	2.61	3.27	2.70	3.33	2.62	3.82	2.63
14 weeks	1.31	2.13	2.27	2.72	3.17	2.62	1.27	2.14	1.29	2.12
Hyperarousal (excluding sleep, PDS)										
Baseline	2.09	0.58	2.15	0.54	2.05	0.60	2.05	0.60	2.14	0.53
14 weeks	0.80	0.74	1.32	0.86	2.00	0.74	0.74	0.75	0.93	0.68
Hyperarousal (excluding sleep, CAPS)										
Baseline	18.29	5.16	18.55	4.62	17.00	5.74	17.47	4.18	19.18	5.97

14 weeks	8.26	7.69	12.28	7.34	17.43	6.28	7.69	7.75	9.49	7.48
Anxiety going to bed										
Baseline	42.54	30.59	33.67	27.98	46.33	26.45	39.43	32.46	41.71	26.45
14 weeks	20.98	30.04	35.17	31.83	38.50	29.04	17.72	25.60	22.56	30.23

Sleep quality

The ANCOVAs showed a significant difference between the conditions for self-reported sleep-quality, $F(2, 109) = 12.77$, $p < .001$, partial $\eta^2 = .190$. Cognitive therapy and supportive therapy led to greater changes in sleep quality than waitlist: baseline-adjusted mean difference = 26.54 (95% CI = 16.11 to 36.98), $p < .001$. Supportive therapy showed advantages over the waitlist for improving sleep quality = 16.10 (95% CI = 3.97 to 22.23), $p = .01$. Finally, cognitive therapy was just superior to supportive therapy: adjusted mean differences for sleep quality = 10.44 (95% CI = .02 to 20.91), $p = .05$. This shows that cognitive therapy was most effective at improving sleep quality.

Insomnia symptoms (from PTSD measures). The ANCOVAs showed a significant difference between the conditions for each of the insomnia measures; PDS insomnia, $F(2, 117) = 15.84$, $p < .001$, partial $\eta^2 = .213$; CAPS insomnia, $F(2, 117) = 5.53$, $p = .005$, partial $\eta^2 = .09$. Cognitive therapy led to greater changes in insomnia than waitlist: baseline-adjusted mean difference for PDS insomnia = - 1.12 (95% CI = -1.52 to -0.72), $p < .001$; CAPS insomnia = -2.00 (95% CI = -3.23 to -0.77), $p = .002$. In contrast, supportive therapy was not superior to the waitlist on CAPS insomnia severity, baseline adjusted mean difference = -0.86 (95% CI = -2.30 to 0.58), $p = .24$, but showed advantages over the waitlist on PDS insomnia severity = -0.52 (95% CI = -0.98 to -0.60), $p = .03$. Cognitive therapy was superior to supportive therapy on PDS insomnia severity = -0.60 (95% CI = -0.99 to -0.21), $p = .003$; but not on CAPS insomnia severity = -1.14 (95% CI = -2.38 to 0.09), $p = .07$. Related-samples McNemar tests showed that with cognitive therapy, $p < .001$, and supportive therapy, $p = .021$, there was a reduction in the proportion of patients with clinically significant

insomnia symptoms between the initial and 14-week assessments, but not in the wait-list group, $p = .69$. At the 14-week assessment, 44.3% of patients who had received cognitive therapy and 63.3% of those who had received supportive therapy continued to report clinically insomnia symptoms, according to the CAPS. This shows that insomnia symptoms were improved to the greatest extent with cognitive therapy, but remained residual for nearly half of patients after treatment.

PTSD symptom severity (excluding sleep). PTSD symptom changes were analysed and reported for comparison. Table 2.2 shows the changes in self-reported PTSD symptoms (excluding sleep). The ANCOVA showed a significant difference between the conditions, $F(2, 117) = 33.60$, $p < .001$. Both treatments led to greater reductions in PTSD symptoms compared to waitlist; baseline-adjusted differences for CT = -16.24 (95% CI = -12.25 to -20.23); EST = - 8.042 (95% CI = -3.42 to -12.67).

Question 2: Does the degree of sleep change depend on the extent to which the therapy focuses on processing trauma memories?

Comparing cognitive therapy and supportive therapy

Sleep Duration. The ANCOVA showed a significant effect of condition, $F(1, 88) = 5.30$, $p = .024$, partial $\eta^2 = .06$. Cognitive therapy led to greater improvement in sleep duration than supportive therapy, baseline-adjusted mean difference = 0.58 (95% CI = .08 to 1.09) (see Figure 2.1 and Table 2.2).

PTSD Symptom Severity (excluding sleep). The ANCOVA showed a significant difference between the conditions, $F(1, 88) = 14.64$, $p < .001$. Cognitive therapy led

to greater improvement in PTSD symptoms than supportive therapy, baseline-adjusted mean difference = 8.164 (95% CI = -3.92 to -12.41).

Question 3: Does the memory-updating procedure facilitate sleep improvements in CT-PTSD?

Comparison of intensive and weekly CT at 3 weeks

Sleep Duration. The ANCOVA showed a significant effect of group (see Table 2.2), $F(1, 82) = 5.75$, $p = .019$, partial $\eta^2 = .07$. Patients receiving intensive cognitive therapy, who had completed the updating memory-updating intervention at this stage (3 weeks), reported sleeping longer than those receiving standard CT, who had not yet updated their memories, baseline-adjusted mean difference = 0.67 (95% CI = .11 to 1.22).

PTSD Symptom Severity (excluding sleep). The ANCOVA showed a significant effect of group (see Table 2.2), $F(1, 82) = 11.65$, $p = .001$, partial $\eta^2 = .124$. Patients receiving intensive therapy reported fewer PTSD symptoms at 3 weeks, than those receiving standard cognitive therapy, baseline-adjusted mean difference = -6.931 (95% CI = -2.89 to -10.97).

Sleep diaries in intensive cognitive therapy: Memory updating

Table 2.2 shows the mean sleep duration for pre, during and post intensive cognitive therapy as assessed with the sleep diary. The ANOVA showed a significant effect of time on self-reported sleep duration, $F(2, 44) = 8.68$, $p = .001$, partial $\eta^2 = .28$. There was a significant linear trend across the three time points $F(1, 22) = 10.27$, $p = .004$. Planned contrasts showed significant differences in sleep duration between the pre and

post-treatment sleep diaries, $F(1, 22) = 10.27$, $p = .004$, partial $\eta^2 = .32$; and between during-treatment and post-treatment diaries, $F(1, 23) = 7.52$, $p = .01$, partial $\eta^2 = .25$. There was also a trend for a difference between pre and during-treatment sleep diaries, $F(1, 28) = 4.13$, $p = .05$, partial $\eta^2 = .13$. Parallel to the results of the questionnaire reported sleep duration, patients receiving intensive therapy reported in the diary an increase in sleep duration of about an hour with therapy (see Table 2.2 and Figure 2.2). This shows that sleep duration significantly improved during intensive CT.

Table 2.3 shows the comparison of sleep duration reported for the nights before and after memory-updating in therapy. There was a significant increase of 41.04 minutes of self-reported sleep from the night before updating to after updating, $t(23) = -2.46$, $p = .02$, partial $\eta^2 = .21$, whereas there was no significant change in sleep duration from the night before a randomly selected pre-treatment day to an equivalent period afterwards (with no intervention), $t(23) = -.27$, $p = .79$, partial $\eta^2 = .003$. This shows that sleep duration improves after memory-updating in CT-PTSD, compared to no intervention.

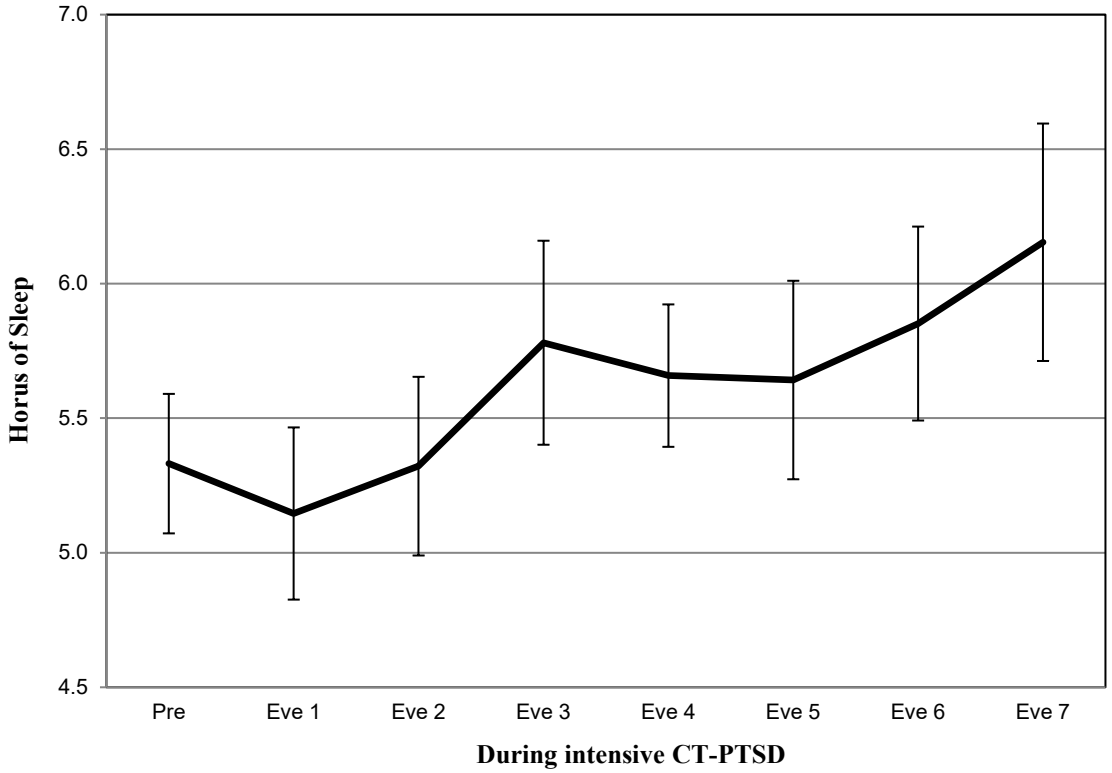


Figure 2.2 Sleep diary data: Mean sleep duration (with standard error bars) during the 7- day treatment phase of intensive Cognitive Therapy for PTSD (n = 32). *Pre = the mean sleep duration reported in the pre-treatment sleep diary given for comparison. Eve = sleep duration that night (Eve 1 would be evening 1 of Day 1 of intensive therapy).*

Table 2.3. Mean sleep duration (hours) and standard deviations before and after memory-updating during intensive Cognitive Therapy for PTSD; and before and after no updating (or intervention).

	Updating (n = 24)		**No Updating (n =24)**	
	Mean	SD	Mean	SD
Pre updating	5.14	1.96	5.52	1.95
Post updating	5.82	2.27	5.40	1.73
Change (in mins)	0.68*** (41.04)	1.36	-0.12 (-7.38)	2.23

*Note. *** = p <.001.*

Question 4: What is the effect of sleep duration on PTSD treatment outcome?

For patients receiving CT-PTSD, shorter sleep duration at baseline correlated with higher PTSD (PDS excluding sleep) symptom severity at baseline, r = -.48 p < .001; post-treatment (14 weeks), r = -.23, p = .007; and at 40-week follow-up, r = -.24, p =

.03. However, regression analyses showed that shorter sleep duration at baseline did not predict PTSD severity at 14 weeks, β = -.12, p = .30, and 40 weeks, β = -.07, p = .55, over and above what could be predicted from initial PDS scores. Similarly, poor sleep at the end of treatment correlated with PTSD severity (PDS excluding sleep) at 40-week follow-up, r = -.31, p = .003, but regression analysis showed that it did not predict PTSD symptoms over and above PTSD severity at the end of treatment, β = -.07, p = .32. This shows that sleep duration at baseline did not predict PTSD treatment outcome over and above what could be predicted by baseline PTSD symptom severity.

Question 5: Symptoms that may be associated with sleep improvement

The ANCOVAs showed significant differences at 14 weeks between conditions for: PDS nightmares, $F(2, 117) = 11.09$, $p < .001$, partial $\eta^2 = .159$; CAPS nightmares, $F(2, 117) = 10.22$, $p < .001$, partial $\eta^2 = .149$; PDS arousal symptoms (excluding sleep), $F(2, 117) = 31.79$, $p < .001$, partial $\eta^2 = .35$; CAPS arousal symptoms (excluding sleep), $F(2, 117) = 21.41$, $p < .001$, partial $\eta^2 = .27$; and anxiety about going to bed, $F(2, 117) = 5.17$, $p = .007$, partial $\eta^2 = .081$. Cognitive therapy led to larger improvements than the waitlist on each of these measures: baseline-adjusted mean difference for PDS nightmares = -0.75 (95% CI = -1.08 to -0.42), p <.001; CAPS nightmares = -2.07 (95% CI = -3.00 to -1.15), p <.001; PDS arousal symptoms (excluding sleep) = - 1.23 (95% CI = -1.53 to -0.92), p <.001; CAPS arousal symptoms (excluding sleep) = -9.91 (95% CI = -12.92 to -6.90), p <.001; anxiety about going to bed = -16.19 (95% CI = -28.85 to -3.53, p <.001. In contrast, supportive therapy was only superior to the waitlist on arousal, PDS arousal = -0.74 (95% CI = -1.09 to -0.39, p <.001; CAPS arousal = -5.96 (95% CI = -9.44 to -2.48), p <.001. Cognitive therapy was superior to supportive therapy on all measures: PDS

nightmares = -0.48 (95% CI = -0.81 to -0.15), p = .005; CAPS nightmares = -1.11 (95% CI = -2.02 to -0.178), p = .02; PDS arousal symptoms (excluding sleep) = -0.48 (95% CI = -0.79 to -0.18), p = .002; CAPS arousal symptoms (excluding sleep) = -3.95 (95% CI = -6.94 to -0.96), p = .010; anxiety about going to bed = -17.29 (95% CI = -30.03; -4.55), p =008.

For participants treated with cognitive therapy (N = 85), change in the frequency of nightmares correlated with changes in sleep duration, PDS nightmares r = .32, p = .003; CAPS nightmares, r = .26, p = .018, as did change in hyperarousal symptoms (excluding sleep), PDS r = .21, p = .056 (trend), CAPS r = .39, p < .001, and change in anxiety about going to bed, r = .35, p = .001. This shows that sleep duration improvements are associated with improvements in nightmares, clinician-assessed hyperarousal and anxiety about going to bed.

Discussion

The present study investigated changes in self-reported sleep with psychological treatments for PTSD. Specifically, it was investigated 1) whether psychological therapies for PTSD lead to an improvement in sleep; 2) whether the improvement in sleep depends on the extent to which the therapy focuses on re-processing the trauma memory; 3) whether improvements in sleep are related to memory-updating interventions in CT-PTSD; 4) what is the effect of sleep duration on PTSD treatment outcome; and explored 5) whether hyperarousal, nightmares and anxiety about going to bed are associated with sleep duration improvements.

The results showed that CT-PTSD, but not supportive therapy, led to greater improvement in self-reported sleep duration in comparison to a waitlist control group

(Question 1). CT-PTSD and supportive therapy also led to greater improvements in self-reported sleep quality and self-reported insomnia symptoms (PDS) than the waitlist, and CT-PTSD led to greater improvements than supportive therapy on both self-reported sleep quality, and self-reported but not clinician assessed (CAPS) insomnia symptoms. This suggests that trauma-focused therapy is more effective than non-trauma-focused therapy for improving self-reported insomnia symptoms in PTSD. Sleep duration increased by nearly one hour on average with CT-PTSD, which focuses on re-processing threatening meanings of the trauma and updating trauma memories with the revised meanings. Sleep duration changed to a significantly lesser extent (around 20 minutes) with supportive therapy, which focuses on current feelings and problems (Question 2). More people had residual insomnia on the CAPS after supportive therapy, than after CT-PTSD. The pattern of results suggests that the sleep changes with CT-PTSD were specific effects of the intervention, rather than effects of the passage of time or non-specific effects of therapy. This conclusion is further supported by the finding that for patients receiving intensive CT, the improvement in sleep duration had already occurred by the 3-week assessment, and that sleep diaries showed a significant increase in sleep duration during the week of intensive treatment (Question 3). These findings suggest that sleep improves with trauma-focused CT, where trauma memories are re-processed and updated. This is consistent with a recent paper showing that sleep duration improved by an average of one hour with weekly CT-PTSD in a large sample of PTSD patients in a routine clinical service (Lommen et al., 2015), and with a recent study showing an improvement in sleep duration after trauma-focused therapies; cognitive processing therapy and prolonged exposure therapy (Galovksi et al., 2009; Gutner et al., 2013). The reported gain of one hour of sleep in CT-PTSD is similar to that observed in successful insomnia treatment with insomnia patients (see Mitchell et al., 2012), and to specific treatment of insomnia in

people with PTSD (Margolies et al., 2013; Talbot et al., 2014), which is encouraging. Sleep quality and insomnia improvements with trauma-focused treatment in the present study are consistent with previous studies showing that CBT for PTSD improves insomnia symptoms in PTSD patients (e.g., Gutner et al., 2013). However, by post-treatment (14 weeks), patients' reported sleep duration was only six hours on average, which is lower than the recommended 7-9 hours for adults (see Hirshkowitz et al., 2015). Furthermore, 43.3% of patients were assessed as continuing to experience clinically significant insomnia symptoms (CAPS). This is consistent with the findings of previous studies that insomnia is commonly residual after CBT for PTSD (Belleville et al., 2011; Zayfert & DeViva, 2004). The pattern of results was the same for sleep and PTSD symptoms (excluding sleep). This suggests that the treatment interventions were having the same effect on both symptom domains, rather than a different effect on sleep and PTSD symptoms (although the effect on PTSD symptoms was not controlled for in the analyses). This is consistent with a previous study showing that sleep and PTSD symptoms change together, in parallel during PTSD treatment (Lommen et al., 2015), and with the results in the present study that baseline sleep was not associated with end of treatment PTSD symptoms, over and above baseline PTSD symptoms. Overall these findings suggest that self-reported sleep duration, quality and insomnia symptoms (difficulties falling and staying asleep) are improved with trauma-focused CT for PTSD, but that insomnia remains residual for nearly half of patients after therapy.

The design of the present study allowed for a closer examination of a core procedure (memory-updating) in CT-PTSD that may be important for facilitating sleep duration improvements with PTSD therapy. Patients in the intensive CT group reported around a 40-minute increase in sleep duration after memory-updating in therapy, whereas

there was no change in sleep duration after an equivalent recording period before therapy, where no intervention was done. This suggests that memory-updating may facilitate the sleep duration improvements seen with CT-PTSD. This finding is in line with a previous study that found an increase in objective sleep duration the night after processing trauma memories with written narrative exposure (Kobayashi et al., 2016). However, in order to conclude that the memory updating intervention in CT-PTSD facilitated sleep improvements, memory updating would need to be compared to an alternative active intervention in CT-PTSD, carried out at the same point in therapy, but that did not include memory-updating. Future studies could investigate this.

The present study also explored symptoms that may be associated with sleep improvements with CT-PTSD, by examining whether arousal, nightmares and pre-bed anxiety were affected by treatment, and whether changes were associated with sleep duration improvements (Question 5). The direction of effects between sleep improvement and improvements in nightmares, arousal and pre-bed anxiety were not determined in this study. However, the results, particularly differences in the effects of trauma and non-trauma-focused psychotherapy, generate some interesting hypotheses about how CT-PTSD may improve sleep duration, based on previously proposed mechanisms of therapeutic change with CT-PTSD (Ehlers et al., 2005).

There are several proposed mechanisms of PTSD symptom change with CT-PTSD (Ehlers et al., 2005). The first is a change in the trauma memory, through elaborating and updating the trauma memory with new meanings. In the current study, this could have affected sleep duration through reducing both daytime and night-time intrusive memories and nightmares, and reducing hypervigilance and hyperarousal, and an overall sense of current threat. The results of the present study were consistent with this interpretation, as only CT-PTSD led to a greater reduction

in nightmares than the waitlist, and nightmare and hyperarousal reduction with CT-PTSD were associated with improvements in sleep duration. For hyperarousal symptoms, supportive therapy also led to greater changes than the waitlist, possibly suggesting that a reduction in hyperarousal may be a less specific pathway to sleep duration improvements in patients with PTSD, than a reduction in nightmares. This would need to be explored in further research.

The second possible pathway of sleep change with CT-PTSD is change in cognitive appraisals and related behaviours (Ehlers et al., 2005). In CT-PTSD, modifying appraisals of the need for vigilance, the safety of the bedroom and of the individual when they sleep, could theoretically lead to sleep duration improvements as a result of reduced pre-sleep hypervigilance, hyperarousal, and avoidance of the bed and sleep. The results of the present study are consistent with this suggestion, as a reduction in anxiety about going to bed was only found with CT-PTSD, and not with supportive therapy, and was associated with sleep duration increases. This may suggest that CT-PTSD leads to reductions in pre-bed anxiety, which is associated with sleep duration increases, although the direction of effects between anxiety and sleep was not determined, and it is plausible that sleep duration improvements may lead to reduced anxiety about going to bed.

The present findings of an improvement in sleep duration with trauma-focused CT lends support to both as possible pathways of change in sleep duration, as in CT-PTSD both the memory is updated and appraisals are modified. More research is required to look at how reductions in re-experiencing, hyperarousal, and appraisal modification may relate to sleep improvements with CT-PTSD, and to determine the direction of effects.

The study found that sleep duration was not an independent predictor of PTSD treatment response over and above PTSD symptom severity (Question 4), suggesting that reduced sleep duration may not interfere with PTSD treatment outcome. This is consistent with Lommen and colleagues' (2015) recent study, which found that poor sleep did not interfere with the overall efficacy of CT-PTSD. Concerns for the effects of sleep disturbances in PTSD treatment comes in part from experimental studies with healthy controls, where variables of interest were often measured after full sleep deprivation rather than sleep disturbance or reduction. The results of the current study raise the possibility that reduced sleep duration may have a less severe impact than total sleep deprivation on factors important in cognitive therapy, such as emotional and cognitive processing. This finding is encouraging as it suggests that PTSD therapy can still be effective in the presence of reduced sleep duration, but does not preclude the possibility that sleep-focused treatment, before PTSD therapy could further enhance treatment gains. A recent study found that sleep-directed hypnosis before PTSD therapy did not augment PTSD treatment gains (Galovski et al., 2016), however the effects of sleep treatments such as CBT for insomnia, have not yet been investigated, and may yield different results.

Limitations and future directions

The present study has a number of limitations. First, the sleep measure available regularly for all groups, at every time point, was self-reported average sleep duration for the previous week, rather than a validated self-report measure of sleep disturbances, or a measure assessing the broad range of sleep disturbances found in PTSD. However, sleep duration provided a useful indicator of sleep change across CT-PTSD, and improvements were also evidenced in sleep quality ratings and self-reported and clinician assessed insomnia symptoms and nightmares, suggesting that

CT-PTSD also had beneficial effects on a broader range of sleep outcomes. Furthermore, objective measures of sleep duration were also not available. Some studies have shown that PTSD patient reports of sleep duration are often consistent with actigraphy (Kobayashi, Huntley, Lavela, & Mellman, 2012; Woodward, Bliwise, Friedman, & Gusman, 1996a), however it remains unknown whether CT-PTSD also has a beneficial effect on objectively measured sleep. Second, it is conceivable that the use of sleep diaries may have had a therapeutic effect on sleep symptoms in the intensive CT group, as self-monitoring sleep before treatment can have a beneficial effect on sleep (Talbot et al., 2014). However, this appears unlikely in the present study, as the standard CT group showed similar gains in sleep duration as the intensive CT group. Thirdly, as previously noted, memory updating was compared to no intervention rather than an alternative active intervention in CT-PTSD, which limits the conclusions that can be drawn from this finding. Finally, there were some limitations with the statistical analyses used. First, ANCOVA was used as the primary analytic strategy as there was very little missing data. However, an approach such as hierarchical linear modelling may have been more appropriate in a longitudinal design such as this, to avoid the limitations of ANCOVA in dealing with missing data. Second, change scores were correlated to investigate whether change in sleep was correlated with change in associated symptoms. However, change scores are limited in not controlling for baseline symptom severity, which would be important to address in future studies. Further research should address these limitations, and investigate whether change in sleep with CT-PTSD is also reflected in objective data. Detailed sleep diaries meeting the recommendations for standardised prospective sleep self-monitoring (Carney et al., 2012) are also required, to assess variables such as sleep onset latency and wake time after sleep onset. Future studies could also examine more closely the mechanisms of improvements in sleep

duration in trauma-focused CBT, and examine the specific effects of memory updating interventions in CT-PTSD by comparing memory updating to a different active intervention in CT-PTSD.

Overall, this study shows that sleep disturbances improved with trauma-focused therapy for PTSD, and sleep duration improved faster when PTSD treatment was delivered intensively over seven days. The results suggest that updating the trauma memory, a key procedure of CT-PTSD, was associated with sleep duration increase, although specific effects of memory updating were not determined. CT-PTSD may affect sleep duration through associated reductions in hyperarousal symptoms, nightmares, and pre-bed anxiety. Sleep duration did not predict PTSD treatment outcome, suggesting that CT-PTSD can be effective in the presence of reduced sleep duration. For many patients sleep difficulties were residual after PTSD treatment, raising the possibility that sleep treatment preceding or following PTSD treatment could enhance sleep gains and perhaps also treatment gains.

Chapter 3: Temporal Changes Between Sleep Disturbances and Posttraumatic Symptoms across Cognitive Therapy for PTSD: Results from an NHS Outpatient Sample.

Introduction

As reviewed in Chapter 1, sleep problems such as reduced self-reported (Calhoun et al., 2007; Hurwitz et al., 1998; Lewis et al., 2009; Straus et al., 2015) and objective sleep duration (Germain, 2006; Straus et al., 2015), and poor sleep quality (Calhoun et al., 2007; Lamarche & Koninck, 2007; Leskin et al., 2002) are common in posttraumatic stress disorder (PTSD), and persist after PTSD treatments (Belleville et al., 2011; Galovski et al., 2009; 2016; Gutner et al., 2013; Lommen et al., 2015; Nishith et al., 2003; Zayfert & DeViva, 2004). Chapter 2 further showed that sleep improved by up to one hour with CT-PTSD, and improvements were associated with improvements in nightmares and arousal symptoms. However, associations do not inform on the direction of effects, and so it remained unclear exactly why sleep duration improved. A recent study by Lommen and colleagues (2015) showed that self-reported sleep (duration and quality) and PTSD symptoms changed simultaneously over ten sessions of CT-PTSD, each predicting subsequent change in the other. Further, it was found that initial sleep quality predicted change in PTSD symptoms over treatment, only in those who were depressed (moderated by depression). The present study aimed to replicate the findings of Lommen and colleagues (2015), and to further build on them by investigating potential mechanisms by which PTSD therapy leads to therapeutic change in sleep. This was done by examining two theoretically plausible mediators of change between sleep and PTSD symptoms; 1) change in appraisals, and 2) change in the flashback-quality of intrusions.

Cognitive Therapy for PTSD

As described in Chapter 1, the cognitive model of PTSD (Ehlers & Clark, 2000) proposes that unhelpful appraisals (e.g., 'I have to be on guard all the time' or 'The world is a dangerous place') induce a sense of current threat that maintains PTSD symptomatology such as hyperarousal and hypervigilance, maladaptive coping strategies, and re-experiencing symptoms (Ehlers & Clark, 2000; Ehlers et al., 2005). A second source of the current threat is thought to be the disjointed nature of trauma memories that leads to easy triggering of intrusive memories with a flashback-quality, i.e., the experience that the memories are happening in the present rather than the past (Ehlers & Clark, 2000). Trauma-focused CT for PTSD (CT-PTSD; Ehlers et al., 2005) therefore aims to elaborate the trauma memory and update the negative trauma appraisals in order to change the meaning of the trauma and reduce PTSD symptoms (see Chapters 1 & 2).

Change in appraisals

Modifying negative appraisals (cognitions), such as those about the need for vigilance ('I have to be on guard all the time') is one proposed mechanism for therapeutic change in CT-PTSD (Dunmore et al., 2001; Ehlers et al., 2005; Ehlers & Clark, 2000; Kleim, Grey, et al., 2013a). A recent study investigating treatment mechanisms in CT-PTSD, found that session-to-session changes in posttraumatic cognitions preceded and predicted subsequent change in PTSD symptomatology, but change in PTSD symptoms did not predict change in posttraumatic cognitions (Kleim, Grey, et al., 2013a). This gave initial support for the assumption that appraisal modification may be a mechanism of therapeutic change in CT-PTSD. To better understand the effects of CT-PTSD on sleep disturbances, it may be important to investigate whether the modification of

negative trauma appraisals may be a mechanism of change in sleep during CT-PTSD. Fear of sleep has been associated with insomnia severity in trauma survivors (Pruiksma et al., 2016). Linking this to the cognitive model of PTSD (Ehlers & Clark, 2000), dysfunctional appraisals such as 'Nowhere is safe' or 'I have to be on guard at all times', which are common in PTSD, could result in fear of sleep. Therefore changes in trauma appraisals could lead to sleep improvements with PTSD therapy. The present study investigated the role of appraisal change in sleep improvement in CT-PTSD.

Change in flashback-quality

The flashback-quality of intrusive re-experiencing (resulting from the disjointed nature of the trauma memory) is a second proposed source of the current threat maintaining PTSD symptomatology, in the cognitive model of PTSD (Ehlers & Clark, 2000). Re-experiencing symptoms are thought to be reduced in CT-PTSD by elaborating and updating the trauma memory in treatment as well as discrimination of intrusion triggers (see Ehlers et al., 2005). Re-experiencing in PTSD can take the form nightmares (APA, 2013). The flashback-quality of intrusions may affect sleep by directly disrupting sleep through nightmares (Woodward et al., 2000) and indirectly through fear of nightmares (Davis et al., 2007; 2011; Davis & Wright, 2007; Krakow et al., 1995). Therefore, in the present study, changing flashback-quality of intrusive re-experiencing with treatment was also investigated as a potential mechanism of sleep improvement with CT-PTSD.

Aims and Research Questions

The aim of this study was to build on the findings of Chapter 2**,** by investigating session-to-session changes in PTSD symptoms and self-reported sleep during CT-PTSD, and examining two possible mechanisms of sleep change with PTSD treatment (change in appraisals and flashback quality). This study aims to add to the findings of

Chapter 2 by examining treatment effects in a routine clinic rather than a randomised controlled trial sample. This will support examination of the generalizability of the effects of CT-PTSD on sleep.

Specifically, as a first step, this study aimed to replicate the research questions and analysis of Lommen and colleagues (2015). The replicated research questions are shown in Table 3.1, along with the results from Lommen et al. (2015). Lommen and colleagues additionally examined whether medication use moderated the effects of sleep problems on PTSD symptom change, however no moderating effect of medication was found, and so medication use was not examined in this study.

Table 3.1 Research questions and results from Lommen et al. (2015)'s study

	Research Question	**Result**
1	What is the relationship between changes in PTSD symptoms and sleep across treatment?	The slopes of change in PTSD symptoms and self-reported sleep over treatment were correlated, and PTSD symptoms and sleep changed in parallel over treatment, neither having temporal precedence
2	Do sleep problems at the beginning of treatment predict poorer response to treatment?	Sleep quality and sleep duration at the beginning of treatment did not predict the slope of PTSD symptoms (except in those who were depressed, see Question 4).
3	Do residual sleep problems at the end of treatment predict poorer long-term outcome over and above PTSD symptoms?	Residual sleep problems at the end of treatment did not predict PTSD at long-term follow-up over and above what could be predicted from PTSD symptoms.
4	Does depression moderate the effects of sleep problems on PTSD symptom change?	Depression moderated the effect of sleep quality on PTSD symptom change. In those with depression, sleep quality predicted slower improvement in PTSD symptoms (slope). It did not moderate the relationship between baseline sleep duration and PTSD symptom change.

As a second step, the study aimed to further investigate possible therapeutic mechanisms of sleep changes. Using latent growth curve modelling to examine the temporal precedence of symptom changes across PTSD treatment (as in Kleim et al., 2013, and Lommen et al., 2015), the following research questions were investigated:

5) Does change in appraisals predict subsequent change in sleep duration/quality, and does it account for the relationship between PTSD symptoms and sleep?
6) Does change in the flashback-quality of intrusions predict subsequent change in sleep duration/quality, and does it account for the relationship between PTSD symptoms and sleep?

It was expected that if sleep improvement results from modification of appraisals, then change in trauma appraisals would show a temporal precedence, and would precede and predict subsequent change in sleep, but not vice versa. Alternately, if change in appraisals depends upon sleep improvement, due to the importance of sleep in memory, learning and emotional memory consolidation, then it would be expected that appraisal change would be preceded and predicted by improvements in sleep. Similarly, if improvements in flashback-quality of intrusions precede sleep improvements, then it would be expected that they would predict subsequent change in sleep, not vice versa.

Methods

Participants

Participants were identified from a sample of 343 PTSD patients aged 18–67 (M = 37.98, SD = 11.26) who attended an NHS outpatient clinic in South London between May 2008 and September 2013 (Ehlers et al., in preparation). To be eligible for inclusion, patients were required to have completed at least 3 (of a possible 10) weekly questionnaire measures for both sleep and PTSD symptoms, to ensure sufficient data points for the analysis. A total of 244 PTSD patients met this criterion and were therefore included in the analysis. The large sample size was important for the latent growth curve approach, where large samples of at least 100 are typically recommended, and larger samples of over 200 preferable (see Curran, Obeidat & Losardo, 2010).

Demographic details for this sample can be found in Table 3.2. All patients had a primary diagnosis of PTSD, as assessed by the Clinician-administered PTSD Scale (CAPS) for DSM-IV (Blake et al., 1995), and the Structured Clinical Interview for DSM-IV (SCID) (First et al., 1996). 45% had a comorbid major depression diagnosis. The majority of patients also reported difficulties falling or staying asleep (86.5%), and nightmares (69.4%), as assessed by the SCID at baseline assessment.

Table 3.2. Demographic information for the patient sample included in analysis (N = 244)

	N	%
Gender		
Male	111	45.50
Female	133	54.50
Marital status		
Married/cohabiting/long-term	95	40.50
Divorced/separated/widowed	30	13.20
Never married	109	46.40
Educational degree		
None	17	8.50
GCSE (or equivalent professional)	77	38.60
A-level	31	15.60
University level	74	37.20
Ethnicity		
Caucasian	156	63.90
Ethnic minority	88	36.00
Trauma type (sought treatment for)		
Witnessing another person hurt/die	25	10.40
Traumatic loss	3	1.20
Sexual assault/ rape	36	14.90
Childhood trauma	1	0.40
Interpersonal	99	41.00
Accidents (incl. RTA)	47	19.5
Terrorist attack	4	1.60
Military	1	0.40
Other	28	11.5
Comorbid Axis 1 disorder		
Comorbid anxiety disorder	157	64.30
Comorbid major depression	110	45.00
Taking psychotropic medication	102	43.40
Sleep (SCID)		
Difficulties falling/staying asleep	109	86.50
Nightmares	86	69.40

N = number of people; % = valid percent.

Treatment

Patients received trauma-focused Cognitive Therapy for PTSD (CT-PTSD, (Ehlers et al., 2005). Full details of the treatment can be found here:

(http://oxcadat.psy.ox.ac.uk/downloads/CTPTSD%20Treatment%20Procedures.pdf/view). The treatment was developed from Ehlers and Clark's model of PTSD (Ehlers & Clark, 2000). As described in Chapter 2, the treatment aims to reduce an individual's sense of current threat, by changing the nature of the trauma memory, modifying problematic negative appraisals of the trauma and its consequences, and reducing behaviours and cognitive strategies that maintain the appraisals and memory features. Patients attended an average of 11 weekly sessions (M = 10.58, SD = 4.53).

Measures

At initial assessment, patients were assessed using the CAPS (Blake et al., 1995) and SCID (First et al., 1996) for DSM-IV. Symptom self-reports were collected at initial assessment and before each treatment session, and at six months and one year post-treatment. Therefore, every patient included in the analysis had an end of treatment score, which was the last available score during treatment. The last available follow-up score was used for the analysis of long-term outcome (long-term follow-up).

The following measures were used to assess symptoms:

PTSD Symptoms (Excluding Sleep)

Self-reported PTSD symptoms were assessed using the 17-item Posttraumatic Diagnostic Scale for DSM-IV (PDS; Foa et al., 1997). The PDS assesses all PTSD symptom clusters specified in the DSM-IV, and asks patients to rate the frequency of their PTSD symptoms over the previous week, on a scale of 0 (*never*), to 3 (*5 times a week/almost always*), with higher scores indicating more severe PTSD symptoms (range: 0–51). The scale has good psychometric properties (Cronbach's alpha = .92) (Foa et al., 1997). For the purpose of this analysis, the item assessing sleep difficulties

(*having trouble falling or staying asleep*) was not included in the PDS sum score, therefore a PDS without sleep sum score was calculated from 16 items (range: 0–48), and will be referred to as **PDSwos**.

Sleep Symptoms

Self-reported Sleep Duration and Quality

Self-reported sleep duration and quality were assessed weekly during treatment. As in Lommen et al., (2015), sleep duration was assessed by asking patients to report on average '*in the past week how much sleep you had per night'.* Sleep quality was assessed by asking patients to rate the quality of their sleep over the previous week on a scale of 0 (*not at all well*) to 100 (*very well*).

Patient Health Questionnaire (PHQ-9) Item 3: Difficulties Sleeping

The PHQ-9 (Kroenke, Spitzer, & Williams, 2001) consists of 9 items assessing the DSM-IV diagnostic criteria for depression. Respondents rate how often in the last 2 weeks they have been bothered by each symptom (e.g., '*Feeling down, depressed or hopeless'*) from 0 (*Not at all*), 1 (*Several days*), 2 (*More than half the days*), to 3 *(Nearly every day*). The scale has good psychometric properties (Cronbach's alpha = .89) and is routinely used in primary care settings (Kroenke et al., 2001). Question 3 on the PHQ-9 '*Trouble falling or staying asleep, or sleeping too much'* was used as a measure of clinically significant sleep problems at initial assessment, end of treatment and long-term follow-up. The sleep item has been shown to correlate significantly with self-reported insomnia symptoms in primary care, $r = .75$, $p < .001$ (Insomnia Severity Index; MacGregor, Funderburk, Pigeon, & Maisto, (2011), and a cut-off of 1 has been shown to indicate significant sleep disturbance with good sensitivity (82.5%) and specificity (84.5%) (MacGregor et al., 2011).

Moderator

Major Depression Diagnosis

Current diagnosis of comorbid major depression was assessed at initial assessment using the SCID for DSM-IV, referring to the previous month (First et al., 1996).

Mediators

Mediators were measured weekly during treatment.

Posttraumatic Cognitions

The 20-item short version of the Posttraumatic Cognitions Inventory (PTCI; Foa, Ehlers, Clark, Tolin, & Orsillo, 1999), was used to assess excessively negative appraisals of the trauma and its consequences, including negative cognitions about the self, the world and self-blame. The PTCI asked patients to rate on a Likert scale how much they agreed with each statement (e.g., '*People are not what they seem*') from 1 (*totally disagree*) to 7 (*totally agree*). Responses across the items were summed to produce a total PTCI sum score, which was used in the analyses. Possible scores range from 1–140, with higher scores indicating more maladaptive appraisals. The measure has been found to have good internal consistency (Cronbach's alpha = .97) and psychometric properties (Foa, et al.,1999).

Flashback-quality

The flashback-quality (FQ) of unwanted trauma memories was also assessed. The questionnaire was a modified version of the scales used by Halligan, Michael, Clark, and Ehlers (2003), and Michael, Ehlers, Halligan, and Clark (2005). Patients were asked to rate the extent to which their intrusions felt: (1) distressing, (2) as if they

were happening now, (3) sense of reliving the moment, (4) disconnected from what happened before and after, and (5) were easily triggered by many different stimuli, each on a scale from 0 (*not at all*) to 100 (*very strongly*). The sum score of these items was used for the analysis (range: 0–500). Higher scores indicated more severe flashback-quality of intrusions (see Appendix A for the scale). The scale had good internal consistency in this sample (Cronbach's alpha = 0.84, N = 243).

Data Analysis

As in Lommen et al. (2015) parallel process latent growth curve modelling (LGM) using Mplus version 7 was used to model the week to week changes in sleep (duration and quality) and PTSD symptoms (PDSwos) over CT-PTSD, and to consider whether week-to-week changes in the proposed mediators (flashback-quality and posttraumatic cognitions) was related to change in sleep duration or quality.

As the average number of treatment sessions attended was 10.58 (SD = 4.53), data from sessions 1-10 only was analysed in the LGM analyses. Six patients were excluded from sleep duration analyses, as outlier analyses suggested that their sleep duration was more than 3 standard deviations above the mean (11 hours and more). The final sample sizes for each LGM analysis (with 3 data points minimum for each variable included) were; *n* = 229 for sleep duration and PDSwos, *n* = 237 for sleep quality and PDSwos. For sleep duration mediation analyses, sample sizes were; *n* = 221 for flashback-quality and *n* = 229 for PTCI. For sleep quality, mediation analysis sample sizes were *n* = 236 for flashback-quality, and *n* = 237 for PTCI. Missing sum scores on PDSwos and sleep variables were estimated using Full Information Maximum Likelihood (FIML).

As in Lommen et al., (2015), the parallel process analysis followed a bottom-up strategy. This involved fitting multiple models to the data (PDSwos and sleep duration/quality scores over treatment), and selecting the best fitting model, to use in testing the research hypotheses. First, it was investigated whether there was significant variance (individual differences) between participants in the intercepts (starting level) and slopes (change over treatment) of the sleep variable and PDSwos. This was done through testing the goodness of fit of different models to evaluate which best represented the change in PDSwos and sleep (duration or quality) over weeks 1-10 of treatment. Five steps were followed (see Table 3.4 and 3.5 for model results): 1) a null model was fitted (Model 1), which had fixed intercepts and modelled no change in PDSwos or sleep over treatment, no change over time and no individual variability in scores; 2) a random intercept model was fitted (Model 2), which allowed for variation in the intercepts (starting levels) between participants (Model 2b included correlations between the intercepts of PDSwos and sleep); 3) a random intercept, fixed slope model was fitted, which models different starting levels, but the same change over time for participants (Model 3); 4) a random intercept, random slope model was fitted (Model 4), which models variation between subjects in starting level and change over time (slope) of PDSwos and sleep (Model 4b added a within construct correlation between intercept and slope for PDSwos and sleep, respectively); 5) the addition of a quadratic term for sleep and PDSwos was investigated (Model 5), to examine whether this improved model fit (Model 5b tested the addition of a quadratic term for PDSwos only, and Model 5c tested the addition of a quadratic term for sleep only).

Second, once the model that best fitted the data was selected, this model was then used to test the research questions for sleep and PDSwos. Question 1 was evaluated by investigating whether the slopes of PDSwos and sleep were significantly correlated.

Question 2 was evaluated by investigating whether the intercept (starting level) of sleep significantly predicted the slope (change over treatment) of PDSwos. Question 3 (the effect of sleep at the end of treatment on PTSD symptoms at long-term follow-up) was evaluated using regression analyses to evaluate whether end of treatment sleep predicted unique variance in PTSD symptoms at long-term follow-up. Question 4, the moderating effect of depression, was investigated by examining the effect of a diagnosis of major depression on the prediction of the PDSwos slope by the sleep intercept. Formally this was conceptualised as moderation as it was tested whether the effect of the moderator (depression) affected the relationship between the predictor (sleep intercept) and the dependent variable (PDSwos), by testing the predictive effect of the interaction term (depression x sleep intercept) on the outcome (PDSwos slope). Finally, Questions 1, 5 and 6 were examined by using cross-lagged path analyses to test the temporal relationship between changes in sleep and PDSwos over weeks 1-10 of treatment (Question 1), and the mediation of this relationship by Posttraumatic Cognitions (Question 5), and Flashback-quality (Question 6). Cross-lagged path analyses involve testing whether change in a variable at time 1 (for example, treatment session 1), predicts subsequent change in another variable at time 2 (for example, treatment session 2). Cross-lagged path analyses were run first between sleep and PDSwos, to examine if change in sleep (duration/quality) at time 1 predicted subsequent change in PDSwos at time 2, and vice versa, and second between sleep, PDSwos and each mediator. The cross-lagged path analyses were run from session 1 to session 10.

Model fit was evaluated using indices; Chi square, comparative fit index (CFI) and root-mean-square error of approximation (RMSEA). Chi square difference was computed to compare the fit of different models, and evaluate if a model was significantly better than

another model. CFI values of >.90 and RMSEA values of < .08 were considered to indicate adequate model fit (Kline, 2010).

Results

Descriptive statistics: Pre to Post Treatment

Sleep, PTSD and depression symptoms, flashback-quality and posttraumatic cognitions at each treatment stage are reported in Table 3.3.

Table 3.3. Mean scores and standard deviations of PTSD symptoms, sleep, appraisals and flashback-quality symptoms (SD) at each treatment stage (intent-to-treat).

	Initial Assessment			End of treatment				Long-term follow-up		
	Mean	**SD**	**N**	**Mean**	**SD**	**N**	***d***	**Mean**	**SD**	**N**
PDS	34.23	9.67	244	14.90	14.02	244	1.61	14.96	13.82	141
PDSwos	31.85	9.34	244	13.77	13.13	244		13.74	12.89	141
Sleep quality	30.29	22.10	238	54.06	27.75	238	.94	51.28	27.50	81
Sleep duration	5.25	1.59	220	6.06	1.79	229	.48	6.35	1.50	77
Flashback-quality	228.78	95.29	229	85.88	108.08	244	1.40	68.58	96.6	85
PTCI	78.98	26.85	231	49.53	31.48	244	1.01	43.41	27.58	86
PHQ-9	16.57	6.90	244	8.00	8.00	244	1.14	8.40	8.11	140
PHQ-9: sleep item	2.39	0.84	244	1.25	1.14	244	1.14	1.26	1.14	139

Note. Paired t-test comparisons for initial assessment to last weekly session, and initial assessment to long-term follow-up were all significant at the p < .001 level. End of treatment is the final score available at the end of treatment. Long-term follow-up is the last available measurement at 6 months or 1 year (whichever was later). d = effect size according to Cohen (1992): 0.20 = small; 0.50 = medium; 0.80 = large.

PTSD Symptoms and Sleep Duration and Quality

Results from the intent-to-treat sample showed that PDSwos significantly decreased by a mean of 18.08 by the end of treatment, and improvement was sustained at long-term follow-up (LTFU). Sleep duration significantly increased by 48.6 minutes by the end of treatment, and showed additional improvement at LTFU. Sleep quality significantly increased by a mean of 23.77 by the end of treatment, which was maintained at LTFU (*p's < .001)* (see Table 3.3). This shows that sleep quality and duration were improved with CT-PTSD. Sleep quality and duration were significantly correlated at each time point (*r's = .49 - .67, p*'s < .001).

Responder Analysis

A responder analysis was also calculated. Patients with a sum score improvement of 50% or more on the PDS were classified as 'responders' (n = 159; 65.2%) and those with less than 50% improvement were classified as non-responders (n = 85; 34.8%). Results showed that in the sleep duration sample, responders (n = 152) had significantly higher end of treatment sleep duration (M = 6.65, SD = 1.57) in comparison to non-responders (n = 77; M = 4.90, SD = 1.54), $t(227) = 7.99$, $p < .001$. Similarly, in the sleep quality sample, responders (n = 157) had significantly higher end of treatment sleep quality ratings (M = 62.69, SD = 25.32) than non-responders (n = 80; M = 37.13, SD = 24.41), $t(235) = 7.44$, $p < .001$. Responders also scored significantly lower on the PHQ-9 sleep item at the end of treatment (M = 0.71, SD = 0.85) in comparison to non-responders (M = 2.24, SD = 0.95), $t(235) = -12.61$, $p < .001$. This shows that treatment responders reported better sleep than non-responders at the end of treatment.

PHQ-9: Sleep Item

On item 3 of the PHQ-9 at initial assessment, out of 244 patients, 234 (95.8%) reported sleep problems 'several days' or more in the previous 2 weeks (score > 0), and 206 (84.7%) reported sleep difficulties 'half the days' or 'nearly every day' (score > 1). The mean frequency of reported sleep problems reduced significantly from initial assessment to end treatment, $t(237) = 13.90$, $p < .0001$ (see Table 3.3). By the end of treatment, fewer (159; 65.2%) patients reported sleep difficulties at least 'several days ' in 2 weeks (score > 0), and 94 (38.52%) reported sleep problems 'more than half the days' up to 'every day' (score > 1). Improvement was sustained at LTFU. This shows that difficulties sleeping were improved with CT-PTSD.

Sleep quality and sleep duration were both significantly, negatively, correlated with the PHQ-9 sleep item at initial assessment (duration, r = -.41, p <.001; quality, r = -.43, p < .001) and end of treatment (duration, r = -.58, p <.001; quality, r = -.45, p < .001).

Follow-up Data

PTSD symptom data was also available at LTFU for 141 out of 244 patients (57.79%). Of these, 77 (67.54%) also had sleep duration data at LTFU, and 78 (68.42%) also had sleep quality data. Those with PTSD symptom follow-up data had less severe PTSD symptoms (PDSwos) at end of treatment (M = 11.73, SD = 11.67), compared to those without follow-up data (M = 16.57, SD = 14.49), t(242) = -2.885, p <0.01. Similarly, those with follow-up sleep duration data had higher end of treatment sleep duration (M = 6.45, SD = 1.54) than those without follow-up data (M = 5.86, SD = 1.84), t(227) = 2.41, p = .017. However, those with sleep quality data at LTFU did not significantly differ from those without, t(235) = 1.84, p = .07.

Posttraumatic Symptoms and Sleep Duration and Quality (Questions 1 and 2)

Model selection

As described, different models were compared to find the model which best represented the data, as indicated by model fit indices. A number of models were fitted for sleep duration (see Table 3.4), showing that the best-fitting model included both random intercepts and slopes for PDSwos and sleep duration (Model 5b). This suggests that there was individual variance in both the starting level (intercept) and change (slope) in PDSwos and sleep duration over time. The inclusion of intercept correlations between PDSwos and sleep duration r = -.59, p < .001 (in Model 2b) significantly improved model fit, $\Delta \chi 2$ = 60.13, Δdf = 1, p < .001, suggesting that severity of PTSD symptoms

and sleep duration at baseline were related. This between-construct (sleep duration and PDSwos) intercept correlation was retained in future models (3 – 5c). The addition of the within construct intercept–slope correlation (in Model 4b) was significant for PDSwos $r = -.20, p < .01,$ but not for sleep duration $r = -.27$, $p > .05$, suggesting that starting level of PTSD symptoms was related to the degree of PDSwos change over treatment, but that the starting level of sleep duration was not related to change in sleep over treatment. However, this addition did not significantly improve model fit, $\Delta \chi 2 = .06$, $\Delta df = 2$, $p > .05$, and so was not retained in future models (5-5c). The quadratic terms for PDSwos (Model 5b) $\mu = .04, p > .05,$ and sleep duration, $\mu = -.01, p > .05$ (Model 5c) were not significant, and the addition did not significantly improve model fit, suggesting that change in sleep duration and PTSD symptoms was best described by a linear increase trajectory. However, although the addition of a quadratic term for PDSwos only (Model 5b) did not significantly improve model fit in comparison to model 4, $\Delta \chi 2 = 2.98$, $\Delta df = 1$, $p > .05$, the model fit index AIC (Akaike information criterion) marginally improved (from 17377.89 (Model 4) to 17376.39 (Model 5b) and therefore the quadratic term for PDSwos only was retained. Model 5b, was therefore considered the model best fitting the data. The final model included a random intercept, random slope, between construct (PDSwos and sleep) intercept correlation, and a quadratic term for PDSwos and a linear trajectory for sleep change over treatment. Following the same model selection process (for full sleep quality results see Appendix B), a random intercept, random slope model best fit the data for sleep quality (Model 5), showing that there was individual variance in the intercepts and slopes of PDSwos and sleep quality (see Table 3.5). These models were used to test Questions 1 and 2 for both sleep duration and quality.

Research question 1: Sleep and PTSD symptoms and sleep across treatment

The slopes of sleep duration and PDSwos over treatment (Model 5b) were significantly correlated, r = -.51, p = .016, showing that an increase in sleep duration across treatment sessions corresponded to a decrease in PDSwos. The addition of the correlation significantly improved model fit from Model 5b, $\Delta \chi 2$ = 16.82, Δdf = 3, p < .001. Similarly, the slopes of PDSwos and sleep quality were significantly correlated, r = -.74, p < 0.001, and the addition of the correlation significantly improved the fit of Model 5, $\Delta \chi 2$ =61.95, Δdf = 2, p < 0.001. This shows that changes in PTSD symptoms and sleep duration and quality were related.

Research question 2: Sleep problems and response to treatment

To examine whether short sleep duration at the start of treatment predicted worse response to treatment, the relationship between the starting level (intercept) of sleep duration and the change in PDSwos (slope) was investigated. Results showed that the intercept of sleep duration significantly predicted the slope of PDSwos, β = -.26, p = .02. The model fit was good, $\chi 2$ = 424.33, df = 208, and the addition of this relationship significantly improved model fit from Model 5b, $\Delta \chi 2$ = 5.88, Δdf = 1, p = .01. The intercept of PDSwos did not significantly predict the slope of sleep duration, β = .08, p = .59 and did not significantly improve model fit from model 5b, $\Delta \chi 2$ = -.43, Δdf = 1, p >.05. The results showed that lower sleep duration at the start of treatment predicted worse (shallower slope) change in PTSD symptoms over treatment, however severity of PTSD symptoms did not influence the change in sleep duration over treatment. Similarly, for sleep quality, the intercept of sleep quality significantly predicted the slope of PDSwos, β = - .35, p = .003, and the addition significantly improved model fit from Model 5, $\Delta \chi 2$ =10.87, Δdf = 1, p < .01. The intercept of PDSwos did not predict the slope of sleep quality over treatment, β = -.06, p > .05, and did not improve model

fit from Model 5, $\Delta \chi 2 = .43$, $\Delta df = 1$, $p > .05$ (see Appendix B for full sleep quality results).

Table 3.4. Model results sleep duration and PTSD symptoms (PDSwos) (n = 229). Table includes χ^2 value and degrees of freedom (df) from model output, model fit indices (CFI and RMSEA), and model estimates of the intercept (μi), slope (μs) and variance for both (σi; σs) for sleep duration and PDSwos.

						PDSwos		Sleep duration		PDSwos		Sleep duration	
Model (MLR)		χ^2	*df*	**CFI**	**RMSEA**	**μi**	**σi**	**μi**	**σi**	**μs**	**σs**	**μs**	**σs**
1	Fixed intercept	1852.67	217.00	0.27	0.18	23.49	--------	5.72	--------	--------	--------	--------	
2	Random intercept	1281.91	215.00	0.53	0.15	23.25	76.18	5.72	1.92	--------	--------	--------	--------
2b	Random intercept (with intercept correlations)*	1221.78	214.00	0.55	0.14	23.26	76.50	5.72	1.93	--------	--------	--------	--------
3	Random intercept, fixed slope	699.04	212.00	0.78	0.10	29.98	91.86	5.39	1.95	-1.80	--------	0.08	--------
4	Random intercept, random slope	433.19	210.00	0.90	0.07	30.62	75.69	5.37	1.65	-2.15	2.20	0.09	0.02
4b	4 with within construct intercept - slope correlation**	432.58	208.00	0.90	0.07	30.62	83.01	5.36	1.95	-2.15	2.37	0.09	0.03
5	4 with quadratic term for sleep and PDS	430.45	208.00	0.90	0.07	30.94	75.95	5.30	1.65	-2.43	2.09	0.13	0.02
5b	Model 5b (Quadratic term only for PDS)***	430.21	209.00	0.90	0.07	30.94	75.95	5.37	1.65	-2.43	2.09	0.09	0.02
5c	Model 5c (Quadratic term only for sleep)	433.46	209.00	0.90	0.07	30.62	75.69	5.30	1.65	-2.15	2.20	0.13	0.02

* Including a correlation between the intercepts of PDSwos and sleep duration, $r = .594$, $p < .001$, significantly improved model fit, $\Delta \chi 2 = 60.13$, $\Delta df = 1$, $p < .001$, and was retained in Models 3 – 5c.

** The within construct correlations between intercept and slope was significant for PDSwos, $r = -.20$, $p < .01$, but not for sleep duration, $r = -.27$, $p > .05$, however it did not significantly improve model fit, $\Delta \chi 2 = .06$, $\Delta df = 2$, $p > .05$, and so was not retained in future models (5 – 5c).

***Not significantly different from Model 4, but the AIC value was lower, indicating better model fit, and so this model is used for hypothesis testing.

Table 3.5. Model results for **sleep quality** and PTSD symptoms (PDSwos) (n = 238). Table includes χ^2 value and degrees of freedom (df) from model output, model fit indices (CFI and RMSEA), and model estimates of the intercept (μi), slope (μs) and variance for both (σi; σs) for sleep quality and PDSwos.

						PDSwos		Sleep Quality		PDSwos		Sleep Quality	
Model (MLR)		χ^2	*df*	**CFI**	**RMSEA**	**μi**	**σi**	**μi**	**σi**	**μs**	**σs**	**μs**	**σs**
1	Fixed intercept	2318.19	217.00	0.26	0.20	29.92	--------	37.18	--------	--------	--------	--------	--------
2	Random intercept	1423.01	215.00	0.58	0.15	23.41	82.36	40.92	340.86	--------	--------	--------	--------
2b	Random intercept (with intercept correlations)*	1340.95	214.00	0.60	0.15	23.43	82.68	40.89	343.59	--------	--------	--------	--------
3	Random intercepts, fixed slope	726.85	212.00	0.82	0.10	30.07	96.42	33.71	351.09	-1.77	--------	1.09	--------
4	Random intercept, random slope	475.72	210.00	0.91	0.07	30.68	79.51	33.25	308.25	-2.10	2.11	20.74	4.28
4b	Model 4 with within construct intercept - slope correlation**	467.18	208.00	0.91	0.07	30.68	89.21	33.15	338.79	2.10	2.28	2.11	4.69
5	Model 5 (Add quadratic term for sleep and PDS)***	448.24	206.00	0.92	0.07	31.03	89.51	31.39	339.78	-2.41	2.16	3.87	4.55
5b	Model 5b (Quadratic term only for PDS)	463.10	207.00	0.91	0.07	31.03	89.71	33.15	339.85	-2.05	2.16	2.11	4.69
5c	Model 5c (Quadratic term only for sleep)	452.31	207.00	0.91	0.07	30.68	89.02	31.39	338.89	-2.10	2.28	3.87	4.55

*Including a correlation between the intercepts of PDSwos and sleep quality, r = -067, p <.001, contributed significantly to model fit, ΔχÇ = 82.06 , Δdf = 2, p <.001, and was retained in future models (3- 5c)

** Within construct intercept and slope correlations were significant for PDS, r = -.22, p < .001, but not sleep quality, r = *-0.17, p > .05*, but significantly contributed to the model fit, Δ $\chi 2$ = 8.54 Δdf = 2, p < .01, and so were retained in future models (4b - 5c)

*** Adding a quadratic term for both constructs was significant sleep quality (μ = -.22, p < .001) but not for PDS (μ = 0.04, p = .053), however the inclusion of both contributed significantly to the model fit, Δ $\chi 2$ = 18.94, Δdf = 2, p <.001. This model was used for hypothesis testing

Research Question 4: Depression as a moderator

Sleep duration and depression

Using the best fitting model for sleep duration and PDSwos (Model 5b), the role of comorbid depression was investigated by adding an interaction term for co-morbid depression to the model. The interaction term was not significant, and did not significantly predict the slope of PDSwos, β = -.02, p = .92. The intercept of sleep duration no longer predicted the slope of PDSwos, β = -.20, p = .12 and neither did depression, β = -.31, p = 0.77, suggesting that depression had no moderating effect on sleep duration.

Sleep quality and depression

An interaction term for depression was added to the best fitting model for sleep quality and PDSwos (Model 5). The results showed that the interaction was significant; the interaction term significantly predicted the slope of PDSwos, β = -.04, p < .01 but the intercept of sleep quality did not, β = -.01, p > .05, suggesting that sleep quality predicts slope of PDSwos only in those who are depressed. A multi-group model with the groups depression/ no depression, further explored and confirmed the interaction effect. The results showed that in those without depression, sleep did not predict the slope of PDSwos, β = -0.20, p > .05, but for those with depression the intercept of sleep still predicted the slope of PDSwos, β = -.51, p < .001. This supports the interaction term that sleep quality at baseline is only related to the slope of PDSwos in those who are depressed. These results support moderation of the relationship between the predictor (sleep quality intercept) and the outcome (PDSwos slope) by comorbid depression, as the combined effect (interaction term) of the predictor (sleep intercept), and moderator (comorbid depression), predicted the outcome variable (PDSwos slope). Further, the

association between the sleep intercept and PDSwos slope was different in those with and without depression, and only significant in the comorbid major depression group. This confirms moderation as the relationship between the predictor (sleep) and outcome (PDSwos) was changed as a result of the moderator variable (depression).

Crosslag Analyses (Research questions 1, 5 and 6)

To investigate the temporal relationship between changes over treatment in sleep variables, PTSD symptoms, posttraumatic cognitions and flashback-quality, three cross-lagged path analyses were run. Autoregressive paths, regression paths (on statements) and correlations were fixed to be equal in all models.

Research Question 1: Sleep and PTSD symptoms and sleep across treatment

To investigate the temporal relationship between changes in PDSwos and sleep duration over treatment, a cross-lagged path analysis was used including cross-lagged paths between PDSwos and sleep duration (with PDSwos predicting subsequent change in sleep and sleep predicting subsequent change in PDSwos) over sessions 1 to 10 of treatment. Cross-lagged paths were fixed as equal over time. The model had nearly adequate fit, $\chi 2$ = 557.93, df = 160, CFI = .89, RMSEA = .10, and cross-lagged paths were all significant. PDSwos predicted change in sleep duration, β = -.14, $p < .001$, and sleep duration predicted change in PDSwos, β = - .12, $p = .01$. Model fit decreased when the model included sleep predicting PDSwos only, $\Delta \chi 2$ =18.42, Δdf = 1, $p <$ .001, or when PDSwos predicted sleep only, $\Delta \chi 2$ = 6.11, Δdf = 1, p = .01. This suggests that sleep duration and PDSwos each simultaneously predicted change in the other, in a bidirectional manner across treatment. The same analysis procedure was followed for sleep quality and found the same pattern of results (see Appendix B for the

full sleep quality results). Change in PDSwos was highly significant predictor sleep quality, β = -.31, $p < .001$, and change in sleep quality was a significant predictor of PDSwos, β = -.19, $p < .01$. This shows that sleep and PTSD symptoms changed in parallel over treatment.

Research Question 5: Sleep, PTSD Symptoms and Posttraumatic Cognitions

To examine whether change in cognitions (PTCI) mediated the bi-directional relationship between sleep duration and PDSwos, cross-lagged paths between PTCI, PDSwos and sleep duration were examined. Model fit was adequate, $\chi 2$ =1613.58, df = 423, RMSEA = 0.11, CFI = 0.81, and PTCI significantly predicted subsequent change in sleep duration across treatment, β = -.01, $p < .01$, but change in sleep duration did not predict subsequent change in PTCI, β = -.14, $p > .05$. When the PTCI was included in the model, PDSwos no longer predicted change in sleep duration, β = -.01, $p > .05$, and sleep duration no longer predicted change in PDSwos across treatment, β = -.09, $p > .05$. This suggests that change in cognitions predicted change in sleep duration, and that PDSwos was not an independent predictor of change sleep duration over and above change PTCI. However, change in PTCI did not significantly predict change in sleep quality, β = -.04, $p > .05$, and change in sleep quality did not predict PTCI, β = -.02, $p > .05$. PDSwos and sleep quality continued to predict subsequent change in each other across treatment. This shows that appraisal change did not predict change in sleep quality.

Research Question 6: Sleep, PTSD symptoms and Flashback-quality of Intrusions

To examine whether change in flashback-quality (FQ) mediated the bidirectional relationship between sleep duration and PDSwos, cross-lagged paths between flashback-quality, PDSwos and sleep duration were examined. Model fit was adequate,

χ^2 = 1360.79, df = 423, RMSEA = .10, CFI = .84, and change in FQ predicted subsequent change in sleep duration, β = -.01, p = .047. Sleep duration did not predict subsequent change in FQ, β = -.79, p = .12. When FQ was included in the model, PDSwos no longer predicted sleep duration, β = -.01, p = .054, and sleep no longer predicted PDSwos, β = -.08, p = .09. This suggests that change in FQ predicted change in sleep, and that PDSwos was not an independent predictor of change in sleep duration, over and above changes in flashback-quality. However, change in flashback-quality did not predict change in sleep quality, β = -.01, p > .05, and change in sleep quality did not predict flashback-quality, β = -.10, p > .05. PDSwos and sleep quality continued to predict subsequent change in each other across treatment.

Sleep and long-term PTSD treatment outcome (Research Question 3)

For the patients who provided PDSwos data at LTFU (n = 141), the average PDSwos score at the end of treatment was 11.72, (SD = 11.67), and 13.74, (SD = 12.89) at LTFU. This shows that PTSD symptom severity at end of treatment and LTFU remained below the clinical cut-off for clinically significant PTSD symptoms on the PDS (cut-off = 18; Ehring et al., 2007), and therefore indicates relatively stable treatment effects. Treatment effects on sleep quality (n = 81) and duration (n = 77) were also stable from the end of treatment (quality, M = 58.21, SD = 26.59; duration, M = 6.45, SD = 1.54) to LTFU (quality, M = 50.74, SD = 27.23; duration, M = 6.35, SD = 1.50).

Regression analyses (Table 3.6) showed that sleep duration at the end of treatment predicted PDSwos at LTFU, but was no longer a significant predictor when PDSwos at end of treatment was included, suggesting that sleep duration at end of treatment did not predict PDSwos at LTFU over and above PDSwos at the end treatment. Regression

analyses with sleep quality showed the same result (see Table 3.6 for regression results). This shows that end of treatment sleep duration and quality did not predict long-term PTSD treatment outcome over and above PTSD symptom severity at the end of treatment.

Table 3.6. Regression results for sleep duration and quality, and PDSwos at end of treatment, predicting PDSwos at long-term follow-up.

	Sleep Duration				**Sleep Quality**			
	b	SE	β	*p*	*b*	SE	β	*p*
Step 1								
Constant	37.71	4.17			25.98	2.36		
Sleep end	-3.89	.65	-.47	.000	-.22	.04	-.44	.000
Step 2								
Constant	8.08	3.57			3.64	2.35		
Sleep end	-.69	.49	-.08	.161	-.003	.03	-.01	.922
PDSwos end	.87	.07	.77	.000	.88	.07	.79	.000

***Note**: Sleep duration: for step 1 R^2= .22, for step 2, R^2= .66; Sleep quality: for step 1 R^2 = .19, for step 2, R^2 = .63. end = end of treatment.*

Discussion

The aim of this study was to investigate the effects of CT-PTSD on the session-to-session changes in sleep duration and quality and PTSD symptoms. It aimed to replicate the results of Lommen et al. (2015) in another patient sample, and expand upon their findings by examining whether change in appraisals and flashback-quality of intrusions mediated the relationship between sleep and PTSD symptoms, and could thus be considered mechanisms of therapeutic change in sleep.

Summary

The results showed that as self-reported sleep duration and quality increased, PTSD symptom severity (PDSwos scores) decreased across treatment. Sleep duration had improved by 48 minutes at the end of treatment, and by over one hour total at LTFU with CT-PTSD. More severe (lower) sleep duration at the start of treatment predicted slower change in PTSD symptoms over treatment. However, PTSD symptom severity at the start of treatment did not predict change in sleep duration. The results of growth

curve modelling and cross-lagged path analysis showed that PTSD symptoms and sleep duration changed simultaneously, in parallel over treatment, each predicting subsequent change in the other. Further analysis of this relationship showed that change in posttraumatic cognitions and change in flashback-quality each predicted change in sleep duration over and above PTSD symptom scores, and mediated the relationship between sleep and PDS scores during treatment, as this relationship ceased to be significant when appraisal change or flashback quality change was included. Change in appraisals or flashback quality were not predicted by change in sleep duration. Similar to the sleep duration results, more severe initial sleep quality predicted slower change in PTSD symptoms over treatment, but initial PTSD symptom severity did not predict subsequent change in sleep quality. When depression was included as a moderator, results showed a significant moderating effect of depression on sleep quality but not sleep duration, showing that lower sleep quality predicts slower change in PTSD symptoms, only in those who are depressed. In contrast to the sleep duration modelling results, changes in appraisals or flashback-quality did not predict change in sleep quality, nor did it account for any variance in the relationship between sleep quality and PDSwos scores. Sleep quality and duration improvements were also reflected in the respective PHQ-9 sleep item, which also showed a significant reduction in the frequency of self-reported sleep problems at post-treatment and LTFU. Finally, sleep duration and sleep quality at the end of treatment predicted PTSD symptoms at long-term follow-up, but not when end of treatment PTSD symptoms were controlled for.

Overall the results suggest that self-reported sleep was improved with CT-PTSD when sleep was not directly targeted in treatment, and that sleep severity at the end of treatment was not related to long-term PTSD treatment outcome over and above residual PTSD symptoms at the end of treatment. Further, the results of modelling

analyses suggest that change in trauma appraisals, and change in flashback-quality of intrusions may be mechanisms of therapeutic change for sleep duration, but not sleep quality. Finally, the results show that sleep improvements were maintained at long-term follow-up, up to one year post-treatment.

Replicated Findings

The results of the present study replicated the majority of the findings by Lommen et al., (2015), in an independent PTSD patient sample. This suggests stability of these findings, and adds to evidence for the effectiveness of CT-PTSD for improving both self-reported sleep duration and quality. To the authors knowledge, the present study and the study by Lommen et al. (2015) are the largest studies to date to investigate the effects of PTSD therapy on sleep outcomes (see Cox & Olatunji, 2016 for a recent review). The replication of these findings is particularly encouraging in light of concerns regarding the reproducibility of psychological research findings, following a recent report showing that only 39% of 100 published studies were successfully replicated in independent samples (Open Science Collaboration, 2015). The findings that replicated Lommen et al. (2015), were that 1) PTSD and sleep changed in parallel over treatment; 2) residual sleep problems did not predict long-term PTSD treatment outcome; and 3) sleep quality predicted PTSD symptom change in those who were depressed.

However, one finding was discrepant; shorter baseline sleep duration in the present study predicted slower change in PTSD symptoms over treatment, which was not found in the study by Lommen et al. (2015). One possible explanation for this discrepancy is that the average duration between the time of the trauma and the initial assessment was 1 ½ years longer in the present study (4.5 years), in comparison to Lommen et al.

(2015) (3.12 years). A more chronic PTSD population in the present study could have more ingrained sleep problems, which could be more likely to slow response to treatment. This finding is also slightly in contrast to the findings in Chapter 2, which showed that baseline sleep duration did not predict end of treatment PTSD symptom severity, when controlling for baseline PTSD symptom severity. However, Chapter 2 looked at overall treatment outcome, whereas the present study examined session-to-session symptom changes, which may differ despite similar overall outcomes in PTSD symptom severity. Although inconsistent with Lommen and colleagues (2015), and to some extent with Chapter 2, these findings are in line with a previous study which found that pre-treatment sleep problems predicted reduced remission from PTSD over 5 years (Marcks, Weisberg, Edelen, & Keller, 2010), and with a study showing that those with persistent sleep difficulties at post-treatment showed less improvement in PTSD symptoms over treatment (Belleville et al., 2011). Overall, these results suggest that reduced sleep duration at baseline may result in slower change in PTSD symptoms over PTSD therapy. Possible reasons for this could be the detrimental impact of sleep deprivation on processes important in PTSD therapy, such as learning and memory (Yoo et al., 2007), fear extinction learning (Kleim, et al., 2013b; Pace-Schott et al., 2012; Pace-Schott, Germain, & Milad, 2015a; Spoormaker et al., 2011), emotional processing and reactivity (Holland & Lewis, 2007; Silvestri, 2005; Wagner et al., 2006; Yoo et al., 2007), which could theoretically slow PTSD symptom improvement.

Depression

Consistent with the findings by Lommen and colleagues (2015), the results of the present study suggest that poor baseline sleep quality is associated with slower recovery from PTSD, only in those with comorbid depression. Lommen et al. (2015) posed a number of possible explanations for this finding, namely that sleep difficulties in those

with PTSD and depression may differ in comparison to those without depression (Woodward, Friedman, & Bliwise, 1996b), and that sleep difficulties associated with depression may interfere more with treatment efficacy. This is plausible, as reduced slow wave sleep, which is one of the few differences found between PTSD patients with and without depression (Woodward, Friedman, & Bliwise, 1996b), has been correlated with reduced sleep quality ratings in individuals with depression (Argyropoulos et al., 2003; Armitage, Trivedi, Hoffmann, & Rush, 1997) and SWS is important in learning and memory (see Walker, 2009), a process important for therapy. Lommen et al. (2015) further suggest that an additional diagnosis of comorbid depression may compound difficulties such as concentrating in therapy sessions, and may affect motivation to engage in therapy, which could result in slower response to treatment. There is some support for this from studies showing that depression may interfere with PTSD treatment gains (Duffy, Gillespie, & Clark, 2007; Tarrier, Sommerfield, Pilgrim, & Faragher, 2000).

Interestingly, depression did not moderate the influence of lower sleep duration on slower PTSD symptom response over therapy. This could suggest that comorbid depression influences sleep quality more than sleep duration. For example, there is evidence that sleep duration is both prolonged and shortened in individuals with major depression (Soehner, Kaplan, & Harvey, 2014; van Mill, Hoogendijk, Vogelzangs, van Dyck, & Penninx, 2010), but up to 90% of those with major depression report poor sleep quality (Riemann, Berger, & Voderholzer, 2001). Therefore, comorbid depression may have less effect on reports of average sleep duration over the previous week, in comparison to sleep quality ratings. Alternatively, it could suggest that the sleep quality ratings were more likely to be subject to a negative perception bias than sleep duration reports, and therefore could be more greatly influenced by depression. This is supported

by studies showing accurate total sleep time estimates in individuals with depression (Argyropoulos et al., 2003; Armitage et al., 1997).

Improvements in Duration and Quality

Sleep duration improved by 48 minutes at post-treatment and over 1 hour by LTFU with CT-PTSD. This is equivalent to sleep duration improvements found in Chapter 2, and to those reported by Lommen et al. (2015). It is also similar to sleep duration increases found when sleep in PTSD is directly targeted with CBT for insomnia (e.g., Talbot et al., 2014; see Ho et al., 2016 for review). The improvements in self-reported sleep quality, and in self-reported difficulties sleeping (PHQ-9) are also consistent with the findings in Chapter 2, and suggest that CT-PTSD improves the subjective experience of overall sleep quality, and reduces the frequency trouble sleeping (PHQ-9). The results showed that sleep improved with CT-PTSD in routine clinical care settings, and sleep gains were maintained to LTFU, conferring good generalizability of the findings from the clinical trial in Chapter 2. These findings are congruent with findings from previous treatment studies that have found significant improvements in self-reported sleep duration (Cooper & Clum, 1989), sleep quality (Belleville et al., 2011; Nishith et al., 2003; Raboni, 2006) or both (Galovski et al., 2009; Gutner et al., 2013; Lommen et al., 2015) with PTSD therapy. Previous studies have often only considered single trauma type populations, such as female sexual assault survivors (Galvoksi et al., 2009; 2016; Gutner et al., 2013; Nishith et al., 2003), kidnap victims (Raboni et al., 2006) or veterans (Cooper & Clum, 1989). Therefore this study adds to the small body of research demonstrating that sleep can be improved in a sample with a wide range of trauma types (Belleville et al., 2011; Lommen et al., 2015; Zayfert & DeViva, 2004), when sleep is not directly targeted in PTSD therapy. Further, few studies have assessed sleep at long-term follow-up, post-treatment (Galovski et al., 2009; Gutner et al., 2013;

Lommen et al., 2015). The results of this study therefore add to the small number of studies which have demonstrated maintenance of sleep improvements at 9 months (Galovski et al., 2009), 2 years (Lommen et al., 2015) and in one instance 5-10 years (Gutner et al., 2013) after PTSD therapy.

Residual Sleep Problems

However, as found in Chapter 2, despite significant improvements, sleep duration at the end of treatment was 6 hours on average. This is consistent with the end of treatment sleep duration reported by Lommen et al. (2015) (6.01 hours), and similar to the end of treatment sleep duration in Chapter 2 (6–6.3 hours), but lower than the recommended adult sleep duration of 7-9 hours (Hirshkowitz et al., 2015). Final sleep quality ratings, while significantly improved, were on average 54 out of 100 at the end of treatment, consistent with Lommen et al. (2015) (55 out of 100). Further, the present study used the PHQ-9 sleep item as an additional measure of sleep disturbance, which indicated that despite significant improvements, by the end of treatment 37.7% of patients were still reporting difficulties sleeping more than half the time in a two week period. This is similar to the finding in Chapter 2, that 43.3% of patients had residual sleep problems post-treatment. This suggests residual sleep difficulties post-treatment for some PTSD patients, consistent with the literature suggesting that between 48 and 70% of PTSD patients experience continuing sleep problems after PTSD treatment (Belleville et al., 2011; Gutner et al., 2013; Galovski et al., 2009; Zayfert & DeViva, 2004). However it should be noted that studies have differed in whether they included non-treatment responders in post-treatment analyses (e.g., Belleville et al., 2011), or only those whose PTSD had remitted (e.g., Nishith et al., 2003; Zayfert & DeViva 2004). Both have merits, however the present study included those (34.8%) who had not recovered from PTSD, which may have slightly increased the percentage of sleep problems post-

treatment. This was supported in the responder analysis, which showed that treatment responders had higher end of treatment sleep duration (6.69 hours), sleep quality and lower PHQ-9 sleep scores, in comparison to non-responders (nearly 5 hours sleep duration). As discussed in Chapter 2, studies have found that sleep duration can be additionally improved in a PTSD patient population when a sleep-focused treatment such as CBT for insomnia (CBT-I) is delivered alongside (Talbot at al., 2014), or after (DeViva, Zayfert, Pigeon, & Mellman, 2005) CBT for PTSD. Therefore sleep-focused therapies, such as CBT-I, may be beneficial both before PTSD therapy, to enhance treatment gains for those suffering from severe sleep problems, and after therapy for those experiencing persistent sleep difficulties.

Treatment Mechanisms: Appraisals and Flashback-quality of Intrusions

Lommen and colleagues (2015) found that PTSD and sleep symptoms (duration and quality) changed in parallel over the course of 10 sessions of PTSD therapy, which was replicated in the present study. It was further found that change in trauma appraisals fully mediated the parallel relationship between changes in sleep duration (not quality) and PTSD symptoms. Change in appraisals predicted subsequent change in sleep duration the following week, but sleep duration did not predict change in appraisals. This suggests that CT-PTSD may improve sleep duration, via change in post-traumatic appraisals, but that appraisal change is not dependent on prior sleep duration improvements. This is consistent with a previous study showing that change in appraisals predicted PTSD symptom reduction in CT-PTSD (Kleim, Grey, et al., 2013a). It also elucidates the findings of Chapter 2 that the memory-updating procedure in CT-PTSD, which can influence change in appraisals (Ehlers & Clark, 2000), was associated with sleep duration improvements (compared to no intervention). Therapy related changes in dysfunctional appraisals about threat (e.g., *'I have to be on guard at*

all times') and vulnerability during sleep, could lead to a reduced the sense of current threat (Ehlers & Clark, 2000; Ehlers et al., 2005), and associated reductions in hyper-vigilance and hyper-arousal at bedtime, and coping strategies such as avoidance of the bed and sleep, thereby improving sleep duration. This is supported by studies showing that fear of lost vigilance has been positively associated with poor sleep in veterans (Pietrzak et al., 2010), and fear of sleep has been related to more severe PTSD and insomnia symptoms in trauma survivors (Pruiksma et al., 2016).

Reduction in the flashback-quality of intrusions is another proposed mechanism of PTSD symptom change (Ehlers et al., 2005) from Ehlers and Clark's (2000) cognitive model of PTSD. Consistent with this, the results of the present study showed that change in the flashback-quality of intrusions mediated the relationship between sleep duration and PDS, supporting the hypothesis that it may be a therapeutic mechanism of sleep improvement with CT-PTSD. Reduced re-experiencing symptoms could improve sleep duration either directly through reduced nightmares resulting in less wake after sleep onset (Davis et al., 2007), or indirectly via reduced avoidance of sleep due to fear of nightmares (Krakow et al., 1995) or intrusive re-experiencing that may occur while trying to fall asleep. This is supported by the findings of Chapter 2 and previous studies showing that nightmares and nightmare distress are significantly reduced with CBT for PTSD (Levrier et al., 2016). Future research should aim to consider these pathways, by further investigating how reduced re-experiencing leads to sleep duration improvements with CT-PTSD.

Appraisal change did not mediate the relationship between sleep quality ratings and PTSD symptoms, nor did flashback-quality of intrusions. This indicates that other treatment mechanisms influence sleep quality ratings. One possible mechanism that was

not explored in the present study is hyperarousal. As discussed in Chapter 1, high arousal is key in many models of insomnia (e.g., Bonnet & Arand; 1997; 2010; Espie, 2002) and is implicated in sleep problems such as increased wake after sleep onset in PTSD (Kobayashi et al., 2014; Kobayashi, Boarts, & Delahanty, 2007; Pace-Schott, Germain, & Milad, 2015b). Chapter 2 showed reductions in arousal were associated with sleep duration improvements, which supports change in hyperarousal as a possible pathway for sleep improvements. Further research should explore the role of hyperarousal, and consider whether it may be a mechanism of change for sleep quality improvements with PTSD therapy.

Limitations and Future Directions

There are a number of limitations that should be noted. Firstly, as in Chapter 2, the sleep measures used were simple retrospective self-report measures of average sleep quality and duration over the previous week, and a single item from the PHQ-9. While these provided useful indicators of sleep improvement, it would be important to examine whether improvements with CT-PTSD are also reflected in objective measures of sleep, such as actigraphy or polysomnography, and to use validated subjective measures to assess the clinical significance of sleep problems post-treatment. Furthermore, in the present study it remained unclear exactly how sleep improved, for example whether sleep onset times were reduced, or whether patients had fewer awakenings after sleep onset. Further research is required using more complex subjective measures (such as sleep diaries) to investigate treatment effects on characteristics that may underlie sleep duration and quality improvements, such as reduced onset latency and wake after sleep onset. Fear of night-time re-experiencing symptoms, and changes with CT-PTSD, could also be considered and related to appraisals. Finally, the results showed that those without long-term follow-up data had more severe PTSD and sleep symptoms at the end

of treatment. Therefore it is unclear whether the results of the present study apply to those who did not participate in the follow-up assessments.

The results of the present study suggest that change in trauma-related appraisals and reduction in flashback-quality of intrusions may be treatment mechanisms for improvement in sleep duration with CT-PTSD. Results from the insomnia literature suggest that appraisals about sleep and pre-sleep thought content contribute to the maintenance of general insomnia (Espie et al., 2014; Harvey & Espie, 2004; Wicklow & Espie, 2000). Future studies should therefore also consider the role of sleep-related appraisals and pre-sleep thought content in sleep disturbances in PTSD, and examine whether PTSD treatment modifies these appraisals and reduces pre-sleep cognitions. Future studies should also consider specifically how the flashback-quality of intrusions may interfere with sleep problems, as well as other possible treatment mechanisms, such as high arousal, that may influence subjective sleep quality in PTSD patients.

Summary

In sum, the present study showed that CT-PTSD improved self-reported sleep duration and quality, and difficulties sleeping, in routine clinical care. The results suggested that baseline sleep duration may interfere with PTSD treatment gains, and lower sleep quality ratings may lead to slower PTSD symptom change in those who are depressed. Consistent with Chapter 2, there was no evidence that sleep at the end of treatment was related to PTSD symptoms at long-term follow-up. Finally, the results showed that change in trauma appraisals and reduction in flashback-quality of intrusions may be treatment mechanisms for sleep duration but not sleep quality improvements. Recommendations for future research include the use of objective sleep measures, and investigation into the role of pre-sleep cognitions in sleep disturbances in PTSD.

Chapter 4: Development and Validation of New Measures assessing PTSD related Pre-Sleep Cognitions and Behaviours

Introduction

Overview

As discussed in Chapter 1, there is good evidence for the role of inadequate sleep hygiene (e.g., Bootzin et al., 1993) and pre-sleep cognitions (see Harvey, 2002) in maintaining insomnia. Insomnia is highly prevalent in PTSD (Ohayon & Shapiro, 2000), and commonly residual after PTSD treatment (Zayfert & DeViva, 2004). Researchers have therefore suggested that factors known to perpetuate insomnia, may also contribute to sleep impairment in PTSD. It would therefore be worthwhile to consider the role of pre-sleep cognitive activity and sleep hygiene in sleep impairment in PTSD. However, the relationship between sleep hygiene and pre-sleep cognitions with insomnia in this population have not been directly investigated, nor do measures exist to assess PTSD-specific pre-sleep cognitions and behaviours that may contribute to poor sleep in PTSD. In this chapter, the development of scales to assess pre-sleep cognitions (the 'Pre-Sleep Cognition Scale') and maladaptive pre-sleep behaviours including sleep hygiene (the 'Pre-Sleep Behaviour Scale') in a PTSD population will be described. The scales include modified items derived from a pre-existing measure of pre-sleep cognitions developed with an insomnia population (Harvey & Espie, 2004), and items derived from the literature on sleep hygiene, with the novel addition of PTSD-specific items. Psychometric properties of the scales will be presented and implications for the use of these tools in clinical populations and treatment studies will be discussed.

Existing measures

There already exist validated measures to assess sleep hygiene (Sleep Hygiene Awareness and Practice Scale, Lacks & Rotert, 1986; Sleep Hygiene Self Test, Blake & Gomez, 1998); Sleep Hygiene Index, Gellis & Lichstein, 2009; Mastin et al., 2006), and pre-sleep cognitive activity (Glasgow Content of Thought Inventory, Harvey & Espie, 2004). However, these measures were developed from evidence that was derived from an insomnia population, and may not apply to a PTSD population, or assess the full range of pre-sleep cognitions and behaviours that may interfere with sleep in PTSD. As reviewed in Chapter 1, relatively little is known about pre-sleep cognitive activity and sleep hygiene in PTSD. However, studies have found that fear of sleep (Pruiksma et al., 2016) linked to nightmares (Davis:2007cs; Davis:2007gi; Davis et al., 2011; Krakow et al., 1995), and fear of the loss of vigilance (Pietrzak et al., 2010) are associated with worse sleep in PTSD. Further, it has been suggested that PTSD-specific behaviours such as checking for safety and avoiding sleep because of fear of nightmares (Davis & Wright, 2007; Krakow, Hollifield, et al., 2001b), may play a role in sleep problems in PTSD. It is possible that PTSD-related pre-sleep cognitions (such as being vulnerable while asleep) may occur alongside pre-sleep cognitions that have been measured, and associated with poor sleep, in insomnia (such as worries about getting enough sleep) (Harvey, 2002; Harvey & Espie, 2004). Similarly, PTSD-related pre-sleep behaviours (such as checking for safety) may occur alongside poor sleep hygiene behaviours (such as irregular bedtimes) that have been measured in insomnia (Gellis & Lichstein, 2009; Mastin et al., 2006). It would therefore be important to assess pre-sleep cognitions and sleep hygiene behaviours in PTSD, and to consider their association with disturbed sleep in PTSD.

Aims of the Present Study

This chapter describes the development and initial validation of two measures designed to assess both insomnia-related and PTSD-related pre-sleep cognitions and pre-sleep behaviours in a PTSD population.

The specific aims of the present study were to 1) develop two measures of pre-sleep cognitions and behaviours in PTSD, 2) to assess their psychometric properties and 3) to investigate whether there are PTSD-specific pre-sleep cognitions and behaviours that discriminate people with PTSD from those with insomnia, depression and traumatised and non-traumatised controls.

Methods

An online study evaluated the reliability of the new questionnaires and examined associations between the new questionnaires with established measures of sleep disturbances and PTSD symptoms.

Participants

A total sample of 285 participants took part in the study between 2013 and 2016 (see Table 4.1 for demographic information). The sample was comprised of 159 women, aged 18-65 (M = 30.32, SD = 11.37). This total sample size was selected to enable factor analysis, in line with recommendations that the sample size should include 10 times as many participants as scale items (Nunnally, 1978), which were between 23 and 29 items in the present study. Post hoc power analysis revealed that the sample size enabled 94% power to detect group differences with a medium effect size. Participants were recruited into one of five groups:

Two control groups:

1) Controls: participants who had not experienced a trauma, and did not have any mental health problems (N = 80)
2) Trauma controls: participants who had experienced trauma, but did not have depression, or PTSD (N = 77)

And three clinical groups:

3) PTSD: participants with PTSD (N = 57)
4) Insomnia: participants with insomnia, but no depression or PTSD (N = 42)
5) Depression: participants with depression but no PTSD (N = 29).

Inclusion criteria for all groups were that they were aged 18–65, had no present or past diagnosis of psychosis or bipolar disorder, could read and write in English, had not reported substance or alcohol dependence, and were not currently receiving psychological therapy, as this may have affected the test-retest reliability analyses. Specific inclusion criteria for the PTSD group were that they had experienced a traumatic event, as defined by the DSM-5 criteria (APA, 2013) and had clinically significant PTSD symptoms. Inclusion criteria for the trauma control group were that they had experienced a traumatic event and did not have clinically significant PTSD or depression symptoms, or any reported mental health problems. The inclusion criteria for non-traumatised controls were that they had not experienced a traumatic event, and did not have clinically significant depression symptoms or any reported mental health problems. Inclusion criteria for the depression group were that they reported clinically significant depression symptoms, and did not report clinically significant PTSD symptoms, and inclusion criteria for the insomnia group was that they reported clinically

significant insomnia, but did not report clinically significant PTSD or depression symptoms.

A total of 420 people responded to the advert and were screened according to inclusion criteria outlined previously, and 354 (84.29%) of these were suitable for one of the study groups. A final sample of 285 people (80.51% of those suitable) completed the online questionnaire, of which 152 (53.3%) had experienced a trauma (see Table 4.1).

A sample of 157 participants (55.1%) (57 trauma, 64 control, 18 PTSD, 8 insomnia, and 10 depression) completed the questionnaire again one week later to assess test-retest reliability.

Table 4.1. Demographic and trauma information for each group

	CONTROL (N = 80)	**TRAUMA (N = 77)**	**PTSD (N = 57)**	**DEPRESSION (N =29)**	**INSOMNIA (N = 42)**
	M (SD)	**M (SD)**	**M (SD)**	**M (SD)**	**M (SD)**
Age (years)	27.23 (9.04)	32.56 (12.31)	33.90 (11.69)	30.75 (15.98)	25.84 (6.81)
	N (%)	**N (%)**	**N (%)**	**N (%)**	**N (%)**
GENDER					
Women	49 (61.3)	43 (55.8)	30 (52.6)	16 (55.2)	23 (54.8)
Men	31 (38.8)	34 (44.2)	27 (47.4)	13 (44.8)	19 (45.2)
ETHNIC BACKGROUND					
Caucasian	32 (88.8)	47 (84.0)	37 (75.5)	13 (76.47)	21 (91.4)
Ethnic minority	4 (11.2)	9 (16.1)	12 (25.3%)	4 (23.53)	2 (8.6)
Missing data	43	21	8	12	19
TRAUMA CHARACTERISTICS					
Traumatised	0 (0)	77 (100)	57 (100)	11(37.9)	7 (16.7)
RTA		11 (15.1)	10 (18.5)	3 (25.0)	1 (14.3)
Non-Sexual Assault		10 (13.7)	5 (9.3)	2 (16.7)	0
Sexual assault		9 (12.3)	9 (16.7)	2 (16.7)	2 (28.6)
Accident/ Natural Disaster		4 (5.5)	3 (5.6)	0	1 (14.3)
Military		2 (2.7)	0	0	0
Witnessing Others die/seriously hurt		11 (15.1)	3 (5.6)	0	3 (42.9)
Child abuse		1 (1.4)	6 (11.1)	0	0
Sudden, traumatic loss		12 (16.4)	5 (9.3)	2 (16.7)	0
Life-threatening illness		5 (6.8)	3 (5.6)	2 (16.7)	0

Torture/ imprisonment		0	2 (3.8)	0	0
Other		8 (10.4)	8 (14.9)	1 (8.3)	0
Missing		4	3	0	0
1-week completed	64 (81.00)	57 (73.1)	18 (31.6)	10 (34.5)	8 (19)

Note. 1 week completed refers to the number of people who completed the questionnaire 1 week later to assess test-retest reliability. Trauma characteristics are for those who had experienced a trauma (n = 152).

Development of Measures

The item-pools for the PTSD sub-scales of the cognition and behaviours measures were developed from the literature, and through discussions with both PTSD patients and expert clinical psychologists in the field of trauma and PTSD. An initial pool of PTSD-related items was generated, and refined through informal interviews and feedback after completion of the scale by a small sample of PTSD patients, healthy trauma survivors, and healthy controls, to check for understanding and repetition. Feedback from clinicians and respondents were incorporated into the final item pool included in the study.

Pre-Sleep Cognition Scale (Initial Item Pool): To assess pre-sleep cognitions related to both insomnia and PTSD, the Pre-Sleep Cognition Scale (PSCS) was developed. Respondents were asked to rate how often each thought had kept them awake over the previous week, on a scale from 0 (*Not at all)* to 3 (*5 or more times a week/nearly every day*). The instructions were phrased to apply to the first sleep onset, as well as sleep onset after waking in the night. The original item pool for the PSCS was made up of 23 items and designed to measure two a priori sub-scales. Fourteen of the items were adapted from the Glasgow Content of Thought Inventory (GCTI), developed by Harvey and Espie (2004), to create a preliminary insomnia-related sub-scale (adapted GCTI; $PSCS_{INSOM}$; 14 items). To reduce participant burden, some of the items from the

original GCTI were combined (e.g. *'Your work/responsibilities'* and *'Your personal life'* were collapsed into *'Everyday worries about work, or home life'*), and some items that could be interpreted as PTSD-related (e.g., *'pictures of things in your mind'* and *'things in your past'*) were removed. Nine items representing empirically and theoretically supported pre-sleep cognitions present in PTSD were used to create a preliminary a priori PTSD-related sub-scale ($PSCS_{PTSD}$; 9 items), (e.g., *'being vulnerable if I sleep'*). Items for both a priori sub-scales were presented in the same questionnaire. Items were summed for each a priori sub-scale to produce scores ranging from 0–42 ($PSCS_{INSOM}$), and 0–27 ($PSCS_{PTSD}$), with a higher score indicating greater frequency of pre-sleep cognitions (see Appendix C for final 21-item scale; $PSCS_{INSOM}$ score range: 0-36, and $PSCS_{PTSD}$ score range: 0–27).

Pre-Sleep Behaviour Scale (initial item pool): This scale was designed as a measure of behaviours characterising poor sleep hygiene. The original item pool consisted of 29 items, with two a priori sub-scales assessing the frequency of problematic pre-sleep behaviours that have been related to insomnia ($PSBS_{INSOM}$; 17 items), or may be related to sleep problems in PTSD ($PSBS_{PTSD}$; 12 items), respectively. The insomnia sub-scale items were generated from the literature, and incorporated the majority of inadequate sleep hygiene behaviours defined by the International Classification of Sleep Disorders, third edition (ICSD-3; American Academy Of Sleep Medicine, 2005), as well as behaviours listed as problematic by experts (Bootzin & Perlis, 1992) and measured in previous scales (Gellis & Lichstein, 2009; Mastin et al., 2006). Some items were collapsed and some not included due to overlap with the Pre-Sleep Cognition Scale (e.g., '*using the bed for worrying or planning'*). The PTSD sub-scale was comprised of maladaptive coping strategies used by people with PTSD that could interfere with sleep, such as avoiding going to bed, and other factors such as checking that the house

is secure. Respondents were asked how often in the last seven days they had performed the behaviours (0 days-7 days). Adaptive pre-sleep behaviours (‘*I went to bed at the same time’*) were reverse scored. Items were summed for each sub-scale ($PSBS_{INSOM}$ score range: 0-119; $PSBS_{PTSD}$ score range: 0-84) with a higher score indicating more maladaptive sleep hygiene (see Appendix D for the final 27-item scale; $PSBS_{INSOM}$ score range: 0–119; $PSBS_{PTSD}$ score range: 0-70).

Existing Measures

To examine the psychometric properties of the Pre-Sleep Cognition Scale and Pre-Sleep Behaviour Scale, participants also completed the following measures:

Pre-sleep cognitive activity and arousal

Glasgow Content of Thoughts Inventory (GCTI) (Harvey & Espie, 2004); The GCTI is a measure of pre-sleep cognitive activity. The scale consists of 25 items and respondents rate how often each thought has kept them awake over the previous 7 days, on a 4-point scale from 1 (*never*) to 4 (*always*). Sum scores range from 0 to 100, and the scale has been found to have good psychometric properties (Cronbach’s $\alpha = .87$). A cut-off score of 42 has been found to discriminate good sleepers from those with insomnia, with a specificity of 83% and a sensitivity of 100% compared to insomnia diagnosis (Harvey & Espie, 2004).

Pre-Sleep Arousal Scale (PSAS) (Nicassio et al., 1985). The PSAS is a 16-item scale with two sub-scales (8 items each) measuring the intensity of somatic (e.g., *‘heart racing’*) and cognitive (e.g., ‘*can’t shut off thoughts’*) arousal, while trying to fall asleep. Participants rate how strongly they generally experience each sensation while attempting to fall asleep, on a scale of 0 (*not at all*) to 5 (*extremely*). Sum scores for

each sub-scale range from 0 to 40. The scale was found to have good psychometric properties for both the cognitive (PSAS-cog; Cronbach's α = .76) and somatic sub-scales (PSAS-som; Cronbach's α = .81) in individuals with insomnia (Nicassio et al., 1985).

Sleep symptoms

Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989) The PSQI has 19 items, and assesses seven components of sleep quality and disturbances over the previous month (sleep duration, efficiency, latency, disturbances, reported quality, sleep medication use and daytime dysfunction). Individual items are rated on a scale from 0 (*not during the last month*) to 3 (*three or more times a week*), and each sub-scale is then rated from 0 (*no difficulty*) to 3 (*severe difficulty*) according to scoring guidelines (Buysse et al., 1989). Sub-scale scores are summed to produce a PSQI global score ranging from 0 to 21. Higher scores indicate more severe global sleep disturbances. A global score of greater than 5 has been found to indicate clinically significant sleep disturbances, discriminating good from poor sleepers with a sensitivity of 89.6% and a specificity of 86.5% (Buysse et al., 1989). To assess time taken to fall asleep, PSQI Component 2 was used (Sleep Latency (SOL); score range: 0-3); and to assess daytime sleepiness and effects of poor sleep, PSQI Component 7 was used (Daytime Dysfunction; score range: 0-3).

Trauma exposure and PTSD symptoms

Life Events Checklist (LEC) (Foa et al., 1997). The LEC was used to assess whether participants had experienced a traumatic event, according to DSM-IV criteria (APA, 2000). It is a self-report questionnaire containing a list of stressful life events (including traumatic events) (see Appendix E for scale). Respondents select 'yes' or 'no' to

indicate whether they have experienced each event in their lifetime. Participants also answered questions from the *PTSD Checklist* (PCL-5) for DSM-5 (Weathers et al., 2013) about the worst event they had experienced, to determine if it met DSM-5 criteria for a traumatic event (Criterion A; APA, 2013).

Posttraumatic Diagnostic Scale (PDS) (Foa et al., 1997). The PDS is a validated measure of DSM specified PTSD symptoms. Participants rate how often they have experienced each symptom over the previous seven days on a three-point scale from 0 (*Not at all*) to 3 (*5 or more times a week/nearly every day*). The scale has been found to have good psychometric properties (Cronbach's α = .92 for total symptom severity; sensitivity = 89%, specificity = 75%) compared to the clinician assessment of PTSD (Foa et al., 1997), and has been found to indicate PTSD when a cut-off of score of 18 or above is used (Ehring et al., 2007). An additional four items were added to assess DSM-5 specified symptoms (APA, 2013). The sum score for the 20 DSM-5 items are reported (range: 0-60). A higher score indicates more severe PTSD symptoms. A sum score excluding the sleep item was also computed for use in the analyses (PDSwos).

Mood and Anxiety Symptoms

Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961); The BDI is a 21-item questionnaire assessing depressive symptoms over the previous two weeks (score range: 0-63). Higher scores indicate more severe depression, and a score of 11 or more on the BDI has been shown to indicate clinically significant depressive symptoms (Beck et al., 1961).

Generalised Anxiety Disorder Scale (GAD-7; Spitzer & Kroenke, 2006) The GAD-7 is a 7-item questionnaire assessing the frequency of general anxiety symptoms over the

previous seven days. Items are summed to produce an overall score (range: 0-21), where higher scores indicate more severe anxiety symptoms.

Screening Questionnaires

At screening participants completed two brief questionnaires to screen for depression and insomnia: 1) the *Insomnia Severity Index* (ISI; Bastien, Vallieres, & Morin, 2001), which assess severity of insomnia symptoms over the previous two weeks. A score of 10 or more has been shown to indicate clinically significant insomnia (Morin, Belleville, Bélanger, & Ivers, 2011); and 2) the *Patient Health Questionnaire* (PHQ-9; Kroenke et al., 2001), which assesses the severity of depressive symptoms over the previous two weeks. A score of 10 or more on the PHQ-9 has been shown to indicate clinically significant depression (Kroenke et al., 2001).

Procedure

Participants were recruited via online adverts in the community in Oxford and at the University of Oxford. Multiple adverts were used to recruit each group, requesting participants who had/had not experienced a trauma, participants who had been experiencing problems falling or staying asleep for two weeks or more (insomnia), and participants who had been experiencing a low mood for two weeks or more (depression). Advert respondents completed online screening questionnaires, which consisted of the LEC (Foa et al., 1997) to identify trauma exposure, questions from the PDS (Foa et al., 1997) to assess PTSD symptoms (for those who reported a traumatic event), and questions about their current and past mental health. Participants responding to adverts for low mood or sleeping problems also completed the PHQ-9 (Kroenke et al., 2001), and the ISI (Bastien et al., 2001) to screen for depression and insomnia, respectively. Participants were initially allocated to a group, and suitable

participants (according to the inclusion criteria outlined previously) were emailed the link to the first online questionnaire pack. Participants indicating clinically significant PTSD (PDS score > 17), depression (PHQ-9 score > 9) and no PTSD (PDS score < 18), or insomnia symptoms (ISI score > 9) with no depression (PHQ-9 score < 10), were allocated to PTSD, depression and insomnia groups respectively. Participants without PTSD were later re-allocated to the depression group if they reported clinically significant depression (BDI score > 20). In the first questionnaire pack, participants completed the same set of questionnaires in the same order. First, participants completed the LEC again, and were asked to identify the worst event they had experienced from those they had selected, and answer questions from the PCL-5 checklist to determine if the event met criteria for a traumatic event (according to DSM-5 Criterion A). Participants were then asked to answer the PTSD symptom measure (PDS) with the 'traumatic event' they had identified in mind. Control participants were asked to answer the PDS with the 'worst event' they had identified in mind, and the wording on the PDS was amended to 'the event' rather than 'the traumatic event/ experience'. After completing the baseline questionnaire pack (Week 1), the Pre-Sleep Cognition and the Pre-Sleep Behaviour Scales were emailed again one week later (Week 2), to examine test-retest reliability.

Analysis

Analyses were conducted using SPSS version 22. Data was checked for skewness and kurtosis, and homogeneity of variance, and non-parametric tests were used where appropriate.

The factor structure of the new measures was examined using Principal Component Analysis (PCA), to estimate the underlying latent factor structure of the measures.

Factors were rotated using orthogonal varimax rotation. Meaningful factors were extracted using both examination of the scree plot (Cattell, 1966), suppression of eigenvalues less than 1, and factor loadings less than 0.4, to determine the simplest factor solution, as the use of one of these methods alone can produce over-extraction of factors (see Matsunaga, 2015). The psychometric properties of the final scales were then examined.

Internal consistency was evaluated with Cronbach's alpha (α), where a score of greater than 0.8 indicates good internal consistency (Nunnally & Bernstein, 1994). Internal consistency analyses were conducted for each sub-scale, using the total sample (N = 285). It has been previously noted that sleep hygiene measures typically have poor internal consistency (e.g., Sleep Hygiene Awareness and Practice Scale, Cronbach's α = .48; Lacks & Rotert, 1986), as they represent a wide range of behaviours that have a causal impact on sleep, rather than one underlying construct, and so would not be expected to be highly inter-related (Mastin et al., 2006). Therefore, for the Pre-Sleep Behaviour Scale, test-retest reliability and discriminative ability were considered more important indicators of reliability and validity for this measure.

For those participants who completed the Pre-Sleep Cognition Scale and Pre-Sleep Behaviour scales a second time, mean total scores for each sub-scale at Week 1 and Week 2 were correlated (intraclass correlation) to examine test-retest reliability.

Concurrent validity was investigated by correlating the Pre-Sleep Cognition Scale with the GCTI (Harvey & Espie, 2004), an established measure of pre-sleep cognitive activity. To examine construct validity, the new measures were correlated with existing measures of sleep quality (PSQI), sleep onset latency (SOL), and pre-sleep arousal

(PSAS). Pre-sleep cognitive activity (GCTI sum score) in patients with insomnia (Harvey & Espie, 2004) has been previously correlated with increased pre-sleep mental arousal (PSAS-cog) and increased self-reported sleep onset latency (Harvey & Espie, 2004), therefore these measures were used to evaluate the construct validity of the Pre-Sleep Cognition Scale. Pre-sleep somatic arousal has also been correlated with poor sleep hygiene in insomnia, and insomnia with depression (Kohn & Espie, 2005), and sleep hygiene has been associated with perceived daytime sleepiness (Mastin et al., 2006). Therefore, measures of pre-sleep somatic arousal (PSAS-som) and daytime dysfunction (PSQI Component 7) were used to evaluate the construct validity of the Pre-Sleep Behaviour Scale. In trauma survivors only (n =152), the PTSD sub-scales of the new measures ($PSCS_{PTSD}$; $PSBS_{PTSD}$) were also correlated with PTSD symptom severity (PDSwos).

To investigate discriminant validity, the ability of the Pre-Sleep Cognition Scale and Pre-Sleep Behaviour Scale to discriminate between experimental groups, and between good and bad sleepers (across all groups) was examined.

Sensitivity (the probability that an individual with the target condition will be correctly identified as having that condition), and specificity (the likelihood that an individual without the condition will be correctly identified as not having it) were examined using Receiver Operating Characteristic (ROC) analysis, to investigate the area under the curve (AUC). An AUC statistic of 0.9 to 1 is thought to indicate excellent test, with high levels of sensitivity and specificity, 0.8 to 0.9 is considered a good test, and below 0.6 is thought to represent a poor test with very little sensitivity or specificity to the target population. Equal importance of sensitivity and specificity was assumed to generate cut-off scores for the PTSD sub-scales of the Pre-Sleep Cognition Scale and

Pre-Sleep Behaviour Scale to identify traumatised individuals with and without PTSD, and for the insomnia sub-scales, to identify poor sleepers and good sleepers. The sensitivity and specificity of the Pre-Sleep Cognition Scale was compared with an established measure of pre-sleep cognitive activity (GCTI) to detect good and bad sleepers within trauma survivors and people with PTSD.

Results

Descriptive statistics

Full sample characteristics are shown in Table 4.2. The severity of sleep disturbances (PSQI global scores) was compared across groups using a one-way ANOVA. There was a significant main effect of group, $F(4, 280) = 66.75$, $p < 0.001$, partial $\eta^2 = .49$ (large effect size). Post hoc comparisons showed that individuals with PTSD scored significantly higher on the PSQI in comparison to all other groups (p's < .001); mean difference (PSQI global score) for depression = 2.55 (95% Confidence Interval (CI) = 0.86 to 4.23), $p < .001$; insomnia = 2.92 (95% CI = 1.42 to 4.42), $p < .001$; control = 6.82 (95% CI = 5.54 to 8.11), $p < .001$; and trauma controls = 5.97 (95% CI = 4.68 to 7.25), $p < .001$. Insomnia and depression did not differ from each other ($p > .05$). The depression group had higher PSQI scores than controls, mean difference = 4.27 (95% CI = 2.67 to 5.88), $p < .001$; and trauma controls = 3.42 (95% CI = 1.82 to 5.02), $p < .001$. Insomnia also had higher PSQI scores than controls, mean difference = 3.90 (95% CI = 2.49 to 5.31), $p < .001$; and trauma controls = 3.04 (95% CI = 1.63 to 4.46). Group comparisons for PTSD, depression and anxiety symptoms, pre-sleep arousal and pre-sleep cognitive activity and behaviours are shown in Table 4.2.

Table 4.2: Descriptive statistics for each group, and test-statistics for group comparison. Group differences are indicated in superscript (e.g., [a, b, c,]), groups sharing the same letter do not differ.

	CONTROL	TRAUMA	PTSD	DEPRESSION	INSOMNIA	GROUP DIFF
	(N = 80)	(N = 77)	(N = 57)	(N = 29)	(N = 42)	
	M (SD)	**M (SD)**	**M (SD)**	**M (SD)**	**M (SD)**	*F* / H
MOOD AND ANXIETY						
BDI	3.82 (4.63) [B]	5.29 (4.77) [B]	23.32 (8.76) [A]	21.48 (7.94) [A]	6.78 (4.85) [B]	H = 148.08***
GAD-7	2.78 (3.22) [C]	2.05 (1.81) [C]	12.50 (5.63) [A]	10.48 (4.81) [A]	5.59 (3.96) [B]	H = 59.00***
PDS (n = 152)		6.75 (5.66) [C]	35.24 (10.88) [A]	16.09 (7.66) [B]	10.71 (6.52) [B, C]	H = 131.24***
SLEEP						
PSQI global score	3.82 (1.79) [C]	4.78 (2.82) [C]	10.77 (3.27) [A]	8.14 (3.23) [B]	7.78 (2.74) [B]	F = 66.75***
Component 2 (SOL)	16.07 (11.17)[B]	20.89 (20.41)[B]	60.96 (64.42) [A]	38.90 (28.32) [A]	40.76 (28.52) [A]	F = 22.16***
Component 7 (Dysf)	0.91 (0.66) [B]	0.88 (0.59) [B]	1.83 (0.86) [A]	1.69 (0.60) [A]	1.19 (0.59) [B]	F = 23.11***
PRE-SLEEP AROUSAL						
PSAS-cog	13.45 (4.99) [C]	14.35 (5.11) [C]	25.43 (8.02) [A]	20.55 (6.70) [A, B]	19.30 (7.10) [B]	H = 92.73***
PSAS-som	9.29 (1.89) [C]	9.85 (2.62) [C]	17.19 (7.51) [A]	12.76 (4.99) [A, B]	10.70 (3.25) [B, C]	H = 67.38***
PRE-SLEEP COGNITIONS						
$PSCS_{INSOM}$	7.59 (6.35) [B]	8.28 (6.42) [B]	18.49 (9.38) [A]	15.13 (7.84) [A]	16.75 (9.07) [A]	H = 78.83***
$PSCS_{PTSD}$	0.98 (1.80) [C]	1.30 (2.00) [C]	9.70 (6.85) [A]	4.28 (3.83) [B]	2.53 (2.78) [B, C]	H = 112.47***
GCTI	37.02 (9.51) [B]	38.32 (9.18) [B]	58.55 (16.74) [A]	51.48 (15.06) [A]	47.95 (12.52) [A]	H = 84.22***
PRE-SLEEP BEHAVIOURS						
$PSBS_{INSOM}$	30.05 (8.46) [B]	32.33 (9.73) [B]	35.91 (13.34) [A]	36.62 (8.03) [A]	33.48 (10.05) [A, B]	H = 15.57**
$PSBS_{PTSD}$	2.29 (3.18) [B]	3.63 (4.88) [B]	10.45 (9.24) [A]	4.03 (5.63) [B]	3.88 (3.41) [B]	H = 51.93***

*PDS is for trauma survivors only (n = 152). Mean scores for the Pre-sleep Cognition Scale and Pre-Sleep Behaviour Scales are for final scales (Appendix C and D), after PCA (PSCS) and internal consistency checks (PSBS). Significant level of group difference indicated by: * $p < .05$; ** $p < .01$, *** $p < .001$*

Factor analysis

Pre-Sleep Cognition Scale

Principal component analysis was conducted on the 23-item Pre-Sleep Cognition Scale (PTSD and insomnia sub-scales combined) using the total sample (N= 285). Factors were rotated using orthogonal varimax rotation. The Kaiser-Meyer-Olkin statistic (Kaiser, 1970) was .94, which indicated 'superb' sampling adequacy (> 0.9) (Hutcheson & Sofroniou, 1999). The correlation matrix indicated that all items were significantly correlated, none at more than .9, suggesting that no items should be deleted.

Using eigenvalues of greater than 1 and suppressing factor loadings of less than 0.4, four factors were extracted, which explained 65.16% of the overall variance, after rotation. Eight out of 23 variables cross-loaded onto two factors. Factor 4 consisted of only two items *'How uncomfortable my sleeping environment is'* and *'noises I hear'*, and all but one item on Factor 3 also cross-loaded onto Factor 1. Examination of the scree plot supported the possibility of a two-factor solution. Therefore, PCA was repeated and the extraction of two factors was requested. The results of the rotated component matrix showed a clear two-factor structure, with no cross-loading items (see Table 4.3). One item (*'How uncomfortable my sleeping environment is'*) did not load onto either factor, and was deleted. A second item (*'noises I hear'*) had a much lower factor loading than all other items (eigenvalue = .45) and was also deleted. The two-factor solution supported the original division of items into insomnia and PTSD related sub-scales (see Table 4.3), and so Factor 1 was labelled the insomnia sub-scale ($PSCS_{INSOM}$; now 12 items) and Factor 2 was labelled the PTSD-sub-scale ($PSCS_{PTSD;}$ 9 items). The psychometric properties of the final 21-item scale (see Appendix C) were then investigated.

Table 4.3. Extracted factors for the Pre-sleep Cognition Scale, with varimax rotation factor loadings.

Original Item Pool	Extracted Components	
	1	2
that I am still not asleep	.857	
how long I have been awake	.813	
that I won't be able to cope with so little sleep	.807	
how getting too little sleep affects me	.768	
how tired/sleepy I feel	.720	
checking the time	.711	
everyday worries (e.g., about work or home life)	.711	
tomorrow (plans, things I have to do)	.700	
how I can't stop my mind from racing	.686	
how restless I feel	.633	
worries about the more distant future	.629	
things that happened during the day	.613	
noises I hear	.446	
how uncomfortable my sleeping environment is (e.g., bed)		
unwanted memories of my trauma		.779
dwelling on my trauma (e.g., asking yourself "why me," "what if" questions)		.759
dwelling on how my life has been changed by the trauma		.750
being vulnerable if I sleep		.740
how afraid I feel		.715
something bad happening to my body if I sleep (e.g., heart attack, stop breathing, will not wake up, will die).		.702
fear of nightmares		.659
how lonely I feel		.603
how angry I feel		.601

Pre-Sleep Behaviour Scale

The correlation matrix indicated that many items in the Pre-Sleep Behaviour Scale did not significantly correlate with each other, with few correlations greater than 0.3, suggesting that the measure represents a varying range of behaviours, rather than one underlying construct of sleep hygiene, and so factor analysis was not supported.

Internal Consistency

Pre-Sleep Cognition Scale

Using the entire sample (N = 285) the 12-item insomnia sub-scale ($PSCS_{INSOM}$) had good internal consistency ($\alpha = .93$), and item deletion alphas were less than .94, indicating that

consistency would not be improved with the deletion of any items. The mean corrected item-total correlation of individual scale items with the sum of all items in the sub-scale was r = .71 (range: r = .61-.82), further indicating good internal consistency. Similarly, internal consistency was high for the PTSD sub-scale ($PSCS_{PTSD;}$ α = .90), and would not be improved with the deletion of items. The mean of the corrected item-total correlations was r = .68 (range: r = .59-.78), indicating a good relationship between each item and the overall measured construct.

Pre-Sleep Behaviour Scale

The insomnia sub-scale ($PSBS_{INSOM}$) had low internal consistency (α = .46), below the generally accepted valued of 0.8 (Nunnally & Bernstein, 1994). Item-total correlations supported the reverse scoring of 4 items on the scale: items 8 (‘*Went to bed at same time’*), 9 (‘*Got up at the same time’*), 10 (‘*Set aside some time to relax before bed’*) and 14 (‘*Read in bed’*), which were all positively correlated with the total score when they were reversed. The mean corrected item-total correlation was r = .16 (range: -.10–.32), which was lower than the acceptable level of 0.3. Internal consistency was also low for the PTSD sub-scale ($PSBS_{PTSD}$; 12 items; α = .48). Item deletion statistics suggested that Cronbach’s α would be improved with the deletion of two items (‘*I checked that my phone was near me before going to sleep*’ and *‘I intentionally slept with background noise on’*) therefore these were deleted, and internal consistency was improved to (α = .59), based on the remaining 10 items. The mean of the corrected item-total correlations was r = .29 (range: .06-.54). Subsequent item deletion alphas showed that consistency would not be improved with the further deletion of any items. The final scale had 27 items ($PSBS_{INSOM}$; 17 items; $PSBS_{PTSD}$; 10 items; see Appendix D for final scale).

Test-Retest Reliability

Pre-Sleep Cognition Scale

The scale had good test-retest reliability. Sum scores for each sub-scale significantly correlated with sum scores one week later: $PSCS_{INSOM}$; ICC = .74, $p < .001$, (95% CI = .66 to .81); $PSCS_{PTSD}$, ICC = .75, $p < .001$, (95% CI = .67 to .81).

Pre-Sleep Behaviour Scale

The scale showed good test-retest reliability for both sub-scales: $PSBS_{INSOM}$, ICC= .74, $p < .001$, (95% CI = .65 to .80); $PSBS_{PTSD}$, ICC = .82, $p < .001$, (95% CI = .75 to .86).

Concurrent Validity

Both sub-scales of the Pre-Sleep Cognition Scale correlated highly with the Glasgow Content of Thought Inventory: $PSCS_{INSOM}$; *rho* = .83, $p < .001$; $PSCS_{PTSD}$; *rho* = .66, $p < .001$, demonstrating good concurrent validity (see Table 4.4).

Construct Validity

Pre-Sleep Cognition Scale

Spearman's rank correlations showed that both sub-scales of the Pre-Sleep Cognition Scale significantly correlated with global sleep quality (PSQI global score), $PSCS_{INSOM}$, *rho* = .72, $p < .001$; $PSCS_{PTSD}$, *rho* = .61, $p < .001$; subjective sleep onset latency, $PSCS_{INSOM}$, *rho* = .57 $p < .001$; $PSCS_{PTSD}$, *rho* = .40, $p < .001$; pre-sleep cognitive arousal (PSAS-cog), $PSCS_{INSOM}$, *rho* = .75, $p < .001$; $PSCS_{PTSD}$, *rho* = .65, $p < .001$, and somatic arousal (PSAS-som), $PSCS_{INSOM}$, *rho* = .51, $p < .001$; $PSCS_{PTSD}$, *rho* = .61, $p < .001$. In trauma survivors (n = 152), the PTSD sub-scale was strongly associated with PTSD symptom severity (PDS) with, *rho* = .83, $p < .001$, and without the sleep item, *rho* = .83, $p < .001$ (see Table 4.4 for full results).

Pre-Sleep Behaviour Scale

Spearman's rank correlations showed that both sub-scales of the Pre-Sleep Behaviour Scale had small (.10) to moderate (.30) correlations with global sleep quality (PSQI), $PSBS_{INSOM}$, *rho* = .27 $p < .001$; $PSBS_{PTSD}$, *rho* = .31, $p < .001$, subjective sleep onset latency, $PSBS_{INSOM}$, *rho* = .26, $p < .001$; $PSBS_{PTSD}$, *rho* = .33, $p < .001$, and daytime dysfunction, $PSBS_{INSOM}$, *rho* = .25, $p < .001$; $PSBS_{PTSD}$, *rho* = .18, $p < .001$. The PTSD sub-scale ($PSBS_{PTSD}$) was moderately correlated with PTSD symptom severity (PDS) with, *rho* = 0.45, $p < .001$, and without the sleep item (PDSwos), *rho* = .43, $p < .001$.

Table 4.4 Non-parametric correlations (Spearman's rank) between Pre-Sleep Cognition (PSCS) and Pre-Sleep Behaviour (PSBS) final scales and established measures.

	GCTI	PSQI	SOL	Daytime Dysf.	PSAS-cog	PSAS-som	PDS	PDSwos
$PSCS_{INSOM}$	0.83**	0.72**	0.58**	0.43**	0.75**	0.51**	0.67**	0.65**
$PSCS_{PTSD}$	0.66**	0.61**	0.40**	0.40**	0.65**	0.61**	0.83**	0.83**
$PSBS_{INSOM}$	0.27**	0.26**	0.14*	0.25**	0.25**	0.20**	0.23**	0.23**
$PSBS_{PTSD}$	0.31**	0.33**	0.22**	0.18**	0.32**	041**	0.45**	0.43**

*Note. Correlations with PTSD symptoms (PDS) were for trauma survivors only (n =152). PDSwos = PDS without the sleep item. SOL = estimated subjective sleep onset latency from PSQI. Daytime Dysf = daytime dysfunction as a result of sleepiness (PSQI component 7). * = p < 0.05; ** = p < 0.01.*

Predictive and Discriminative Validity: Discriminating Groups

Pre-Sleep Cognition Scale

For the insomnia sub-scale, ($PSCS_{INSOM}$), a Kruskal-Wallis test showed that there was a significant main effect of group; H(4) = 78.83, $p < .001$. Planned pairwise comparisons, with adjusted p values and effect sizes (*r*), showed no differences between controls and trauma controls ($p > .05$), or between the depression, insomnia and PTSD groups ($p's > .05$). However, the depression group scored significantly higher on the $PSCS_{INSOM}$ than controls, $p < .001$, $r = .42$, and trauma controls, $p < .01$, $r = .38$, as did the PTSD group (control, $p < .001$, $r = .59$; trauma control, $p < .001$, $r = .54$), and insomnia group (control, $p < .001$, $r = .49$; trauma control, $p < .001$, $r = .43$) (see Figure 4.1). The PTSD sub-scale ($PSCS_{PTSD}$) showed a slightly different pattern of results. A Kruskal-Wallis

test showed that there was a significant main effect of group, H(4) = 112.47, $p < .001$. Pairwise comparisons showed that there was no significant difference between the insomnia and controls, trauma controls, or depression groups (*p's* > .05). However, the PTSD group scored significantly higher on the $PSCS_{PTSD}$ than all other groups (controls, $p < .001$, $r = .72$; trauma controls, $p < .001$, $r = .74$; insomnia, $p < .001$, $r = .62$; depression, $p < .05$, $r = .43$), and the depression group scored significantly higher than controls, $p < .001$, $r = .45$, and trauma control groups, $p < .001$, $r = .46$, (see Figure 4.2 and Table 4.2). All comparisons showed medium ($r = .3$) to large ($r = .5$) effect sizes (Cohen, 1992).

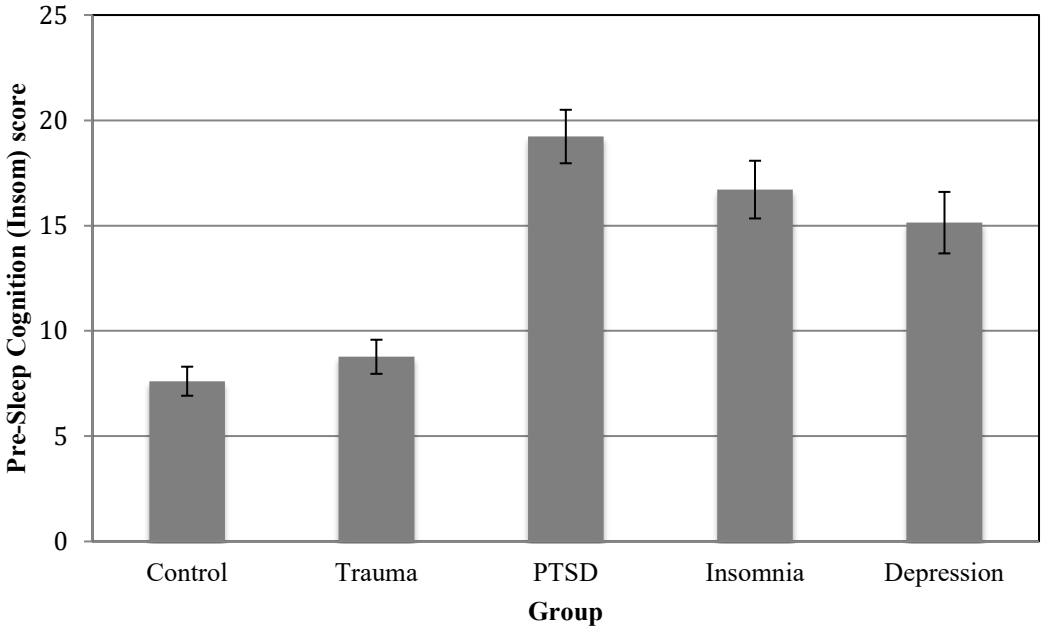


Figure 4.1. Pre-Sleep Cognition Scale (insomnia sub-scale ($PSCS_{INSOM}$); extracted Factor 1) mean scores and standard error bars for each group (N = 285).

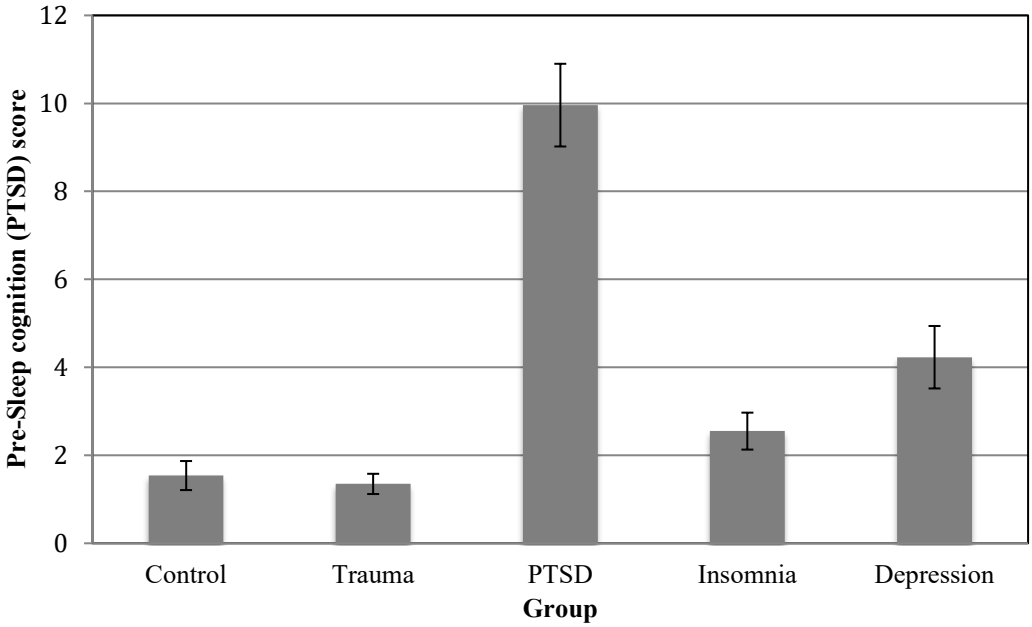


Figure 4.2. Pre-Sleep Cognition Scale (PTSD sub-scale ($PSCS_{PTSD}$); extracted Factor 2) mean scores and standard error bars for each group (N = 285).

Pre-Sleep Behaviour Scale

There was a significant main effect of group on the insomnia sub-scale ($PSBS_{INSOM}$), according to the Kruskal-Wallis test, $H(4) = 15.57$, $p < 0.01$. Planned pairwise comparisons, with adjusted p values and effect sizes (r), showed that the PTSD group, $p = .46$, $r = .23$, and depression group, $p = .01$, $r = .33$, scored significantly higher on the $PSBS_{INSOM}$ than the control or trauma control groups. There were no other significant differences between the groups (see Figure 4.3 and Table 4.2). There was also a significant main effect of group on the PTSD sub-scale ($PSBS_{PTSD}$), $H(4) = 51.93$, $p < .001$. Pairwise comparisons revealed that the PTSD group scored significantly higher on the $PSBS_{PTSD}$ than controls, $p < .001$, $r = .56$, trauma controls, $p < .001$, $r = .46$, depression, $p < .01$, $r = .39$, and insomnia groups, $p < .01$, $r = .41$. There were no other differences between the groups ($p > .05$) (see Figure 4.4 and Table 4.2).

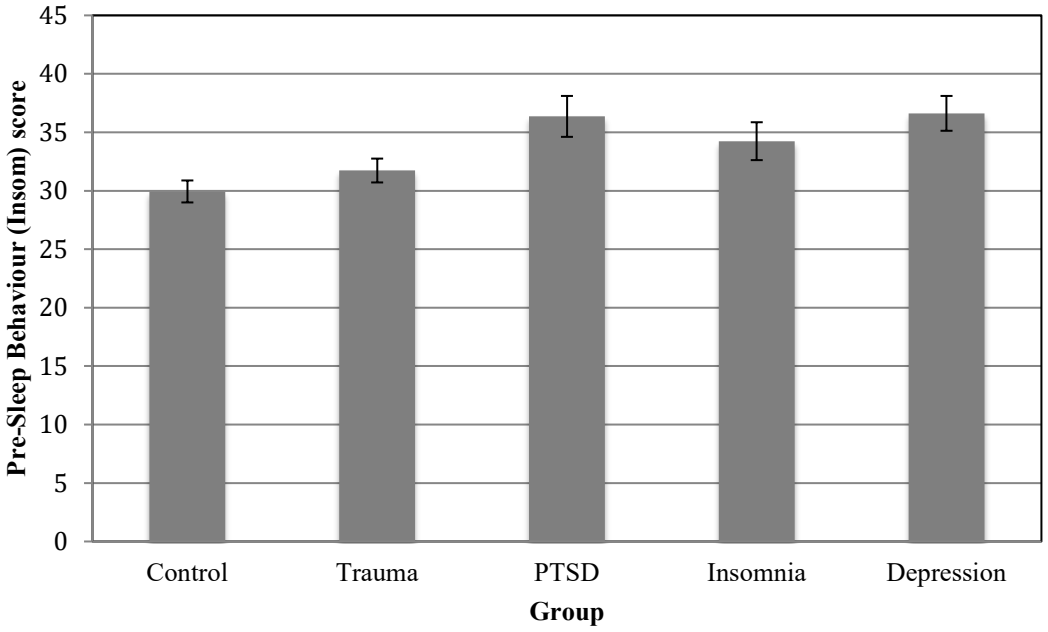


Figure 4.3. Pre-Sleep Behaviour Scale (insomnia sub-scale; $PSBS_{INSOM}$) mean scores and standard error bars for each group (N = 285).

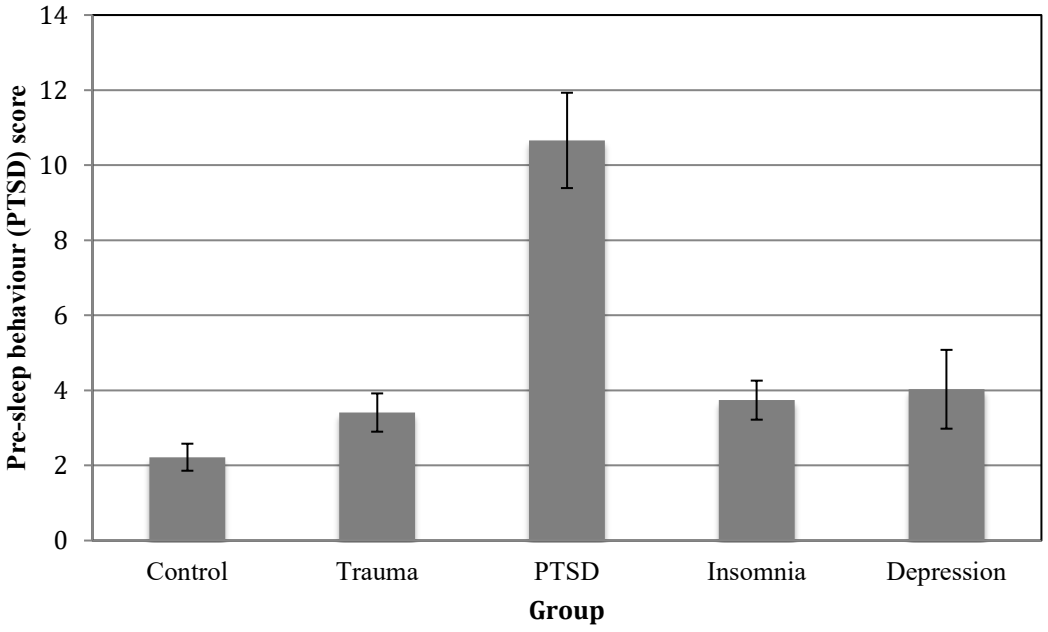


Figure 4.4. Pre-Sleep Behaviour Scale (PTSD sub-scale; $PSBS_{PTSD}$) mean scores and standard error bars for each group (N = 285).

Predictive and Discriminative Validity: Discriminating Sleeper Status

Groups were collapsed and divided into good (*n* = 136; PSQI global score < 6) and poor sleepers (*n* = 149; PSQI global score > 5). The ability of the Pre-sleep Cognition

and Pre-Sleep Behaviour Scales to discriminate between good and poor sleepers was tested in the entire sample, using Mann-Whitney U tests, with effect sizes (*r*) reported. Results showed that on the Pre-Sleep Cognition Scale, poor sleepers scored significantly higher on insomnia-related cognitions, $PSCS_{INSOM}$, U = 3075.00, $p < .001$, $r = .63$, and PTSD-related pre-sleep cognitions, $PSCS_{PTSD}$, U = 4344.00, $p < .001$, $r = .51$, than good sleepers, with large effect sizes (see Figures 4.5 and 4.6). Similarly, on the Pre-Sleep Behaviour Scale, poor sleepers scored higher on insomnia-related, $PSBS_{INSOM}$, U = 7075.7, $p < .001$, $r = .26$, and PTSD-related pre-sleep behaviours, $PSBS_{PTSD}$, U = 6668.5, $p < .001$, $r = .30$, than good sleepers, with small effect sizes (see Figures 4.7 and 4.8).

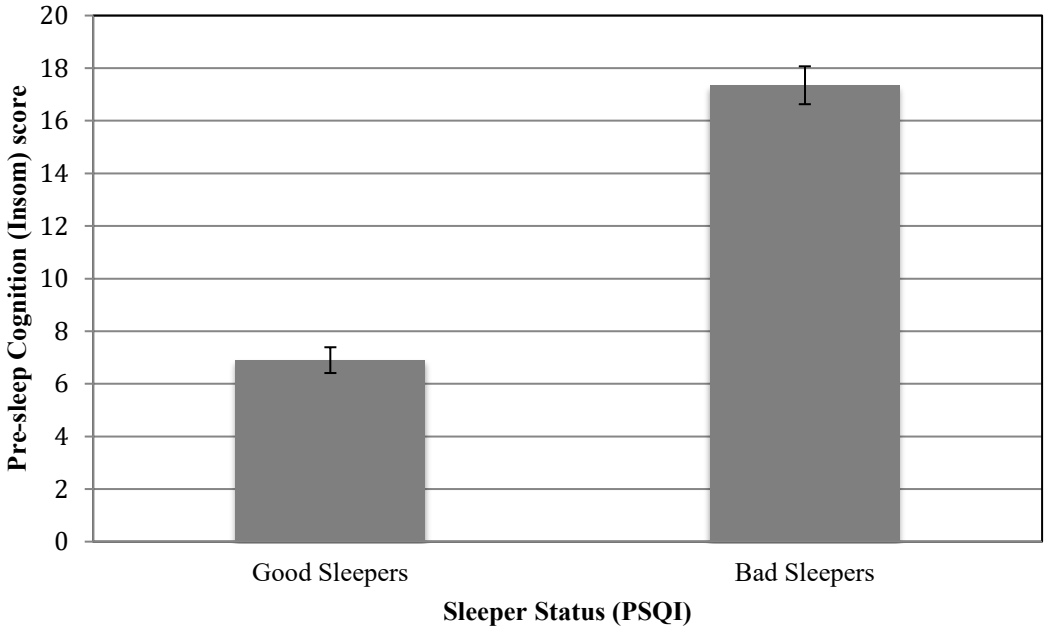


Figure 4.5. Pre-Sleep Cognition Scale (insomnia sub-scale ($PSCS_{INSOM}$); extracted Factor 1: mean scores and standard error bars for good sleepers (PSQI global score < 6; n = 136) and poor sleepers (PSQI global score > 5; *n* = 149).

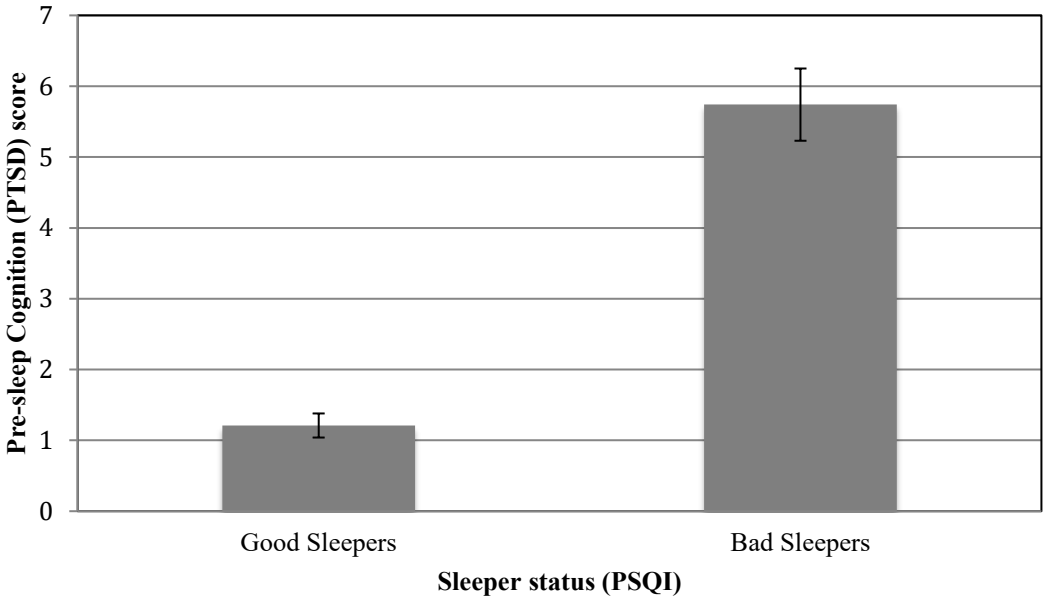


Figure 4.6. Pre-Sleep Cognition Scale (PTSD sub-scale ($PSCS_{PTSD}$); extracted Factor 2: mean scores and standard error bars for good sleepers (PSQI global score < 6; *n* = 136) and poor sleepers (PSQI global score > 5; *n* = 149).

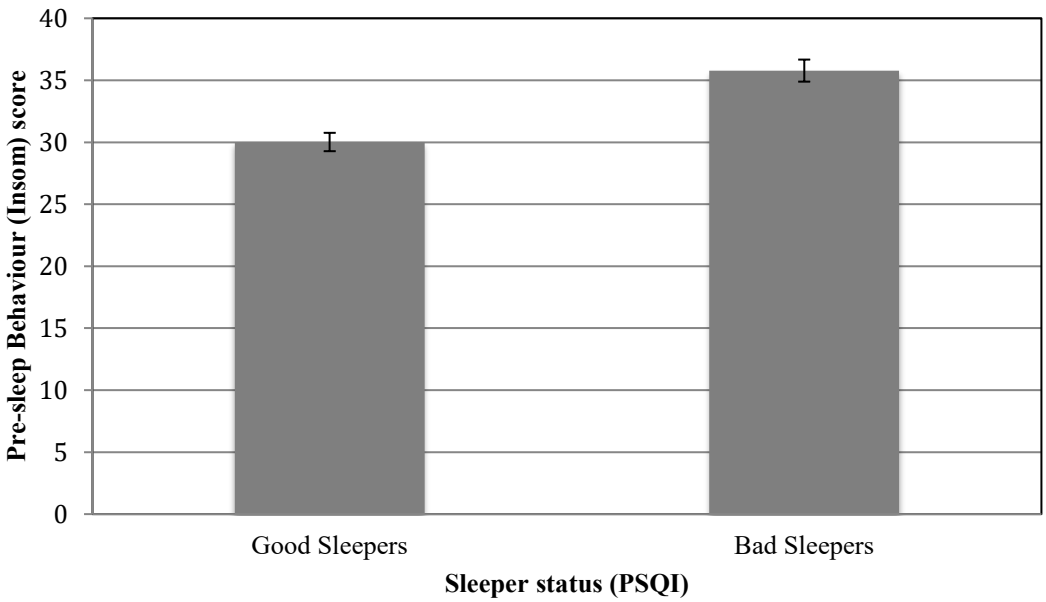


Figure 4.7. Pre-Sleep Behaviour Scale (insomnia sub-scale; $PSBS_{INSOM}$) mean scores and standard error bars for good sleepers (PSQI global score < 6; *n* = 136) and poor sleepers (PSQI global score > 5; *n* = 149).

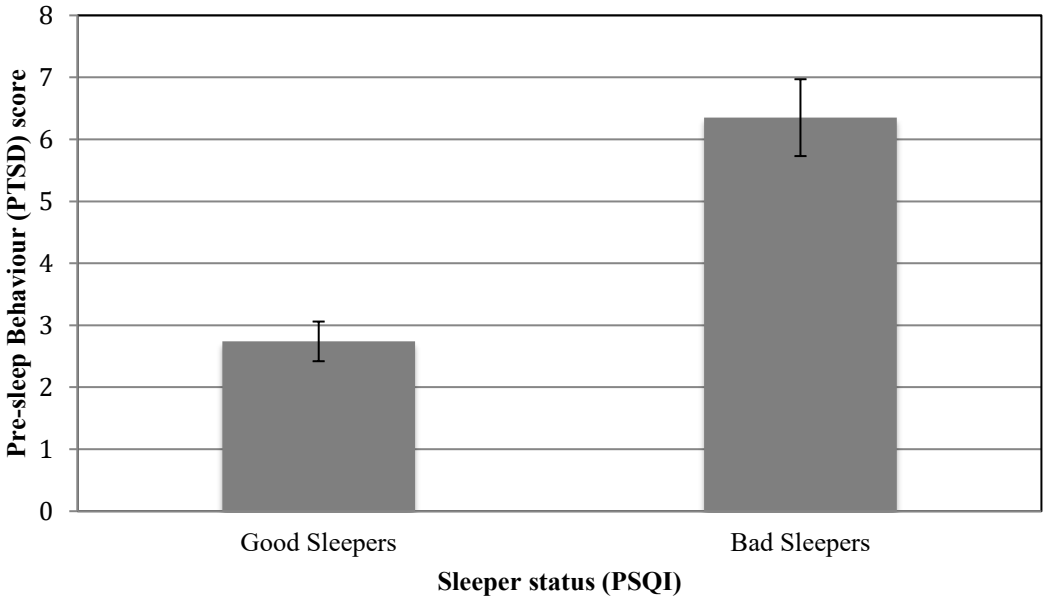


Figure 4.8. Pre-Sleep Behaviour Scale (PTSD sub-scale; $PSCS_{PTSD}$) mean scores and standard error bars for good sleepers (PSQI global score < 6; *n* = 136) and poor sleepers (PSQI global score > 5; *n* = 149).

Sensitivity and Specificity

Good sleepers vs. bad sleepers

Sensitivity and specificity of the insomnia sub-scales to discriminate good (*n* = 136) and poor sleepers (*n* = 149) was examined using the entire sample (N = 285). For the Pre-Sleep Cognition insomnia sub-scale ($PSCS_{INSOM}$), the area under the ROC curve (AUC) was 0.85, (95% CI = .80 to .89), indicating an 85% chance that a randomly selected poor sleeper (PSQI global sum score > 5) would have a higher $PSCS_{INSOM}$ score than a randomly selected good sleeper (PSQI global sum score < 6). A cut-off score of 10 on the $PSCS_{INSOM}$ yielded a sensitivity of 81.2%, correctly identifying 121 out of 149 poor sleepers, and a specificity of 73.4%, correctly 100 out of 136 good sleepers. The group was split into those scoring above or below 10 on the $PSCS_{INSOM}$. Results showed that those scoring above the cut-off had significantly higher PSQI global scores, with a large effect size, U = 17451, $p < .001$, $r = .63$.

The Pre-Sleep Behaviour insomnia sub-scale ($PSBS_{INSOM}$) had an AUC of 0.65 (95% CI = .59 to .72), indicating low sensitivity and specificity. A cut-off score of 29 correctly identified 41.9% (57 out of 136; specificity) of good sleepers (PSQI <6), 73.8% (110 out of 149; sensitivity) of poor sleepers (PSQI > 5). Individuals scoring at or above the cut-off had significantly higher PSQI global scores with a small effect size, U = 11383, $p <$ .01, r = 0.17.

Trauma Survivors: PTSD vs. no PTSD

Sensitivity and specificity of the PTSD sub-scales to discriminate trauma survivors with and without PTSD was examined in the sample of trauma survivors only (n = 152). For the PTSD sub-scale of the Pre-Sleep Cognition Scale ($PSCS_{PTSD}$), the AUC was 0.91, (95% CI = .88 to .96). A cut-off score of 3 correctly identified 91.2% (52 out of 57) of participants with PTSD (sensitivity), and 70.6% (161 out of 228) of those without PTSD (specificity). Trauma survivors were split according to whether they scored above or below the cut-off, and were compared on sleep quality (PSQI global score) and PTSD symptom severity without the sleep item (PDSwos). Mann-Whitney U tests showed that those with $PSCS_{PTSD}$ scores above 3 scored significantly higher on the PSQI, U = 4690, p< .001, r = 0.56, and on the PDSwos, U = 3649, p < .001, r = .69, with large effect sizes.

For the PTSD-sub-scale of the Pre-Sleep Behaviour Scale ($PSBS_{PTSD}$), the AUC was .73, (SE = .04; 95% CI = .65 to .82), indicating a fair test. A cut-off score of 2 correctly identified 82.1% trauma survivors with PTSD (46 out of 57; sensitivity), and 50.9% (112 out of 228) of trauma survivors without PTSD (specificity). A Mann-Whitney U test showed that those scoring 2 or above on the $PSBS_{PTSD,}$ reported higher PDSwos, U =

2772, $p < .001$, $r = .33$, and PSQI global scores, U = 4009, $p < .001$, $r = .35$, with medium effect sizes.

Trauma survivors with good vs. bad sleep: Comparing the sensitivity and specificity of the Pre-Sleep Cognition Scale and Glasgow Content of Thought Inventory

The sensitivity and specificity of the Glasgow Content of Thought Inventory and the Pre-Sleep Cognition Scale to correctly identify trauma survivors with and without sleep problems was examined. The established GCTI cut-off of 42, which has previously correctly identified 100% of individuals with insomnia (sensitivity) (Harvey & Espie, 2004), was used in the sample of trauma survivors (n = 152). Using this cut-off, the GCTI correctly identified 80.90% (72/89) of poor sleepers (sensitivity) and 79.4% (50/63) of good sleepers (specificity) (according to the PSQI). The insomnia and PTSD sub-scales of the Pre-Sleep Cognition Scale were combined to produce an overall sum-score (PSCSsum). A PSCSsum cut-off of 10 correctly identified 88.8% (79/89) of poor sleepers (sensitivity), and 69.8% (44/63) of good sleepers (specificity). The scales were also examined in the PTSD group only (n = 57). The GCTI (cut-off of 42) correctly identified 88.2% (45/51) of poor sleepers (sensitivity) and 50% (3/6) of good sleepers (specificity). A PSCSsum cut-off of 15 correctly identified 92.2% (47/51) of poor sleepers (sensitivity) and 66.7% (4/6) good sleepers (specificity). These results indicates that in trauma survivors (with and without PTSD) the sensitivity of the GCTI for detecting poor sleepers was lower than has previously been reported in people with insomnia, and slightly lower than the sensitivity of the Pre-Sleep Cognition Scale, although the GCTI had higher specificity. In people with PTSD, the GCTI still had good sensitivity for detecting poor sleepers, and slightly lower sensitivity and specificity than the Pre-Sleep Cognition Scale. This suggests that adding PTSD-related cognitions results in a higher sensitivity of pre-sleep cognition measures for detecting poor sleepers in a PTSD population.

Discussion

The present study described the development and initial validation of two measures to assess both PTSD-related and insomnia-related pre-sleep cognitive activity and behaviours. Further, it investigated if there were PTSD specific pre-sleep cognitions and behaviours that related to poor sleep and discriminated people with PTSD from those with insomnia, and depression. Notably, this is the first known study to use measures typically used in insomnia research with a PTSD population, and to measure insomnia and PTSD-related pre-sleep cognitive activity in PTSD.

Summary

Overall, the Pre-Sleep Cognition Scale had good psychometric properties. The insomnia sub-scale discriminated those with poor and good sleep and the PTSD sub-scale discriminated trauma survivors with and without PTSD. The combined sum-score of the Pre-Sleep Cognition Scale (both sub-scales) showed good sensitivity for detecting sleep problems in trauma survivors, and within a PTSD population, and this sensitivity was slightly higher than the sensitivity of an established measure of pre-sleep cognitive activity in insomnia (GCTI), although both discriminated well. People with PTSD reported pre-sleep cognitive activity and behaviours that were specific to PTSD, which were associated with worse sleep, longer sleep onset latencies, and elevated pre-sleep arousal. The Pre-Sleep Behaviour scale showed low internal consistency suggesting low homogeneity of items, but good test-retest reliability and some discriminant validity. The utility of the Pre-Sleep Cognition Scale for measuring pre-sleep cognitive activity frequency and content in PTSD is supported, although replication of the psychometric properties in an independent sample is required.

Pre-Sleep Cognition Scale: psychometric properties and associations with existing measures

Factor analysis resulted in the extraction of two factors, which confirmed the insomnia ($PSCS_{INSOM}$), and PTSD ($PSCS_{PTSD}$) sub-scales. The insomnia sub-scale assessed pre-sleep cognitions commonly reported as interfering with sleep in people with insomnia (Harvey & Espie, 2004), that had kept the respondent awake while trying to fall asleep, such as '*Everyday worries about work, or home life*'. The PTSD sub-scale assessed pre-sleep cognitive activity specific to PTSD that had kept them awake while trying to fall asleep, such as '*Being vulnerable if I sleep'* or *'Dwelling on how my life has been changed by the trauma'.* Both the insomnia and PTSD related pre-sleep cognition sub-scales had good test-retest reliability. Both sub-scales had good internal consistency indicating that items on each sub-scale were measuring one underlying construct, and good concurrent validity, correlating highly with the Glasgow Content of Thought Inventory, an existing validated measure of pre-sleep cognitive activity in insomnia (Harvey & Espie, 2004).

Both Pre-sleep Cognition sub-scales also had good construct validity, as insomnia and PTSD pre-sleep cognitions each correlated positively with more severe sleep problems (PSQI global score), longer reported sleep onset times, and increased reported pre-sleep cognitive (PSAS-cog) and physiological (PSAS-som) arousal. This means that participants with a greater frequency of pre-sleep insomnia or PTSD-related cognitions also reported higher pre-sleep arousal and more severe sleep difficulties. This demonstrates construct validity as it is consistent with findings from previous studies that pre-sleep cognitive activity is associated with poor sleep and insomnia (Harvey, 2002; 2003; 2010; Harvey et al., 2005; Harvey & Espie, 2004), and interferes with sleep by prolonging sleep onset latency (Ansfield et al., 1996; Gross & Borkovec, 1982). The

association between PTSD pre-sleep cognitions, sleep disturbance, and sleep onset time suggests there are PTSD-specific pre-sleep cognitions (such as worrying about being vulnerable while asleep), which are associated with poor sleep in PTSD, although this does not indicate causality. However, it is important to note that the wording of the scale (as adapted from previous measures) asks the respondent 'how often has each thought kept you awake'. Therefore, while associations between the scale and measures of sleep disturbance and sleep onset latency could reflect an association between more pre-sleep cognitions and longer sleep onset, it may also reflect a confound in that respondents are asked how often the thoughts have *kept them awake*, rather than how often they occurred, and so may instead be associated with longer sleep onset latencies and sleep disturbance for this reason. However, the association between pre-sleep cognitive activity and higher pre-sleep arousal does support the construct validity of the scale, and this is also consistent with findings from previous studies in insomnia (Harvey & Espie, 2004; Wuyts et al., 2012), and further suggests that PTSD-related pre-sleep cognitions are also related to elevated mental and physiological arousal, which is associated with poor sleep in PTSD, as in insomnia (see Espie, 2002; Harvey & Espie, 2004). However the psychometric properties of the scale would need to be replicated, before conclusions could be drawn about associations with sleep and arousal.

Pre-sleep cognition scale: Group discrimination

Both sub-scales of the Pre-Sleep Cognition Scale showed good discriminative validity. More frequent insomnia-related cognitions successfully discriminated poor sleepers from good sleepers with good sensitivity and specificity suggesting, consistent with the literature, that higher pre-sleep cognitive activity can discriminate people with insomnia from good sleepers (Harvey, 2002; 2010; Harvey & Espie, 2004). Individuals with depression, insomnia and PTSD reported equally frequent insomnia-related

cognitions, and significantly more than the control groups. These results show similar frequencies of insomnia-related pre-sleep cognitive activity in insomnia, depression and PTSD. The PTSD group reported more frequent PTSD-related pre-sleep cognitions than any other group, which discriminated the PTSD group from other clinical groups associated with poor sleep, and could discriminate trauma survivors with and without PTSD, and trauma survivors with good and bad sleep, with good sensitivity and specificity. This provides preliminary evidence that the Pre-Sleep Cognition Scale may be a tool to discriminate people with insomnia with and without PTSD, although replication of the psychometric properties is required.

In sum, the findings provide initial evidence in support of the psychometric properties of a measure to assess the frequency of pre-sleep cognitions in PTSD. The findings suggest that there are similarities and differences between pre-sleep cognition content in PTSD and insomnia, but that both types of content are associated with poor sleep. This is consistent with suggestions that similar mechanisms may underlie insomnia with or without a mental health problem (Kohn & Espie, 2005).

Pre-Sleep Behaviour Scale: Psychometric properties and associations with existing measures

In contrast, the Pre-sleep Behaviour Scale had weaker psychometric properties. Factor analysis was not appropriate, as the majority of the scale items did not correlate, indicating a heterogeneous set of items. This was also reflected in the relatively low internal consistency of both sub-scales. This was expected, from the results of previous sleep hygiene scales which have also shown poor internal consistency (Blake & Gomez, 1998; Brown, Buboltz, & Soper, 2002; Lack & Rotert, 1986), and from recommendations that test-retest reliability and construct validity are more appropriate

indicators of scale utility for measures of sleep hygiene (Mastin et al., 2006). Both sub-scales had good test-retest reliability. However, correlations between the sub-scales and measures of sleep, sleep onset latency and daytime sleepiness (PSQI and $PSBS_{INSOM}$ r = .18; $PSBS_{PTSD}$ r = .25) were low, and lower than those found in previous studies (e.g., PSQI and Sleep Hygiene index, r = .48; Mastin et al., 2006) indicating relatively poor construct validity for both sub-scales. Previous sleep hygiene measures associated with poor sleep have often included items that overlap with measures of cognitive activity (Gellis & Lichstein, 2009), which may have contributed to previous stronger associations between sleep hygiene measures, poor sleep and reported arousal. Cognitive items were not included in the PSBS due to overlap with the $PSCS_{INSOM,}$ which may in part explain the poorer psychometric properties of the PSBS compared to previous scales. Previous authors have suggested that the same sleep hygiene behaviours may have different consequences for good and poor sleepers (Kohn & Espie, 2005). This may also be true here; the same frequency of sleep hygiene behaviours may affect healthy controls and poor sleepers with and without a mental health problem differently, impacting associations between the scale and sleep measures. Both the insomnia and PTSD sub-scales were associated with pre-sleep physiological arousal, consistent with previous studies relating poor sleep hygiene and somatic arousal (Kohn & Espie, 2005).

Pre-Sleep Behaviour Scale: Group discrimination

Group comparisons showed that the insomnia sub-scale effectively discriminated good and poor sleepers, with poor sleepers reporting worse sleep hygiene. More insomnia related behaviours discriminated PTSD and depression from controls, but could not discriminate the clinical groups from each other (insomnia, PTSD, depression), or insomnia from controls. The PTSD sub-scale showed slightly better discriminant validity, as higher scores discriminated PTSD from depression and insomnia, and from

both control groups, showing that participants with PTSD reported more PTSD related pre-sleep behaviours than other groups. It could not discriminate depression from insomnia, or either from the control groups. Sensitivity and specificity were low for both sub-scales, suggesting that although the scale may have some clinical use, it would not be an appropriate tool for diagnostic purposes.

In sum, the scale may have some utility in measuring the frequency of pre-sleep behaviours, particularly PTSD related, for descriptive purposes or clinical use, but would not be useful diagnostically, or as a research tool due to its weak psychometric properties.

Other group differences

There were a number of other differences between the clinical groups that were not the focus of this study, but are worth noting, as they may have some theoretical and clinical implications. Overall sleep quality was lowest in the PTSD group. The clinical groups did not differ in frequency of insomnia cognitions, but PTSD-related pre-sleep cognitive activity, PTSD symptoms (which include general hyperarousal), and pre-sleep somatic and cognitive arousal were higher in PTSD than insomnia but did not differ between PTSD and depression, and PTSD-related pre-sleep cognitions were higher in PTSD than depression and insomnia. This is consistent with studies showing that psychopathology may be associated with higher pre-sleep arousal, compared to insomnia (Kohn & Espie, 2005). It is perhaps also consistent with suggestions that insomnia alone and in PTSD may have both similarities and differences (Ulmer et al., 2011). These findings could suggest that the combination of elevated PTSD symptoms, pre-sleep arousal, and pre-sleep cognitive activity of both insomnia- and PTSD-related content could lead to worse sleep problems in PTSD compared to insomnia and other clinical groups associated with

poor sleep (depression). However these group differences do not indicate the direction of effects. In the present study, people with depression also had more frequent PTSD-related pre-sleep cognitions than those with insomnia, which could possibly be explained by higher mean sub-clinical PTSD symptom severity in traumatised individuals with depression (PDS = 16.09) in comparison to insomnia (PDS = 10.71).

In sum, the findings of associations between pre-sleep cognitions, arousal and poor sleep in this study, support previous associations between pre-sleep cognitive activity and insomnia (Harvey, 2002; Harvey et al., 2005), and expand this to apply to sleep problems associated with a mental health problem such as PTSD (see also Kohn & Espie, 2005). However, conclusions must be interpreted cautiously as this study only provides the first preliminary evidence of the psychometric properties of the Pre-Sleep Cognition Scale, and replication is required.

Limitations and Future directions

The present study had a number of limitations. Firstly, confirmatory factor analysis was not conducted. Recruiting an independent sample and confirming the factor structure of the new measures would be important. Secondly, measures of self-reported rather than objective arousal were used, and so further investigation is required to investigate whether associations between the Pre-Sleep Cognition Scale and somatic and cognitive arousal are also evidenced in objective arousal measures in PTSD. Similarly, sleep was self-reported rather than objectively measured, and further investigation is required to determine whether the Pre-Sleep Cognition Scale and Pre-Sleep Behaviour Scale are also related to objective measures of poor sleep. Thirdly, clinical diagnoses of insomnia and depression were not confirmed with clinician assessment, and so differences may exist between individuals with diagnosed insomnia and depression, particularly those seeking

treatment, compared to the participants reporting insomnia and depression in this study. This study only provides initial evidence of the psychometric properties of the Pre-Sleep Cognition Scale, therefore future research should aim to replicate these findings, and investigate the psychometric properties of the Pre-Sleep Cognition Scale in clinical, ideally treatment-seeking populations. A number of experts have recommended including measures of pre-sleep cognitions, behaviours and arousal with sleep outcome measures when investigating the experience of insomnia (Kohn & Espie, 2005), and when investigating the effects of treatment on sleep disturbances (Harvey, 2002). Therefore future studies investigating the effect of sleep or of PTSD treatment on insomnia in PTSD could include measures of PTSD-related and insomnia-related pre-sleep cognitions. This would help determine whether insomnia and PTSD treatments, both of which improve sleep in PTSD (Gellis & Lichstein, 2009; Belleville et al., 2009; 2011; Lommen et al., 2015; Margolies et al., 2013; Talbot, 2014; Ulmer et al., 2011), also produce change in pre-sleep cognitions after PTSD treatment. For example, it is possible that trauma-focused therapy for PTSD improves PTSD but not insomnia-related cognitions. Persistence of insomnia-related pre-sleep cognitive activity could theoretically contribute to the persistence of clinical sleep problems after otherwise effective PTSD treatment (Belleville et al., 2009; Galovski et al., 2009; Gutner et al., 2013; Zayfert & DeViva, 2004). Finally, as noted, a limitation of the Pre-Sleep Cognition Scale is the potential confound between the wording of the scale and measures of sleep disturbance. It would be of interest to investigate associations between the Pre-Sleep Cognition Scale and measures of sleep disturbance when the wording of the measure is adapted to ask how often each of the cognitions have occurred while trying to fall asleep, rather than asking how often they have kept you awake. This would be interesting to determine if it is the presence or frequency of the cognitions that is associated with poor sleep, or whether the frequency of certain cognitions may be similar

between groups, but be associated with poor sleep only in certain groups or individuals within groups.

Conclusion

In conclusion, this chapter presented the development and preliminary validation of two measures to assess both PTSD-related and insomnia-related pre-sleep cognitive activity (Pre-Sleep Cognition Scale) and behaviours (Pre-Sleep Behaviour Scale). The Pre-Sleep Cognition Scale had good psychometric properties, and PTSD-related cognitions, discriminated people with PTSD from insomnia and depression, and correlated with arousal and poor sleep. The Pre-Sleep Behaviour Scale had weak psychometric properties, and may have some utility for descriptive purposes and perhaps clinical purposes to measure maladaptive behaviours that could be targeted in treatment, but is not recommended for diagnostic use. Future studies should aim to further investigate the psychometric properties of the Pre-Sleep Cognition Scale in clinical samples, and examine the contribution of pre-sleep cognitive activity to sleep problems in PTSD, and investigate the impact of PTSD treatment on pre-sleep cognitions. This may enhance understanding of the nature of insomnia and factors contributing to poor sleep in PTSD, which may help to refine treatments targeting sleep in PTSD, and the persistence of sleep problems following PTSD treatment.

Chapter 5: The relationship between trauma exposure and PTSD with objective and subjectively measured sleep disturbances, physiological arousal and pre-sleep cognitions.

Introduction

As outlined previously, research has shown that sleep problems, such as insomnia, are common in PTSD and typically persist after CBT for PTSD (Belleville et al., 2011; Galovski et al., 2009; Gutner et al., 2013), when other PTSD symptoms have resolved (Zayfert & DeViva, 2004). A number of explanations have been proposed to account for persistent sleep problems after otherwise effective PTSD treatment, including factors known to maintain general insomnia, such as persistent hyperarousal (Zayfert & DeViva, 2004) and pre-sleep cognitive activity (Chapter 4). However, little is known about their role in sleep problems in PTSD, and further investigation is required. Comparing trauma survivors with and without PTSD, and non-traumatised controls would help to discover factors associated with poor sleep in PTSD, which may be implicated in the maintenance of the disorder. Better understanding the nature of sleep problems in PTSD and its contributing factors could inform on how to improve residual sleep problems after PTSD therapy.

As previously described in Chapters 1 and 4, pre-sleep cognitive activity is implicated in the maintenance of insomnia (Harvey, 2002; Harvey & Espie, 2004). Chapter 4 showed that more frequent pre-sleep cognitive activity was associated with more severe sleep disturbances in PTSD. People with PTSD reported frequent pre-sleep cognitive activity similar to the cognitions reported in insomnia. In addition, cognitions with

content that was specific to PTSD were associated with worse sleep, and it was suggested that they may play a role in maintaining insomnia in PTSD. Hyperarousal is key in many models of insomnia (Bonnet & Arand, 1997b; Espie et al., 2006; Riemann et al., 2010), and is also a symptom of PTSD (APA, 2013), and proposed to be a neurobiological underpinning of insomnia in PTSD (Germain, 2013; Sinha, 2016). In line with this, Chapter 4 showed that people with PTSD reported elevated pre-sleep cognitive and somatic arousal compared to controls, and more severe sleep disturbances. However, Chapter 4 did not include objective measures of sleep or arousal, and PTSD diagnosis was determined from self-report measures. As outlined in Chapter 1, despite consistent evidence of subjective sleep problems in PTSD, evidence of objective sleep disturbance is mixed, possibly due to differences in the measurement environment, such as home-based versus laboratory recordings (Germain et al., 2006). For example, PTSD patients have (anecdotally) reported having slept better when a researcher is 'on guard' in lab settings (Woodward, Bliwise, Friedman, & Gusman, 1996a), than at home, where objective sleep initiation and maintenance problems are more commonly detected (Germain et al., 2006; Herbst et al., 2010). This emphasises the importance home-based sleep assessment in PTSD. Further research that includes clinician diagnosis, and home-based objective indicators of sleep and arousal would add to the findings of Chapter 4, by investigating whether group differences are also evidenced in objective measures and when diagnosis is clinician assessed.

As described in Chapter 1, basal diurnal cortisol and heart-rate can be used as objective indicators of hyperarousal, and alterations in both have been found in PTSD. Cortisol is often measured as an indicator of hypothalamic-pituitary adrenal gland (HPA) axis (stress response system) functioning, which is thought to be dysregulated in PTSD (Yehuda et al., 1990). Therefore cortisol can be conceptualised as an indicator of

hyperarousal, and is referred to as such in this chapter. However it should be noted that cortisol is not a direct measure of hyperarousal. Rather, it reflects the activity of the HPA-axis and activation of the stress response system. The HPA-axis has also been associated more generally with sleep regulation (Saper et al., 2005). Cortisol is secreted with a circadian rhythm, peaking 30-60 minutes after waking (Pruessner et al., 1997), and then decreasing over the course of the day (Keenan et al., 2004). PTSD has been associated with lower cortisol compared to controls, particularly in the afternoon and evening (Yehuda et al., 1996), and in the first half of the night (van Liempt, Arends, Cluitmans, Westenberg, Kahn, & Vermetten, 2013a). These lower levels are thought to reflect dysregulation of the HPA-axis, as low cortisol may result from evidenced increases in number and sensitivity of glucocorticoid receptors in the hypothalamus, resulting in an increased feedback sensitivity (Yehuda, 2006; Yehuda, Boisoneau, Mason, & Giller, 1993). But the results of studies are mixed, as some studies have instead found higher cortisol (which may also indicate dysregulation of the HPA-axis), and some have found no differences in cortisol between people with PTSD and controls (see Klassens et al., 2012; Meewisse et al., 2007 for review). However, studies have been criticised for combining traumatised and non-traumatised controls into one control group for comparison to PTSD. Cortisol differences are more commonly found between PTSD and non-traumatised controls, than between PTSD and traumatised controls (see Meewisse et al., 2007). Alterations in the HPA-axis have also been described in healthy traumatised controls compared to non-traumatised controls (de Kloet et al., 2007; Klaassens et al., 2010), suggesting that trauma exposure itself may alter HPA-axis functioning, and emphasising the importance of separating trauma exposed and non-exposed control groups. Lower cortisol (HPA-axis dysregulation) has also been associated with more severe PTSD symptoms (Olff, Guzelcan, de Vries, Assies, & Gersons, 2006; Wessa et al., 2006), and dysregulated HPA-axis activity has been

associated with fragmented sleep in PTSD (van Liempt, Arends, Cluitmans, Westenberg, Kahn, & Vermetten, 2013a), perhaps due to awakenings interfering with the benefits of sleep, and resulting in alterations in stress hormones (Steiger, 2007). Heart-rate and heart-rate variability (HRV) can be used as non-invasive measures of autonomic arousal, and sympathetic nervous system involvement, which has been associated with sleep regulation (Saper et al., 2005). In healthy individuals the parasympathetic nervous system is dominant, reflected in low resting heart-rate and high HRV. Altered HRV during sleep has been found in insomnia (Bonnet & Arand, 1997a; Spiegelhalder et al., 2011), supporting theories that persistent hyperarousal disrupts sleep in people with insomnia (Bonnet & Arand, 1997b; 2010; Espie et al., 2006; Perlis et al., 1997; Riemann et al., 2010). Similarly, higher autonomic arousal during sleep has been found in PTSD, reflected in higher nocturnal heart-rate in PTSD, compared to a mixed control group (Woodward et al., 2009), and compared to traumatised controls (van Liempt, Arends, Cluitmans, Westenberg, Kahn, & Vermetten, 2013a). Higher sympathetic activation (altered HRV) has also been found during sleep in people with PTSD compared to traumatised controls (Kobayashi et al., 2014; Mellman et al., 2004). However, one recent study found increased heart-rate, but after controlling for REM sleep percentage, did not find increased autonomic nervous system (ANS) arousal during sleep in PTSD compared to traumatised controls (Kobayashi, Lavela, Bell, & Mellman, 2016a).

Aims of the present study

This chapter presents a study designed to further investigate factors that may be associated with sleep disturbances in PTSD, such as pre-sleep cognitive activity and hyperarousal (including nocturnal autonomic arousal, i.e. HRV). It builds on the

findings of Chapter 4 by including objective measures of both sleep and arousal, and by using clinician assessment to determine PTSD diagnosis.

Research questions and hypotheses

To address these aims, the study specifically investigated the following questions;

1) Do people with PTSD and trauma exposed and non-exposed controls without PTSD differ in sleep disturbance severity, pre-sleep cognitive activity and objective physiological arousal during the day (cortisol) and during sleep (HRV)?
2) Are measures of objective arousal associated with pre-sleep cognitive activity, PTSD symptoms and sleep in people with PTSD?
3) Does pre-sleep cognitive activity mediate the relationship between reported sleep disturbance severity and PTSD symptoms in PTSD?

In line with the literature and the results of previous Chapters, it was hypothesised that:

1) People with PTSD will show more severe sleep problems, pre-sleep cognitive activity, and higher arousal (reflected in lower daytime cortisol levels, and altered HRV during sleep) than trauma exposed and non-exposed controls.
2) Indicators of hyperarousal (cortisol levels, nocturnal HRV) will be associated with worse sleep, and more pre-sleep cognitive activity.
3) Pre-sleep cognitive activity will account for significant variance in sleep disturbance, partly mediating the relationship between PTSD symptoms and sleep.

Methods

Participants

A total sample of 115 participants (80 women) took part in the study (Mean age: 32.73, SD: 11.73), which included 30 non-traumatised control participants, 43 trauma-exposed participants without PTSD, and 42 people with PTSD (comprised of 30 treatment-seeking PTSD patients recruited from NHS services, and 12 recruited from the community). The sample size was selected based on power calculations using effect sizes observed in previous studies (e.g., Pietrzak et al., 2010; medium effect size) to give a power of 95% to detect differences in self-reported sleep between groups at $\alpha = .05$. Power analysis determined that a sample size of 130 was required, but 115 were recruited which gave an actual power of 92.23% to detect group differences with a medium effect size. Inclusion criteria for all groups were that participants were aged between 18 and 65, could read and write in English, had no history of or current bipolar or psychosis, no current substance or alcohol dependence, and if they were taking psychotropic medication had been on a stable dose for at least 2 months. Additional inclusion criteria for the PTSD group was that they had experienced a traumatic event as defined by Criterion A of the DSM-5 (APA, 2014), and had a current diagnosis of PTSD. Inclusion criteria for the control group was that they had never experienced a Criterion A traumatic event, and reported no current mental health problems. Inclusion criteria for the trauma control group was that they had experienced a Criterion A traumatic event, but did not meet criteria for a current diagnosis of PTSD. Table 5.1 shows demographic characteristics and comparison between groups, PTSD and depression symptom severity for each group, and trauma characteristics for the PTSD and trauma control participants. The groups did not differ in age, gender distribution and medication use, or type of psychotropic medication use, and among trauma

survivors (n = 85), there was no difference in trauma type (interpersonal versus non-interpersonal) between PTSD and trauma controls (see Table 5.1). The groups differed on ethnicity distribution, as the PTSD group had more people of ethnic minority than controls or trauma controls. The effect of ethnicity (caucasian vs. ethnic minority) on sleep disturbance (PSQI), cortisol, and HRV was checked, by entering ethnicity as a covariate into each of these analyses. There was no significant main effect or interaction with experimental group (control, trauma, PTSD), and so ethnicity was not included as a covariate in analyses. The distribution of participants reporting physical health conditions was also higher in the PTSD group. As with ethnicity, the effect of physical health problems on sleep (PSQI), cortisol, and HRV were checked by entering health problems as a covariate into the analyses. Physical health problems also had no main effect on any of the measures, and no interaction with group, and so was not included as a covariate in analyses. Analyses without ethnicity or physical health problems as a covariate are reported.

PTSD symptom severity (PDS) was compared between trauma survivors with and without PTSD. People with PTSD had significantly higher PDS scores compared to trauma survivors without PTSD, $t(74) = 6.96$, $p < .001$**.** People with PTSD recruited from the community and treatment-seeking patients did not differ on PTSD symptom severity $t(39) = 0.51$, $p = .62$; BDI, $t(36) = .74$, $p = .47$, or sleep severity (PSQI global score) $t(39) = .63$, $p = .53$.

Recruitment and ethics

The study received NHS ethical approval from the South-Central Oxford C Research ethics committee (Ref 14/SC/0198). Recruitment began in June 2014 and ended in April 2016. Control and traumatised control participants were recruited via adverts within the

University of Oxford, on the departmental website, and on online community forums in Oxford, which were 'Daily info' and 'Gum-tree'. Participants who responded to adverts completed a set of short online screening questionnaires to determine whether they may be suitable for one of the study groups. Participants with PTSD were recruited from participating NHS treatment clinics in London and Oxford. These were the 'Centre for Anxiety Disorders and Trauma', and Lambeth and Lewisham IAPT services, all within the South London and Maudsley NHS trust, and the Oxford Centre for Anxiety Disorders and Trauma, at the University of Oxford. As part of routine clinical care at each clinic, participants provided consent to be contacted about on-going research studies. Patients who had consented and met inclusion criteria for the study were contacted via phone about the research study, and received a full study information sheet in the post. Participants provided full informed consent at the research session. Traumatised controls meeting criteria for PTSD at interview were re-allocated to the PTSD participant group, and referred for PTSD treatment where appropriate.

Table 5.1. Demographic information and PTSD and depression symptom severity for each group, and statistical comparison of groups on distributions (x^2) and mean scores (F or *t*).

	CONTROL (N = 30)	**TRAUMA-CONTROL (N = 43)**	**PTSD (N = 42)**	**STATISTICAL SIGNIFINCANCE *(x^2, F, or t, p)***
	M (SD)			
AGE (years)	31.17 (10.38)	34.02 (14.01)	32.51 (9.93)	*F*(2, 109) = .53, *p* =.59
	N (Valid %)			
GENDER				
Women	23 (76.7%)	31 (72.1%)	26 (61.9%)	
Men	7 (23.3%)	12 (27.9%)	16 (38.1%)	$x^2(2) = 2.1, p = .37$
Education (years)	17.43 (2.85)	16.40 (2.65)	15.63 (3.54)	*F*(2, 107) = 2.10, *p*=.06
ETHNIC BACKGROUND	N (%)			
Caucasian	29 (96.7%)	35 (81.4%)	28 (66.6%)	
Ethnic minority	1 (3.3%)	8 (18.6%)	14 (33.4%)	$x^2(2) = 9.93, p = .007$
PTSD SYMPTOMS & MOOD	Mean (SD)			
PDS (Trauma survivors; n = 85)[2]		8.4 (6.78)	35.10 (11.45)	*F*(2, 105) = 114.55, *p*<.001
BDI	4.78 (5.59)	7.93 (7.43)	23.21 (9.02)	*F*(2, 107) = 58.72, *p* <.001
MEDICATION USE	N (%)			
No medication	18 (60%)	30 (69.8%)	22 (52.4%)	
Non-psychotropic medication	10 (33.3%)	10 (23.3%)	10 (23.8%)	
Use of psychotropic medication (all)	2 (6.7%)	3 (7.0%)	10 (23.8%)	Med use: $x^2(4)$ = 7.76, *p* = .10
Psychotropic: SSRIs	1 (3.35%)	3 (7%)	8 (19.05%)	
Psychotropic: Benzodiazepines	1 (3.35%)	0	1 (.02%)	
Sleeping medication (Narcotic)	0	0	1 (.02%)	Type of Psychotropic: $x^2(4) = 7.39, p = .12$
PHYSICAL HEALTH PROBLEMS				
Physical health problems	2 (8%)	5 (11.6%)	14 (35.0%)	$x^2(2) = 9.95, p = .007$
SMOKER				
Smoker	2	3	8	$x^2(2) = 3.96, p = .14$
TRAUMA TYPE (trauma survivors; n = 85)				
RTA		6 (14%)	8 (20.5%)	
Non-Sexual Assault[1]		5 (11.6%)	3 (7.7%)	
Sexual assault[1]		5 (11.6%)	10 (25.6%)	
Accident		2 (4.7%)	0	
Natural Disaster		0	1 (2.6%)	
Military		1 (2.3%)	0	
Witnessing Others die/seriously hurt		5 (11.6%)	1 (2.6%)	
Childhood abuse[1]		3 (8.0%)	5 (12.8%)	
Sudden, traumatic loss		7 (16.3%)	1 (2.6%)	
Life-threatening illness		3 (7.0%)	0	
Armed robbery[1]		1 (2.3%)	0	
Imprisonment		0	1 (2.6%)	
Other		5 (11.6%)	8 (20.5%)	*Interpersonal vs. non-interpersonal trauma: $x^2(1) = 1.59$, p = .26*
TRAUMA CHARACTERISTICS				
Time since Trauma (years)		10.12 (10.18)	8.23 (9.71)	t(78) =.85, *p* = .39

Note (Table 5.1.).

[1] Trauma type distribution was compared by collapsing groups into interpersonal[1] and non-interpersonal trauma types and comparing these.
[2] Due to missing data, the sample sizes were: Trauma, n = 35, PTSD, n = 41.
Trauma type and characteristics are for trauma survivors only (n= 85). Time since trauma was calculated as the time (years) from trauma to study participation date. Med use = comparison of groups on any medication use (psychotropic, non-psychotropic, no medication). Type of psychotropic = comparison of groups on type of psychotropic medication used (including narcotics).

Measures

Clinician Assessment

Clinician-administered PTSD Scale for DSM-5 (CAPS). The CAPS (Weathers et al., 2013) is a clinician-administered measure of the severity of PTSD symptoms. The CAPS was administered by the author of this thesis, and used to determine PTSD diagnosis according to DSM-5 criteria (APA, 2013), for trauma controls and participants with PTSD.

Symptom Measures

Life Events Checklist (LEC). The LEC (Foa et al., 1997) is a self-report questionnaire containing a list of stressful life events (including traumatic events) according to DSM criteria. Respondents indicate whether they have experienced each event in their lifetime. The LEC was administered to determine whether participants had experienced a Criterion A traumatic event, according to DSM-5 criteria (APA, 2013), and to identify a negative life event experienced by non-traumatised control participants (see Appendix E for scale).

Posttraumatic Diagnostic Scale (PDS). The PDS (Foa et al., 1997) is a validated self-report measure assessing the severity of DSM specified PTSD symptoms. Participants

rate the frequency of each symptom over the past week from 0 (*Not at all*) to 3 (*5 or more times a week/nearly every day*). Items are summed, and higher scores indicate more severe symptoms. The 17-item DSM-IV (APA, 2000) version of the PDS was administered, along with four additional items assessing severity of DSM-5 (APA, 2013) specified PTSD symptoms. Sum scores of the 20 DSM-5 relevant items will be reported (range: 0–60). A PDS sum score without the sleep item (PDSwos) was also computed for use in analyses (range: 0–57).

Beck Depression Inventory (BDI). The BDI (Beck et al., 1961) is a widely used 21-item questionnaire assessing the severity of depressive symptoms over the previous two weeks. Scores range from 0–63, higher scores indicate more severe depression.

Posttraumatic Cognitions Inventory (PTCI). The 20-item short version of the PTCI (Foa, Ehlers, Clark, Tolin, & Orsillo, 1999b), was used to assess excessively negative appraisals of the trauma and its consequences. Respondents rate their agreement with each appraisal from 1 (*totally disagree*) to 7 (*totally agree*). Items are summed to produce a total score (range: 1–140), with higher scores indicating more maladaptive appraisals. The measure has been found to have good internal consistency (Cronbach's alpha = .97) and psychometric properties (Foa, Ehlers, Clark, Tolin, & Orsillo, 1999a)

Pre-Sleep Cognition Scale (PSCS) (Woodward & Ehlers, in prep; see Chapter 4, Appendix C). The PSCS is 21-item scale measuring the frequency of pre-sleep cognitions during sleep onset. Respondents rate how often each thought kept them awake over the previous week on a scale from 0 (*Not at all*) to 3 (*5 or more times a week/nearly every day*). Items are summed (range: 0–63), and higher scores indicate greater frequency of interfering pre-sleep cognitive activity. The scale includes two

sub-scales assessing insomnia related pre-sleep cognitions ($PSCS_{INSOM,}$ range: 0–36) and PTSD related pre-sleep cognitions ($PSCS_{PTSD,}$ range: 0-27). The scale has been found to have good psychometric properties (see Chapter 4).

Subjective sleep measures

Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989). The PSQI was used to measure the overall severity of sleep disturbances. It is a 19-item scale, widely used to assess the global severity of sleep disturbances. Respondents rate the occurrence of sleep disturbances over the previous month on a scale from 0 (*not during the last month*) to 3 (*three or more times a week*). The scale includes 7 sub-scales assessing different aspects of sleep dysfunction, which sum to a global score ranging from 0-21, where higher scores indicate more severe sleep disturbances. The scale has been found to have good psychometric properties, and a cut-off score of greater than 5 is commonly used to indicate clinically significant sleep disturbances (Buysse et al., 1989), and insomnia with a sensitivity of 98.7% and specificity of 84.4% (Backhaus, Junghanns, Broocks, Riemann, & Hohagen, 2002).

Pittsburgh Sleep Quality Index Addendum for PTSD (PSQIA) The PSQIA (Germain et al., 2005) consists of seven items assessing the severity of PTSD related sleep disturbances over the past month (e.g., '*memories or nightmares of the trauma', 'severe anxiety or panic not related to traumatic memories'*). Respondents rate the frequency of each disturbance on a scale from 0 (*not during the last month*) to 3 (*three or more times a week*), summed to produce a score ranging from 0-21. Higher scores indicate more severe PTSD related sleep disturbances (Germain et al., 2005).

Sleep Diary. The sleep diary was used to prospectively monitor participants' sleep over

seven days. The sleep diary was adapted from the Pittsburgh Sleep Diary (Monk et al, 1994), and followed the recommendations for sleep research (Buysse, Ancoli-Israel, Edinger, Lichstein, & Morin, 2006) and the prospective self-monitoring of sleep as outlined by Carney and colleagues (2012). Participants completed the diary twice a day, once in the morning (answering questions about their sleep the previous night) and evening (answering questions about naps, exercise, medication use (type, dose, time), drug and alcohol use that day). The diary questions enabled the calculation of the following sleep parameters; total sleep time (TST; time in bed minus time spent trying to fall asleep, and awake after sleep onset), sleep onset latency (SOL; time taken to fall asleep) sleep efficiency ((time asleep/time in bed) x 100), sleep quality (*'overall how well did you sleep'* rated from 0 '*not at all well'* to 100 '*extremely well'*) and duration of wake after sleep onset (WASO). Additional questions were added which asked respondents to rate *how anxious they were about going to bed that night* (from 0 '*not at all'* to 100 '*extremely'*); to report how many nightmares they had ('*How many nightmares did you have in total last night?'*); whether the nightmare was trauma or non-trauma-related (*'Were your nightmares a memory of or related to your trauma?'* yes/no); and rate how distressed they were in response to nightmares (from 0 '*not at all*' to 100 '*extremely*'). Control participants reported nightmares, and nightmares related to the negative event they had identified on the LEC. Nightmare frequency was calculated as the number of days nightmares were had on for nightmares that were trauma related and non-trauma related. See Appendix F for sleep diary instructions and items included in these analyses.

Objective sleep measures

Actigraphy. Actigraphy was used as an objective measure of sleep and wake.

Participants wore an actigraphy wristband (GeneACTIV; ActivInsights, Ltd., Kimbolton, UK) on their non-dominant wrist for seven days while completing the sleep diary. Actigraphy is a commonly used tool in the assessment and treatment of insomnia (Buysse et al., 2006; Ancoli-Israel et al., 2003). It uses an accelerometer to measure motion, from which sleep and wake can be estimated. Actigraphy has been used with people with PTSD (see Cox & Olatunji, 2016; Kobayashi et al., 2014), and has shown consistency with sleep diary reports in a PTSD population (Kobayashi et al., 2012). Sampling frequency was set at 100 Hz, and raw data was extracted in 1-minute epochs, using the GeneACTIV PCsoftware (ActivInsights, Ltd., Kimbolton, UK), and analysed using a novel algorithm (Tsanas,..Woodward et al., in prep), developed in MATLAB (version R2016a, The MathWorks, Inc., Natick, Massachusetts). The algorithm automatically analysed raw data indices of tri-axial movement (motion and arm angle in three dimensions), temperature, and light exposure, to estimate sleep-onset and sleep-offset times from which objective estimates of time in bed, total sleep time, and sleep efficiency were calculated. The GeneACTIV device z-axis has been validated against traditional actigraphic counts measured using the Actiwatch, showing 'almost perfect' agreement between sleep parameter estimates, although tri-axial measurement is recommended as a more advanced and accurate measure (Lindert & Van Someren, 2014).

Objective arousal measures

Heart-rate and cortisol were assessed as indicators of physiological arousal.

Heart-rate. Heart-rate was assessed over a 24-hour period (including over-night) in patients own homes, using a Polar RS800CX (Polar Electro Oy, Kempele, Finland; 1000 Hz) ambulatory heart-rate monitor, which records inter-beat intervals (IBIs). The

device consists of a chest strap and a wireless watch receiver, worn on the wrist. Polar heart-rate devices are commonly used for research purposes, including with trauma exposed individuals (e.g., Ehring, Ehlers, Cleare, & Glucksman, 2008b), and have shown good reliability and validity compared to simultaneous electrocardiogram (ECG) recordings, correlating between 0.9 -1.0 (Engström, Ottosson, & Wohlfart, 2012; Weippert et al., 2010). For data analysis, a 5-minute segment was selected from the recording during actual sleep (selected to be 2 hours after sleep onset and confirmed as sleep against actigraphy). The sleep diary and actigraphy sleep parameters informed identification of sleep onset time. Raw data was extracted from the device using the Polar ProTrainer software (version 5, Polar Electro, Oy, Kempele, Finland), and exported to MATLAB (version R2016a, The MathWorks, Inc., Natick, Massachusetts) for data cleaning and analysis. To clean the data, samples were automatically processed to exclude non-reasonable heart-rate values (below 30 and higher than 200), followed by the use of mean filtering, which replaces non-reasonable values with values from the mean of the segment. The data was then visually inspected to confirm artefact removal. To evaluate heart-rate variability (HRV), the frequency domain method was used, by applying the fast-Fourier transformation (FFT) to the R-R interval (RRI) time-series, to calculate the spectral power of the low frequency (LF) range (.04 to .15 Hz) and high frequency (HF) range (.15 to .4 Hz), from which the LF/HF ratio was calculated. The HF range is mediated by the parasympathetic nervous system, and the LF/HF ratio indicates sympathovagal balance, with higher LF/HF ratio values indicating greater sympathetic dominance (Lahiri, Kannankeril, & Goldberger, 2008). In addition, mean heart-rate (HR) was calculated from the RRI time-series, for baseline and for the selected sleep segment.

Cortisol. Salivary cortisol was measured as an indicator of HPA-axis functioning, to assess arousal. To measure diurnal variation (short daytime profile) of free cortisol, participants collected their saliva samples in 7ml plastic bijou bottles (Sterilin) via the passive drooling method, at 8am, 4pm, and 10pm on the second measurement day, the day after the session. Samples were stored at -20°C, prior to analysis. Samples were analysed using a radioimmunoassay (assay analysis was conducted by Middleton, B. at the University of Surrey, method adapted from; Riad-Fahmy, Read, Gaskell, Dyas, & Hindawi, 1979; Seth & Brown, 1978), to assess free cortisol levels at each time point. The staff who conducted the assay analysis were blinded to group allocation. Analysis of cortisol concentration (nmol/l) was carried out in duplicate, and the duplicate mean was used in the analysis.

Procedure

Suitable participants attended the research session at the Institute of Psychiatry, Kings College London, or the Oxford Centre for Anxiety Disorders, University of Oxford, and then completed 7 days of home-based measurement after the session. Upon arrival participants completed a general demographic information sheet. Participants were given the actigraphy wristband to wear on their non-dominant hand for 7-days, and shown how to wear the polar heart-rate monitor, wearing the watch receiver on their dominant hand. To assess baseline autonomic arousal, resting (baseline) heart-rate was measured for 2 minutes; participants were asked to sit still and quietly until they were told the 2 minutes had ended. The researcher kept their head bowed and their eyes lowered during measurement. Participants were then asked to wear the monitor continuously for 24 hours, including over-night, and to remove it the next day. Participants then completed the LEC to assess for trauma exposure, and trauma-exposed participants were assessed for current and past PTSD diagnosis using the CAPS

(Weathers et al., 2013). Participants were given the sleep diary and asked to complete it every morning and evening for seven days. Standardised instructions were printed in each sleep diary, read aloud to all participants, and their understanding was checked. Finally, participants were given three bijou bottles to collect their saliva samples in at 8am, 4pm and 10pm the following day. Bottles were pre-labelled with the expected date and time for each participant. Participants were asked to use the relevant pot to collect their sample at the exact time specified, and to do so by passive drooling into the pot until the indicated volume (1ml) was reached. Participants were asked to avoid eating food, drinking (except water), brushing their teeth, or smoking 1 hour prior to collecting the sample. The importance of collecting the samples at the specified time was emphasised, but to confirm compliance, participants were asked to make a note on the pot if they collected the sample at a different time, and that there would be no penalty for doing this. Participants stored the samples in their home refrigerators, and returned them to the experimenter at the end of the measurement week, along with the other equipment. At the end of the session, participants completed a questionnaire pack, to assess self-reported PTSD, sleep and mood symptoms. Trauma-exposed participants were asked to answer the PTSD symptom measures (PDS, PTCI, PSQIA) in relation to the traumatic event, and control participants answered them in relation to the negative event they had identified on the LEC (Foa et al., 1997).

Data Analysis

Analyses were conducted in IBM SPSS statistics (version 22.0). Data was checked for assumptions of normality and homogeneity, and non-parametric tests were used where appropriate.

In order to examine group differences in sleep, pre-sleep cognitive activity and arousal (Question 1), groups were compared on measures of sleep, arousal, and pre-sleep cognitive activity, using ANOVAs or Kruskal-Wallis tests in case of non-normal distributions. Overall group effects are reported, and effect sizes (ES) are reported as partial $\eta 2$, with small ES ≥ 0.01; medium ≥ 0.06 and large ≥ 0.14.

To test for group differences in sleep disturbances, one-way ANOVAs and planned contrasts compared groups (control, trauma, PTSD) on subjective (Sleep diary, PSQI, PSQIA) and objective (actigraphy) sleep parameters. Subjective and objectively derived estimates of sleep duration were compared using Spearman's rank correlations. To test for group differences in pre-sleep **cognitive activity**, a Kruskall-Wallis test compared groups on PSCS sum, and $PSCS_{PTSD}$ and $PSCS_{INSOM}$ scores. To investigate group differences in **cortisol**, the area under the curve with respect to ground (AUCg), and with respect to increase (AUCi) were calculated for each participant and compared between groups (see Fekedulegn et al., 2007 for formula). The AUCg is the total area under the curve of all measurements (with respect to zero), and the AUCi is calculated as the area under the curve with respect to the baseline measurement (in this case 8am) for each individual. Where the final measurement value is lower than baseline (as would be expected from a daytime profile), the AUCi sign will be negative. The AUCi represents a measure of change over time, and the AUCg is assumed to represent total hormonal output (Fekedulegn et al., 2007). To examine group differences in the daytime profile of cortisol, one-way ANOVAS compared groups on mean AUCi and AUCg. Group differences in mean cortisol were analysed using a repeated-measures ANOVA with between subjects factor 'group' (control, trauma, PTSD) and within-subjects factor 'sampling time' (8am, 4pm, 10pm). To test for group differences in nocturnal **autonomic arousal**, a one-way ANOVA compared groups on LF/HF ratio (HRV)

during sleep. As smoking, age, gender and medication use were comparable between the groups, these were not co-varied in the cortisol or HRV analyses. Physical health problems and ethnicity were not included as covariates in analyses, as preliminary analyses showed they had shown no significant effect on sleep, cortisol or HRV measures.

To examine associations between sleep, objective arousal, pre-sleep cognitive activity and PTSD symptoms in trauma survivors (n = 85), measures of objective arousal were correlated (Spearman's rank) with subjective and objective sleep measures (PSQI, sleep diary, actigraphy), PTSD symptom severity (PDSwos), and Pre-Sleep Cognition sub-scale scores (Question 2).

The relationship between PTSD symptoms, pre-sleep cognitive activity, and sleep disturbance (PSQI global score) at baseline (Question 3) was examined using a three-step hierarchical multiple regression in the PTSD group.

Results

Research Question 1: Group differences in subjective and objective sleep, pre-sleep cognitive activity, and objective arousal.

Subjective Sleep: Pittsburgh Sleep Quality Index (and addendum) and Sleep Diary

Full descriptive and test-statistics are reported in Table 5.2. The ANOVA showed a significant main effect of group on PSQI global score. People with PTSD reported more severe subjective sleep disturbances (higher global scores) than controls, or trauma controls, who did not differ (Figure 5.1). Of the PTSD group, 90.5% (38 of 42) had

clinically significant sleep problems at baseline, according to the PSQI global score (> 5). ANOVAS showed a significant main effect of group on sleep diary variables. People with PTSD reported longer sleep onset latencies, lower sleep quality, shorter sleep duration, lower sleep efficiency, and more time awake after sleep onset (although number of awakenings after sleep was equivalent across groups) compared to controls or trauma controls, who did not differ. People with PTSD also reported more PTSD-related sleep disturbances (higher PSQIA sum scores) than controls or trauma controls, who did not differ. In the sleep diary, people with PTSD also reported more frequent non-trauma nightmares than controls and trauma controls, and people with PTSD reported more trauma-nightmares compared to trauma controls. Trauma controls and people with PTSD did not differ on diary reported nightmare distress to both trauma and non-trauma related nightmares. People with PTSD also reported significantly more anxiety about going to bed than controls, or trauma controls, who did not differ. In sum, these results show that people with PTSD reported more severe sleep problems than the control groups.

Table 5.2. Descriptive and test-statistics for sleep measures, pre-sleep cognitive activity (PSCS) and posttraumatic cognitions (PTCI) for each group.

	Control (N = 30)	**Trauma (N = 43)**	**PTSD (N = 42)**	**Test-statistic**
	Mean (SD)			*F* / *t* /Kruskal
SYMPTOMS AND APPRAISALS				
PDSwos (Trauma survivors, n = 85)		7.69 (6.31)	32.83 (10.91)	t = -12.02, *p* <.001
PTCI (n = 85)		72.21 (36.63)^{B}	134.83 (43.78) ^{A}	t = -6.92, *p* <.001
PITTSURGH SLEEP QUALITY INDEX				
PSQI (Global score)	4.73 ^{B} (1.80)	5.39 ^{B} (2.61)	11.05 (3.46) ^{A}	F = 60.1, *p* <.001
Sleep Quality	.08 ^{A}(0.14)	1.09 ^{A} (0.89)	2.12^{B} (0.64)	F = 29.39, *p* <.001
Sleep Onset Latency	1.24 ^{B}(0.44)	1.44 ^{B} (0.61)	2.11 ^{A} (0.76)	F = 16.73, *p* <.001
Sleep Duration	0.30 ^{A}(.54)	0.25 ^{A} (.59)	1.38^{B} (1.03)	F = 27.01, *p* <.001
Sleep Efficiency	0.43 ^{A}(0.68)	0.47 ^{A} (0.83)	1.68^{B} (1.21)	F = 25.52, *p* <.001
Sleep Disturbances	1.10 ^{A}(0.31)	1.37 ^{A} (0.58)	1.83^{B} (0.70)	F = 14.89, *p* <.001
Daytime Dysfunction	1.03 ^{B}(0.72)	0.93 ^{B} (0.67)	1.68 ^{A} (0.92)	F = 10.69, *p* <.001

Sleep Medication	.00 ^{B}(0)	.09 ^{B} (.038)	.61^{A} (1.05)	F = 3.85, *p* = 03
PSQI-A (total)	1.90 ^{B} (1.95)	3.33 ^{B}(2.35)	8.28 ^{A}(3.72)	H = 53.95, *p* <.001
Hot flashes	.30 ^{B} (.70)	.42 $^{B\,A}$(.70)	.98 ^{A}(1.17)	H = 8.75, *p* = .013
General nervousness	.60 ^{B} (.81)	.98 ^{B}(.89)	1.89 ^{A}(1.05)	H = 26.87, *p* <.001
Trauma nightmares	.10 ^{B} (.31)	.35 ^{B}(.53)	1.76^{A}(1.09)	H = 53.20, *p* <.001
Anxiety or panic	.20 ^{B} (.84)	.47 ^{B}(.77)	1.15 ^{A} (.96)	H = 24.76, *p* <.001
Bad dreams not related to trauma	.57 ^{B} (.90)	.91$^{B\,A}$(.92)	1.40^{A}(1.05)	H = 13.04, *p* =.001
Terror/screaming	.03 ^{B} (.18)	.12 ^{B}(.32)	.55 ^{A}(.78)	H = 18.13, *p* <.001
"Acting out" dreams	.10 ^{B} (.31)	.09 ^{B}(.36)	.61^{A}(.74)	H = 20.47, *p* <.001
SLEEP DIARY				
Sleep Quality (0-100)	67.90 ^{A}(19.33)	62.20 ^{A} (17.96)	44.34 ^{B}(17.07)	F = 8.71, *p* <.001
Sleep Onset Latency	15.70 ^{B}(8.63)	20.71 ^{B}(17.15)	34.80 ^{A}(28.39)	F = 17.2, *p* = .002
Sleep Duration (Hrs)	7.43 ^{A}(0.86)	6.92 ^{A} (1.25)	5.99 ^{B}(1.73)	F = 10.76, *p* <.001
Sleep Efficiency (%)	85.26 ^{A}(6.83)	81.67 ^{A}(10.54)	70.39 ^{B}(19.66)	F = 11.69, *p* <.001
Wakings (mins)	11.72 ^{B}(10.50)	18.19 ^{B}(16.42)	38.30 ^{A}(34.35)	H = 13.85, *p* = .001
Non-trauma nightmare frequency	.53 ^{B}(1.14)	.77 ^{B}(.09)	1.71 ^{A}(1.88)	H = 13.70, *p* =.001
Non-trauma nightmare distress (0-100)	10.33 ^{B}(19.62)	33.07 ^{AB} (23.40)	42.60 ^{A}(24.46)	H = 12.45, *p* = .002
Trauma nightmare frequency (n = 85)	----------	.19 (.55)	1.00 (1.36)	t = -3.63, *p* <.001
Trauma nightmare distress (0-100) (n = 85)	----------	58.89 (19.17)	56.43 (20.82)	t = .26, *p* =.80
Pre-bed anxiety (0-100)	6.46 ^{B} (10.59)	14.9 ^{B} (16.52)	36.74 ^{A}(20.90)	H = 37.81, *p* <.001
ACTIGRAPHY				
Time in Bed	7.46 ^{B}(1.12)	7.83 ^{A}(1.24)	7.02 ^{B} (1.59)	F = 3.38, *p* = .038
Sleep Duration[1]	7.01 ^{A}(1.18)	7.28 ^{A}(1.20)	5.74 ^{B}(1.96)	F = 10.94, *p* <.001
Sleep Efficiency (%)	93.97%	92.98%	81.77%	
PRE-SLEEP COGNITION SCALE (PSCS)				
PSCS (SUM)	9.27 ^{B}(8.18)	12.16 ^{B}(9.57)	31.12 ^{A}(16.38)	H = 43.59, *p* <.001
$PSCS_{INSOM}$	7.70 ^{B}(7.22)	10.21 ^{B}(7.16)	18.90 ^{A}(10.28)	H = 28.51, *p* <.001
$PSCS_{PTSD}$	0.85 ^{B} (1.26)	1.73 ^{B}(2.89)	9.14 ^{A}(6.77)	H = 62.42, *p* <.001

[1]Sleep duration was calculated as objective time in bed minus subjective time awake in bed.

PSQI = Pittsburgh sleep quality index, PSQIA = PSQI addendum for PTSD. Nightmare frequency refers to the number of days that nightmares were had. Test statistics (F/Kruskal Wallis/independent t-test) and significance levels (p) are shown for main effect of group, and results of pairwise comparisons are indicated in superscript ($^{A, B}$), where groups that do not differ share the same letter.

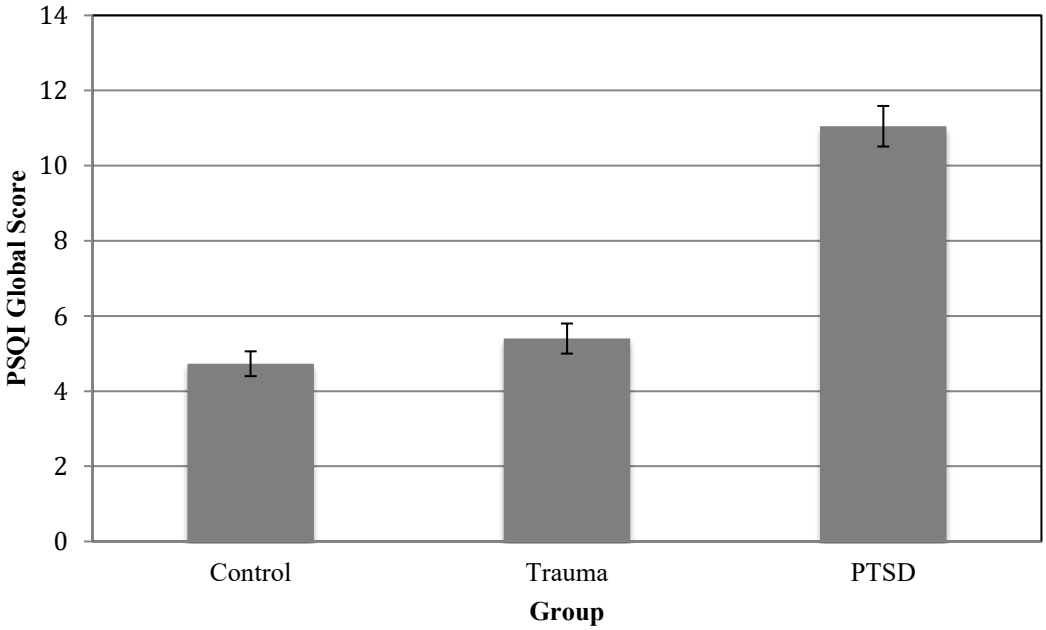


Figure 5.1. Mean PSQI global sum score (standard error bars) for each group.

Objective Sleep: Actigraphy

Full descriptive and test-statistics are reported in Table 5.2. Group differences in subjective sleep were also reflected in objective data. The ANOVA showed a significant main effect of group on mean objective sleep duration. PTSD patients had significantly shorter sleep durations than controls and trauma controls, who did not differ. The mean correlation between sleep diary and actigraphy derived estimates of sleep duration (across all groups) was $r = .50$, $p < .001$, and daily correlations between actigraphy and the sleep diary ranged from, $r = .29$ - $.69$, p's $< .05$. This suggests some consistency between self-report and objectively measured sleep duration.

Pre-Sleep Cognitive Activity

Descriptive and test-statistics are shown in Table 5.2. Kruskal-Wallis tests showed a significant main effect of group on pre-sleep cognitions. The PTSD group scored higher on the PSCS and PSCS insomnia and PTSD sub-scales than controls, or trauma controls, who did not differ.

Objective Arousal: Cortisol

Descriptive and test statistics are shown in Table 5.3. For the analysis, 9 participants were excluded for non-compliance with sampling times (2 control, 3 trauma controls and 4 PTSD), and 8 had missing data (1 control, 3 trauma, 4 PTSD). A total of 94 participants had data at every time all three time points (control n = 27, trauma n = 36, PTSD n = 31). See Table 5.3 for final sample sizes for each group.

The mixed ANOVA showed a significant main effect of 'sampling time' $F(2, 182) = 127.27$, $p < .001$, partial $\eta 2 = .07$ (see Figure 5.2 and Table 5.3), no significant effect of 'group', $F(2, 91) = 1.34$, $p = .27$, and a group x time interaction for quadratic effect of time only, $F(2, 91) = 3.25$, p=.04, partial $\eta 2$= .07, indicating group differences in change over time. One-way ANOVAs showed that there was a significant main effect of group at 4pm only, $F(2, 96) = 3.45$, $p = .036$, and not at 8am $F(2, 97) = 1.20$, $p = .31$, or 10pm, $F(2, 95) = 1.30$, $p = .28$. Post-hoc comparisons between groups at 4pm revealed that the PTSD group had significantly lower cortisol at 4pm in comparison to trauma controls, mean difference = -1.65 (95% CI = -3.16 to -.12), $p = .03$, and did not differ compared to controls, mean difference = -1.18 (95% CI = -2.8 to .46), $p = .20$. Trauma controls and controls also did not differ, mean difference = .45 (95% CI = -1.15 to 2.06), $p = .78$. One-way ANOVAs showed no significant main effect of group on AUCg, $F(2, 93) = 1.73$, p =.18, or AUCi, $F(2, 93) = 1.55$, $p = .22$.

Table 5.3. Mean (standard deviation) cortisol (nmol/l) at each sampling time, and derived cortisol parameters (AUC) for each group.

	Control (n = 27)	**Trauma (n = 36)**	**PTSD (n = 31)**
Cortisol	**M (SD)**	**M (SD)**	**M (SD)**
8am[1]	13.30 (6.68)	10.77 (6.68)	11.12 (8.56)

4pm[2]	4.35 (1.44)	4.80 (3.77)	3.16 (1.76)
10pm[3]	3.13 (3.01)	2.28 (1.03)	2.53 (2.07)
AUCg	5636.54 (2103.91)	4790.06 (1780.12)	4690.35 (2398.67)
AUCi	-5803.85 (3830.26)	-4000.43 (3364.00)	-5178.60 (5148.94)

[1]Sample sizes are: Control n =27; Trauma n = 37; PTSD n = 34, [2] N: Control n =27; Trauma n = 37; PTSD = 33 [3] Sample sizes are: Control n = 27 Trauma n = 36 PTSD n = 32. AUCi = area under the curve with respect to increase; AUCg = area under the curve with respect to ground.

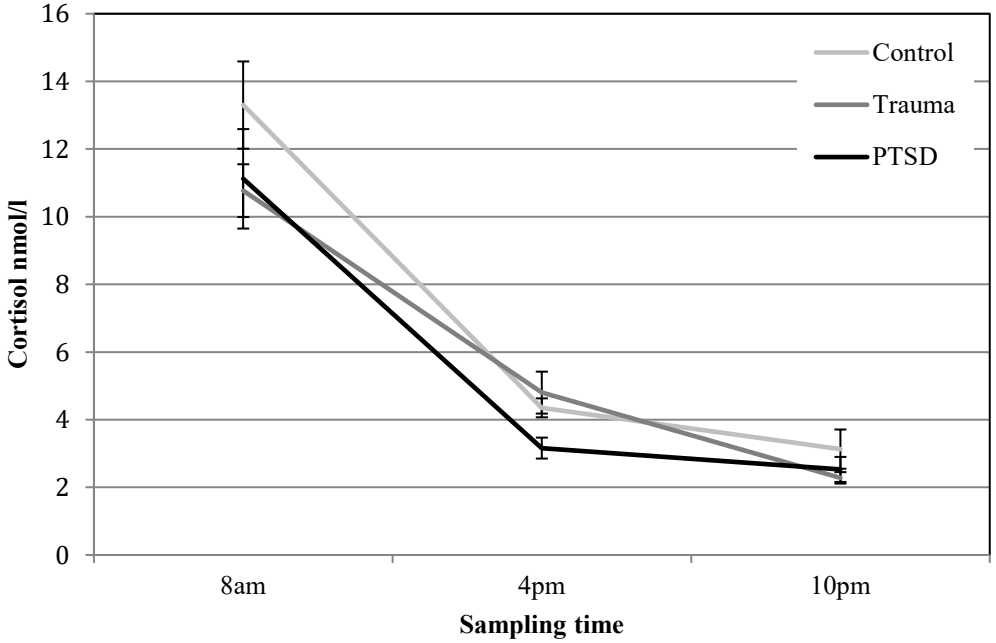


Figure 5.2. Graph illustrating diurnal cortisol curve: mean cortisol levels (nmol/l), at each sampling time for each group.

Objective arousal: heart-rate variability

Descriptive and test-statistics are shown in Table 5.4. For this analysis, 17 participants (4 controls, 8 trauma, 5 PTSD) had to be excluded. These were: 2 for using anti-hypertensive/cardiac medication (1 trauma, 1 control), 14 for drinking (more than one drink) prior to bedtime (6 trauma controls, 4 controls, and 5 PTSD), and 1 for cannabis use before bedtime (control). Data was missing for 24 participants (8 controls, 8 trauma, 8 PTSD), due to recording failure or device removal by participants, and so the final sample size for analysis was *n* = 74. See Table 5.4 for final sample sizes for each group.

The ANOVA showed a significant main effect of group on LF/HF ratio during sleep, $F(2, 57) = 4.10$, $p = .02$. Post-hoc comparisons showed that people with PTSD had significantly higher LF/HF ratios during sleep than controls, $p = .03$. PTSD and trauma controls did not differ, $p > .05$, and trauma controls did not differ from controls $p > .05$. This suggests higher sympathetic dominance during sleep in people with PTSD. The groups also did not differ on baseline heart-rate or heart-rate during sleep (see Table 5.4).

Table 5.4. Descriptive and test-statistics for heart-rate and LF/HF ratio values for each group.

	Control (n = 18)	Trauma (n = 27)	PTSD (n = 29)	Test-statistic
	M (SD)	M (SD)	M (SD)	M (SD)
LF/HF RATIO				
Baseline[1]	3.70 (1.25)	3.59 (1.04)	4.40 (1.69)	F = .37, p = .70
Sleep[2]	3.46 (.91)[B]	3.76 (0.48) [A B]	4.03 (.78)[A]	F = 4.10, p = .02
HEART-RATE (BPM)				
Baseline	74.15 (11.25)	72.84 (10.15)	78.12 (13.40)	F = .67, p = 52
Sleep	63.65 (11.84)	67.90 (14.65)	69.13 (11.35)	F = 1.77, p = .18

Test statistics are shown for main effect of group, and results of pairwise comparisons are indicated in superscript ([A, B]), where groups that do not differ share the same letter. [1]Sample sizes were; control, n = 18; trauma, n = 21; PTSD, n = 29. [2]Sample sizes were; control, n = 11; trauma, n = 27; PTSD, n = 21.

Research Question 2: Association between objective arousal, PTSD symptoms, sleep and pre-sleep cognitive activity in PTSD.

In people with PTSD (N = 42), objective arousal (heart-rate, LF/HF ratio, cortisol) was correlated with subjective sleep parameters (sleep onset latency; SOL), sleep duration (TST), number of awakenings (WASO no.), duration of awakenings (WASO min), overall sleep quality (SQ) and objective sleep duration (TST Acti) from the first recording night (i.e. the night before the day on which cortisol samples were taken). Objective arousal measures were also correlated with pre-sleep cognitive activity ($PSCS_{INSOM}$ and $PSCS_{PTSD}$), and PTSD symptom severity, excluding sleep (PDSwos). Significant correlations are reported, and full results are shown in Table 5.5.

Spearman's rank correlations showed that heart-rate during sleep significantly, positively correlated with $PSCS_{INSOM}$ scores, *rho* = .55, *p* = .02, $PSCS_{PTSD}$ scores, *rho* = .54, *p* = .02, and PSQI global score, *rho* = .56, *p* = .02. LF/HF ratio during sleep was significantly, negatively correlated with subjective number of awakenings, *rho* = -.48, *p* = .04. This indicates that higher autonomic arousal correlated with more pre-sleep cognitive activity (PTSD and insomnia-related) and more sleep disturbances (heart-rate), but fewer awakenings (LF/HF). Heart-rate and LF/HF ratio did not correlate with sleep onset time, number of awakenings or total sleep time (subjective or objectively measured) (Table 5.5).

Mean cortisol at 8am, 4pm or 10pm did not significantly correlate with any sleep measures, *p*'s >.05, nor did AUCi or AUCg. However cortisol at 8am, and AUCg significantly, negatively correlated with PTSD related pre-sleep cognitive activity, 8am, *rho* = -.37, *p* = .04; AUCg, *rho* = -.37, *p* = .03. These results show that lower morning, and overall cortisol were associated with more PTSD-related pre-sleep cognitive activity.

Table 5.5. Spearman's rank correlations within the PTSD group (N = 42), between objective arousal measures, PTSD symptoms, sleep measures, and pre-sleep cognitive activity.

	PDSwos	PSQI	SOL	WASO no.	WASO min.	TST	SQ	TST Acti	$PSCS_{INSOM}$	$PSCS_{PTSD}$
LF/HF_{SLEEP}	.02	.42	.35	-.48*	-.21	-.38	-.07	.05	.21	.19
HR_{SLEEP}	.41	.56*	.25	-.07	.17	-.40	-.30	-.01	.55*	.54*
Cortisol										
8am	-.02	-.31	.16	-.003	.19	.11	-.02	-.03	-.15	-.37*
4pm	-.27	.05	-.04	-.33	-.12	-.08	.29	.34	-.09	-.30
10pm	-.17	-.01	.19	-.14	.06	-.34	.09	.30	-.14	-.13
AUCg	-.12	-.08	.11	-.19	.17	-.09	.09	.04	-.11	-.37*
AUCi	-.09	.23	-.08	-.02	-.18	-.10	.21	.17	.05	.27

Note. LF/HF_{SLEEP} and $HR_{sleep=}$ LF/HF ratio or HR during sleep. SOL = subjective sleep onset latency; WASO no. = subjective number of wakings, WASO min = subjective duration of wake after sleep (mins); TST = subjective total sleep time; SQ = subjective sleep quality; TST Acti = actigraphy estimated total sleep time. Significance level indicated by * p <.05; ** p <.01; **p <.001.

Research Question 3: The role of pre-sleep cognitive activity in the mediation of subjective sleep disturbances in PTSD.

Analyses were conducted in the PTSD group, two people had missing data on one measure, so the final sample was $n = 40$. Preliminary analyses were conducted to ensure no violation of the multicollinearity assumption between proposed predictor variables; PTSD symptom severity, excluding sleep (PDSwos) and pre-sleep cognitive activity ($PSCS_{INSOM}$ and $PSCS_{PTSD}$). As the correlation between $PSCS_{INSOM}$ and $PSCS_{PTSD}$ was high, i.e. above .70, $r = .75$, $p < .001$, the composite PSCS sum score of both sub-scales was used, rather than entering the individual sub-scales. Following recommendations by Baron and Kenny for mediation analysis (1986), hierarchical multiple regression analysis was conducted to test for mediation of the relationship between PTSD symptoms and sleep, by pre-sleep cognitive activity (Table 5.6 and Figure 5.3). First, simple linear regression established a significant direct relationship between PDSwos and the outcome, sleep disturbance (PSQI global score), $R^2 = .19$, $F(1, 39) = 9.13$, $p = .004$ (Step 1), and between the potential mediator (pre-sleep cognitive activity; PSCS sum) and sleep disturbance (PSQI), $R^2 = .38$, $F(1, 39) = 23.51$, $p < .001$. Second, a significant relationship was established between PTSD symptoms and pre-sleep cognitive activity (mediator), $R^2 = .36$, $F(1, 39) = 20.91$, $p < .001$. Finally, PTSD symptoms (Step 1) and then pre-sleep cognitive activity (Step 2) were entered into the model, together accounting for 38.3% of the total variance in PSQI global score. PTSD symptoms no longer predicted PSQI when pre-sleep cognitions were included in the model, beta = .12, $t = .73$, $p = .47$. Pre-sleep cognitive activity continued to predict PSQI even when PTSD symptom severity was controlled for, beta = .54, $t = 3.37$, $p = .002$, and explained an additional 19% of variance, R^2 change = .19, $F(2, 39) = 11.51$, $p < .001$. This suggests that pre-sleep cognitive activity fully mediates the relationship between PTSD symptom severity and sleep disturbance.

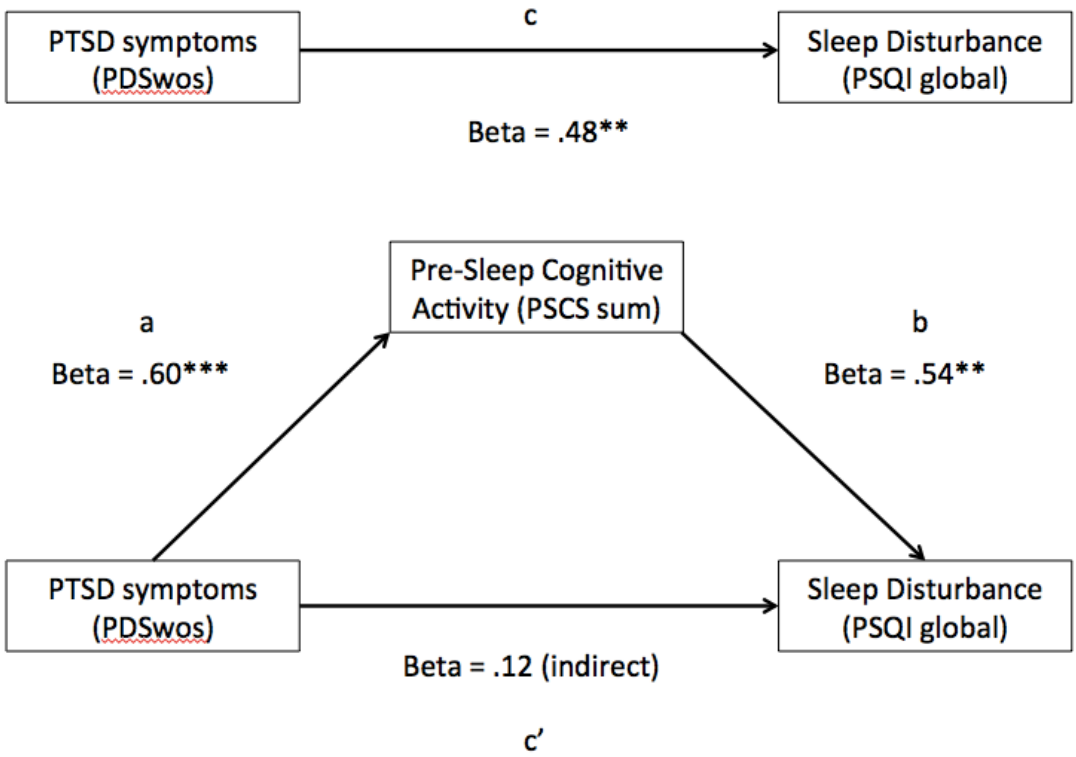


Figure 5.3: Illustration of full mediation of relationship between baseline PTSD symptoms (PDSwos) and sleep disturbances, by pre-sleep cognitive activity (PSCS sum) in PTSD group (n = 40). Model shows direct pathway from PDSwos to PSQI (c), from PDSwos to PSCS (a), from PSCS to PSQI (controlling for PDSwos) (b), and the indirect pathway from PDSwos to PSQI, when PSCS is included in the model (c').

Table 5.6. Hierarchical multiple regression results for the PTSD group (n = 40).

	b	Standard Error	β	*p*	R^2
Step 1					
Constant	6.52	1.60		<.001	
PDSwos	.14	.05	.44	.004	.19
Step 2					
Constant	6.35	1.42		<.001	
PDSwos	.04	.05	.12	.47	
PSCSsum	.11	.03	.54	.002	.38**

Note. Step 1 = PDSwos predicting PSQI global score. Step 2 = PDSwos then PSCS sum entered as predictors of PSQI global score. R^2 change significant at *p < .05; ** = < .01; *** = < .001.

Discussion

Summary

This study aimed to investigate factors that may be associated with sleep disturbances in PTSD, such as pre-sleep cognitive activity and hyperarousal (including nocturnal autonomic arousal, i.e. heart-rate and variability). The results confirmed most of the

hypotheses; 1) In comparison to both control groups, people with PTSD had more severe sleep disturbances (reduced duration, quality, longer sleep onset latency, more wake after sleep, more nightmares), shorter objective sleep duration, and more pre-sleep cognitive activity. People with PTSD had lower cortisol at 4pm, compared to trauma controls, but not compared to controls. People with PTSD had higher sympathetic activation (LF/HF ratio) during sleep compared to controls, but not trauma controls, indicating higher autonomic arousal during sleep in PTSD; 2) In the PTSD group, higher objective arousal (lower morning and overall cortisol, and higher nocturnal heart-rate) was associated with worse subjective sleep disturbances, and more pre-sleep cognitive activity. However, higher sympathetic activation was associated with fewer subjective awakenings; 3) In PTSD patients, pre-sleep cognitive activity accounted for significant variance in sleep disturbances and mediated the relationship between PTSD symptoms and sleep disturbances. The results of this study will hopefully help to identify factors associated with sleep disturbances in PTSD.

Group differences: Subjective and objective sleep

The results replicated the findings of Chapter 4, showing that sleep disturbances are more severe in people with PTSD, compared to traumatised and non-traumatised controls. It adds to Chapter 4 by showing that group differences (between PTSD, trauma controls and controls) in subjective sleep disturbances are also reflected in objective measures, and group differences in self-reported pre-sleep hyperarousal (Chapter 4) are also reflected in differences on measures nocturnal autonomic arousal (LF/HF). This suggests that it is more than just the subjective experience of sleep and pre-sleep arousal that is more severe in PTSD, but that sleep is objectively shorter and arousal is higher, in comparison to trauma survivors without PTSD, and controls. This challenges concerns that PTSD patients may under-estimate sleep duration and disturbances

(Hurwitz et al., 1998; Klein et al., 2003; Woodward, Bliwise, Friedman, & Gusman, 1996a), and is consistent with studies showing similar actigraphy and diary reported sleep duration estimates in PTSD (Kobayashi et al., 2012). It also adds to the literature on objective sleep disturbances in PTSD (reviewed in Chapter 1), where differences in objectively measured sleep in PTSD compared to trauma survivors have not been consistently found. This study suggests that there are differences in objectively measured sleep, using actigraphy, between PTSD, trauma controls, and non-traumatised controls. This is consistent with studies that have found differences between people with PTSD and healthy controls (Calhoun et al., 2007; Straus et al., 2015; Ulmer et al., 2009), and between trauma survivors with and without PTSD (Klein et al., 2003), although three studies have not found differences between people with PTSD and controls (Dagan et al., 1997; Engdahl et al., 2000; Kobayashi et al., 2014). This study found no objective sleep differences and no differences in subjective sleep severity (diary and PSQI) between trauma-exposed and non-exposed controls, suggesting that trauma exposure in the absence of PTSD was not associated with subjective or objective sleep disturbances. However it should be noted that trauma controls did report more non-trauma nightmares on the PSQIA, although this was not reflected in sleep diary reports. Trauma controls also did not differ in their reported distress at trauma nightmares compared to PTSD, but they reported having trauma-related nightmares less frequently than people with PTSD. This is consistent with studies showing that trauma exposure in the absence of PTSD can affect sleep (see Sinha, 2016). It is also consistent with evidence that PTSD patients are more likely to report nightmares that are similar or replicative to the trauma, compared to trauma survivors without PTSD (Mellman & Kulick-Bell, 1995), and compared to trauma survivors with nightmares but no PTSD (van der Kolk, Blitz, Burr, Sherry, & Hartmann, 1984). This suggests that although trauma survivors have trauma-related nightmares infrequently, when they occur they are

experienced as equally distressing to the trauma nightmares experienced by people with PTSD. This is consistent with findings that nightmare distress in trauma survivors is positively associated with the degree of nightmare similarity to the trauma (Davis et al., 2007).

Heart-rate and heart-rate variability

Sympathetic nervous system activation (LF/HF) during sleep was elevated in PTSD, compared to controls, but not compared to trauma controls, indicating elevated autonomic nervous system (ANS) arousal during sleep, which has been suggested to contribute to sleep problems in PTSD (van Liempt, Arends, Cluitmans, Westenberg, Kahn, & Vermetten, 2013a; Woodward et al., 2009). This finding is consistent with previous studies showing heightened nocturnal ANS activity in PTSD compared to a mixed (trauma and non-trauma-exposed) control group (Woodward et al., 2009), but is inconsistent with studies showing differences between PTSD and trauma controls without PTSD (Kobayashi et al., 2014; Mellman et al., 2004; van Liempt, Arends, Cluitmans, Westenberg, Kahn, & Vermetten, 2013a). In the present study, in the PTSD group higher heart-rate during sleep was associated with more insomnia-related and PTSD-related pre-sleep cognitive activity, and more severe sleep disturbances (PSQI). This pattern of results suggest that autonomic arousal may be associated with worse sleep and more pre-sleep cognitive activity in PTSD, although results should be interpreted with caution as samples sizes were small, and the direction of effects cannot be determined. One possibility is that pre-sleep cognitive arousal may increase physiological arousal which could interfere with sleep (Gross & Borkovec, 1982; Harvey, 2002). Another possibility is that sleep disruption could lead to greater sympathetic activation in response, consistent with suggestions that sleep regulates ANS activity (Viola et al., 2002). In the PTSD group, higher sympathetic activation

(LF/HF ratio) during sleep was associated with fewer subjective awakenings. This was unexpected. However, some studies have found that autonomic arousal and sleep duration were not associated in people with PTSD. This has led to the suggestion there may be a dissociation between ANS activity and sleep in PTSD (Kobayashi et al., 2014), which may help to explain the finding in the present study. In sum, the results tend to suggest that elevated autonomic arousal in PTSD is associated with worse subjective sleep. The results are consistent with general associations between the sympathetic nervous system and sleep regulation (Saper et al., 2005) and evidence that the autonomic nervous system may influence sleep (Bonnet & Arand, 1997b). It also fits with proposed models of persistent physiological arousal underpinning primary insomnia (Bonnet & Arand, 1997b; Riemann et al., 2010), and sleep problems in PTSD (Germain, 2013; Sinha, 2016). However, the direction of effects cannot be determined in this study, and sample sizes were small, so results must be interpreted cautiously, and further research is required.

Cortisol

The study showed that the groups differed in their daily rhythm of cortisol. People with PTSD had lower cortisol at 4pm compared trauma controls, but not controls. This is consistent with previous studies, which have found lower afternoon cortisol in PTSD (e.g., Yehuda et al., 1996) indicating dysregulated HPA-axis (stress response) system functioning. However, the results of previous studies are mixed with many finding no evidence of lower cortisol in PTSD (e.g., Wessa et al., 2006; and see Klaassens et al., 2012 and Meewisse et al., 2007 for reviews), and some finding lower evening cortisol (Young & Breslau, 2004). Further, studies more commonly find differences between PTSD and healthy controls, rather than PTSD and trauma-exposed controls (Meewisse et al., 2007).

In people with PTSD, lower morning (8am) cortisol, and lower overall cortisol (AUCg), were associated with more PTSD pre-sleep cognitive activity. This is consistent with previous associations between low cortisol and maladaptive trauma appraisals, where it has been suggested that cognitive appraisals, i.e. about a perceived threat, may impact the neuroendocrinological stress response system (Olff, Langeland, & Gersons, 2005). It is also consistent with associations found between lower awakening cortisol and more sleep-related cognitions in people with insomnia, where low cortisol has been suggested to be a biomarker of poor subjective sleep (Backhaus, Junghanns, & Hohagen, 2004). However, in the present study low cortisol was not associated with worse sleep in PTSD, which is inconsistent with some previous studies (Backhaus et al., 2004). This could be due to small sample sizes in the present study, particularly as previous studies have noted that due to large individual variability, homogenous samples are typically required for studies investigating cortisol (Yehuda, 2006), and therefore the results of the present study should be interpreted cautiously. In sum, the results may indicate an alteration in HPA-axis activity in people with PTSD, reflected in lower afternoon cortisol levels. However, further research with larger sample sizes is required.

The role of pre-sleep cognitive activity

As found in Chapter 4, the PTSD group reported more frequent pre-sleep cognitive activity of both insomnia and PTSD-related content, than controls and trauma controls. Pre-sleep cognitive activity mediated the relationship between PTSD symptoms and sleep, suggesting that PTSD symptoms may affect sleep disturbances via increased pre-sleep cognitive activity. One possible pathway for this effect is that more severe PTSD symptoms may result in more PTSD-related thoughts and worry about nightmares and threat in the pre-sleep period, which could lead to more severe sleep disturbances such

as longer sleep onset latency and shorter sleep duration. The results suggest that, as in primary insomnia (Harvey, 2002), pre-sleep cognitive activity contributes to sleep disturbances in PTSD, and may be one of a number of pathways via which PTSD symptoms disturb sleep. This is consistent with suggestions that insomnia may develop into an independent problem in PTSD, which may account for its persistence after PTSD treatment, in the absence of PTSD symptoms (Zayfert & DeViva, 2004).

Limitations, strengths and future research

The study has a number of limitations. Firstly, the cortisol analysis may have been under-powered to detect associations between cortisol and sleep parameters. This was confirmed with post-hoc power analysis showing that the sample size of 42 yielded a power of 63% to detect a correlation of 0.3. Secondly, a large number of variables can affect cortisol levels, including age, gender, medication, metabolism, mood, substance and alcohol use, nicotine, and environmental stressors (Rasmusson, Vythilingam, & Morgan, 2003; Yehuda, 2006), many of which can be difficult to control when home sampling methods are used, as in this study. Patient reporting was relied upon to confirm compliance with sampling times and guidelines, and so it is unknown if other variables could have biased the samples. Waking time can also influence morning cortisol, and as samples were collected at set-times rather than natural wake-time, this could have influenced morning waking samples and AUC calculations. Future research should aim to use larger sample sizes, and should combine controlled laboratory and home-based saliva sampling methods to control possible confounding variables, and should also collect cortisol samples upon natural awakening. Thirdly, sleep stage was not measured in this study, and so it is possible that participants may have been in different sleep stages when the heart-rate measure was taken. This could have affected the results, as sympathetic activation can vary as a function of sleep stage (Bonnet &

Arand, 1997a), and the length of a sleep cycle varies between individuals. In addition, studies have found differences in sympathetic tone between PTSD and trauma controls only in REM sleep (Mellman et al., 2004), and another study found higher HR only in NREM in PTSD, compared to trauma controls (Kobayashi, Lavela, Bell, & Mellman, 2016a). Therefore, it would be important to assess sleep stage in future studies examining sympathetic activation in PTSD. Finally, when investigating associations between arousal, sleep symptoms and pre-sleep cognitive activity, correlations were not bonferroni corrected, as they were planned associations. However, issues with multiple testing (correlations) may have led to inflation of the alpha error rate, which could have led to some correlations becoming significant by chance. Significant associations should therefore be interpreted with appropriate caution. The strengths of the study are that it provides novel findings demonstrating the role of pre-sleep cognitive activity in mediating sleep disturbances in PTSD. It contributes to the small body of literature on sleep disturbances in PTSD compared to trauma exposed and non-exposed controls, and demonstrates associations between sleep, hyperarousal and pre-sleep cognitive activity in PTSD. Future research should aim to further investigate the effects of PTSD therapy on pre-sleep cognitive activity and hyperarousal and consider the role of persistent arousal and pre-sleep cognitive activity in maintaining sleep problems after PTSD therapy.

Conclusion

In sum, the results showed that sleep, physiological hyperarousal and pre-sleep cognitive activity are elevated in PTSD. The results suggest that sleep disturbances in PTSD could be related to factors known to maintain primary insomnia, such as hyperarousal and pre-sleep cognitive activity, and that PTSD symptoms may in in part disturb sleep via pre-sleep cognitive activity. The study adds to understanding of the

nature of sleep disturbances in PTSD, and highlights possible targets for intervention to further improve comorbid sleep problems in PTSD therapy.

Chapter 6: The Effects of Cognitive Therapy for PTSD on objective and subjectively measured sleep disturbances, hyperarousal and pre-sleep cognitions.

Introduction

Research has shown that sleep problems, such as insomnia, are often persistent in patients treated with Cognitive Behavioural Therapy (CBT) for posttraumatic stress disorder (PTSD) (Belleville et al., 2011; Galovski et al., 2009; 2016; Gutner et al., 2013), including those patients whose PTSD has resolved with treatment (Zayfert & DeViva, 2004). The results of Chapters 2 and 3 showed that sleep quality and duration improved with Cognitive Therapy for PTSD (CT-PTSD) (Ehlers et al., 2005), along with nightmares and hyperarousal symptoms (Chapter 2), and simultaneously with improvements in traumatic appraisals, flashback-quality of intrusions, and PTSD symptoms (Chapter 3). Nevertheless, in Chapters 2 and 3, about 40% of PTSD patients reported residual insomnia symptoms after treatment, consistent with previous studies (Belleville et al., 2011; Galovski et al., 2009; Gutner et al., 2013). Researchers have suggested that chronic insomnia may persist after PTSD therapy, in the absence of PTSD symptoms, due to perpetuating factors known to maintain general insomnia, such as persistent hyperarousal (Zayfert & DeViva, 2004). In Chapter 5, more frequent pre-sleep cognitive activity and hyperarousal were associated with sleep disturbances in PTSD. However, only little is known about their role in the persistence of sleep problems after PTSD therapy, and further research is required to investigate factors that may perpetuate sleep complaints.

As described in Chapter 5, basal diurnal cortisol, heart-rate and heart-rate variability can be used as objective indicators of hyperarousal, and alterations in both have been found in PTSD. However, as noted in Chapter 6, cortisol is a measure of HPA-axis activity rather than a direct measure of hyperarousal. Chapter 5 showed that people with PTSD had increased sympathetic activation during sleep compared to controls (but not trauma controls), indexed by a higher LF/HF ratio (a frequency domain measure of heart-rate variability; HRV). This was consistent with previous studies, which have found elevated nocturnal heart-rate and altered HRV (more sympathetic activation) in PTSD compared to controls (Woodward et al., 2009). However, studies have also shown altered HRV in PTSD compared to trauma-controls (Kobayashi et al., 2014; Mellman et al., 2004; van Liempt, Arends, Cluitmans, Westenberg, Kahn, & Vermetten, 2013a). In Chapter 5, autonomic arousal (higher heart-rate) during sleep was associated with worse subjective sleep disturbances (but altered HRV, reflecting more sympathetic activation, was associated with fewer awakenings), and it was suggested that heightened autonomic arousal may be linked to disturbed sleep in PTSD, consistent with theories that hyperarousal may underpin insomnia in PTSD (Sinha, 2016; Germain, 2013). The few treatment studies conducted have shown that after PTSD therapy daytime HRV (Tan, Dao, Farmer, Sutherland, & Gevirtz, 2011) and HRV during sleep (Nishith et al., 2003) were increased, indicating reductions in autonomic arousal with psychotherapy for PTSD. Cortisol provides a measure of hypothalamic-pituitary adrenal gland (HPA) axis functioning (rather than a direct measure of hyperarousal), and lower levels of cortisol, reflecting HPA-axis dysregulation, have been (inconsistently) found in PTSD (see Klassens et al., 2012; Meewisse et al., 2007), particularly in the afternoon and evening (Yehuda et al., 1996), HPA-axis activity has also been associated with fragmented sleep in PTSD (van Liempt, Arends, Cluitmans, Westenberg, Kahn, & Vermetten, 2013a). Chapter 5 found lower afternoon cortisol in PTSD compared to trauma controls.

Treatment studies have found increased plasma cortisol with psychotherapy for PTSD (Olff, de Vries, Guzelcan, Assies, & Gersons, 2007), resting salivary cortisol has been found to significantly decrease with PTSD therapy in treatment responders (Gerardi, Rothbaum, Astin & Kelly, 2010), and one study has shown that higher bedtime cortisol predicted greater PTSD symptom reduction with therapy (Yehuda et al., 2014). The results of these studies may indicate an influence of PTSD treatment on HPA-axis activity, which could indicate an adaptive decreased reactivity to stressors. Studies have also shown that administering cortisol reduced PTSD re-experiencing and hyperarousal symptoms in 66.7% of patients, which has been linked to the inhibiting effects of high cortisol on memory retrieval, possibly attenuating over-retrieval of traumatic memories (Aerni et al., 2004). In sum, these studies show that hyperarousal and HPA-axis activity may be associated with sleep complaints in PTSD, and warrants further investigation into its association with sleep problems after PTSD therapy.

Aims of the present study

This Chapter presents a study designed to further investigate the effects of CT-PTSD (Ehlers et al., 2005) on sleep disturbances. It builds on the findings of Chapters 2 and 3, by examining whether sleep improvements with CT-PTSD are also reflected in validated subjective sleep questionnaires, detailed sleep diary reports, and in objective sleep measures. It will add to the findings of previous studies, as only two studies have investigated PTSD treatment effects on objective sleep measures, using laboratory-based polysomnography (PSG) (Raboni et al., 2006; Nishith et al., 2003), and none have used home-based objective sleep assessment to investigate PTSD treatment effects on sleep. Studies have found discrepancies between PTSD patient reports and objective measures of sleep complaints (Klein et al., 2003), and it has been suggested that home-based sleep assessments are more likely to detect objective sleep abnormalities

(Germain et al., 2006; Herbst et al., 2010), as PTSD patients often feel safer in laboratory settings than at home, where reported sleep disturbances occur (Woodward, Bliwise, Friedman, & Gusman, 1996a). Actigraphy was used in the present study to measure patients' sleep in their homes. While PSG is the gold standard of objective sleep assessment, actigraphy can offer unobtrusive means of objectively estimating sleep and wake (e.g., Ancoli-Israel et al., 2003). This study also examined possible explanations for persistent sleep problems after PTSD treatment, by investigating treatment effects on variables hypothesised to be associated with disturbed sleep in PTSD, namely pre-sleep cognitive activity, hyperarousal (daytime cortisol), and autonomic arousal during sleep (HRV). This is the first known study to combine cortisol, heart-rate and objective and subjective sleep measures in an investigation of PTSD treatment effects on sleep.

This Chapter describes the results of follow-up assessments conducted as part of the study in Chapter 5. Follow-up assessments took place after PTSD patients had received CT-PTSD, or after an equivalent 3-month wait for trauma controls.

Research questions and hypotheses

To address these aims, the study specifically investigated the following questions:

1) Does CT-PTSD lead to improvements in subjective and objective measures of sleep, pre-sleep cognitive activity (PTSD and insomnia related) and physiological arousal (cortisol) and sympathetic activation during sleep (HRV)?
2) Do sleep problems persist after otherwise effective PTSD treatment, when other PTSD symptoms have resolved?
3) Does pre-sleep cognitive activity play a role in reported sleep problems after PTSD recovery?

4) What factors are associated with sleep disturbance improvements and persistence after effective PTSD therapy? (exploratory analyses)
5) Does sleep severity at pre-treatment predict PTSD symptom severity at post-treatment? (replication analyses of Chapters 2).

In line with the literature and the results of previous chapters, it was hypothesised that:

1) Sleep, arousal (cortisol will increase and LF/HF ratio will reduce) and pre-sleep cognitive activity will improve with effective treatment. Pre-sleep cognitive activity specific to PTSD will reduce to a greater extent with treatment than insomnia related pre-sleep cognitive activity.
2) Sleep problems will be residual for up to half of recovered PTSD patients.
3) In trauma survivors recovered from PTSD, PTSD symptoms will not predict sleep disturbance severity, but pre-sleep cognitive activity will account for significant variance in sleep disturbances.
4) Sleep improvements with therapy will be associated with change in PTSD symptoms and appraisals, as shown in Chapters 2 and 3. In those recovered from PTSD at post-treatment, sleep disturbance severity may be associated with higher post-treatment arousal or insomnia-related pre-sleep cognitive activity reflecting the role of insomnia related maintenance factors in persistent sleep problems after otherwise effective therapy.
5) Pre-treatment sleep duration and quality will not be associated with post-treatment PTSD symptom severity, as in Chapter 2. This will also be reflected in validated subjective measures of sleep disturbance (PSQI), diary measures, and objective measures of sleep duration.

Methods

Participants

A total sample of 73 trauma survivors (50 women, 23 men), aged 18-65 (M: 34.33, SD: 12.67), took part in the study. The sample was comprised of two groups; 30 PTSD patients (treatment-seeking, recruited from NHS services), and 43 trauma-exposed participants without PTSD (trauma controls). The sample size was calculated to detect medium effect sizes for sleep, cortisol and HRV changes with CT-PTSD, as observed in previous chapters for sleep (Chapter 2, Chapter 3), and from previous studies on salivary cortisol (Gerardi et al., 2010), and HRV (Nishith et al., 2003). Power analyses determined that a sample of 132 was required to give a power of 95% to detect medium effect sizes. As recruitment aims were not met, post-hoc power analyses revealed that the recruited sample size (N = 73) yielded 76% power to detect treatment effects on sleep outcomes in a mixed ANOVA. Participants were recruited as part of the wider study described in Chapter 5. Inclusion criteria are the same as in Chapter 5. To be included, it was required that participants were aged between 18 and 65, could read and write in English, had no history of or current bipolar or psychosis, no current substance or alcohol dependence, and if they were taking psychotropic medication had been on a stable dose for at least 2 months. Additional inclusion criteria for the PTSD group were that they had experienced a traumatic event as defined by Criterion A of the DSM-5 (APA, 2014), had a current diagnosis of PTSD, and were not currently undergoing treatment for PTSD. Inclusion criteria for the trauma control group were that they had experienced a Criterion A traumatic event, but did not meet criteria for a current diagnosis of PTSD, and were not receiving psychotherapy. Figure 6.1 shows the recruitment flow-chart for PTSD patients, Table 6.1 shows demographic characteristics, symptom severity, and trauma characteristics.

Of the treatment-seeking PTSD patients, 23 were assessed again 3 months later, after a course of PTSD therapy. Seven patients were not assessed as they could no longer be contacted or had dropped out of treatment. As a comparison, 29 traumatised control participants were assessed again after 3 months (with no intervention) to check for effects of re-assessment. Therefore the final sample follow-up sample sizes were 23 people with PTSD and 29 trauma controls. This sample size (N = 52) provided 61% power to detect medium effect sizes.

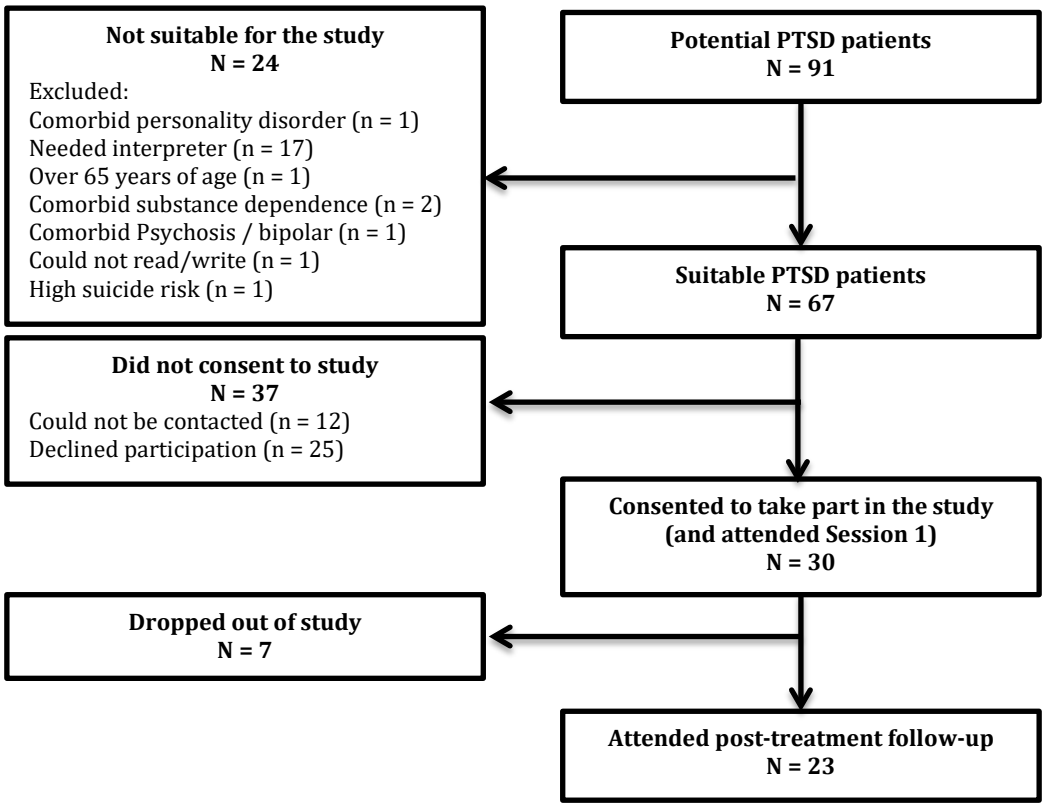


Figure 6.1. Recruitment flow-chart for PTSD patients from referral into the study to post-treatment assessment (n = 23).

Table 6.1. Demographic characteristics and test statistics for PTSD and trauma controls at Session 1.

	TRAUMA-CONTROL (N = 43)	PTSD (N = 30)	STATISTICAL SIGNIFINCANCE (x^2 or t, p)
	M (SD)		
AGE	34.02 (14.01)	34.82 (10.41)	$F(1, 69)$ .06, p = .80
GENDER	**N (%)**		
Women	31 (72.1%)	19 (63.3%)	
Men	12 (27.9%)	11 (36.7%)	$x^2(1) = .63$, p= .43
Education (years)	16.40 (2.65)	15.04 (3.91)	$F(1, 65) = 2.78$, p = .10
ETHNIC BACKGROUND	**N (%)**		
Caucasian	35 (81.4%)	18 (60%)	
Ethnic minority	8 (18.6%)	12 (40%)	$x^2(1) = 4.07$, p = .044*
PTSD SYMPTOMS & MOOD	**N (%)**		
PDS (Trauma survivors; n = 85)[1]	8.4 (6.78)	34.83 (12.24)	$t(63)$ = -10.-97, p <.001***
BDI	7.93 (7.43)	22.52 (8.09)	$t(68)$ = -7.73, p <.001***
MEDICATION USE	**N (%)**		
No medication	30 (69.8%)	14 (46.7%)	
Non-psychotropic medication	10 (23.3%)	9 (30.0%)	
Use of psychotropic medication (all)	3 (7.0%)	7 (23.3%)	
Psychotropic: SSRIs	3 (7.0%)	6 (22.2%)	[2]Medication use: $x^2(2)$ 5.33, p = .07
Psychotropic: Benzodiazepines	0	0	
Psychotropic: Narcotic	0	1 (3.7%)	Type of Psychotropic: $x^2(1) = .48$, p = .49
PHYSICAL HEALTH PROBLEMS	**N (%)**		
Physical health problems	5 (11.6%)	11 (39.3%)	$x^2(1) = 7.43$, p = .006**
SMOKER	**N (%)**		
Smoker	3	5	$x^2(1) = 1.7$, p = .19
TRAUMA TYPE (trauma survivors; n = 85)	**N (%)**		
RTA	6 (14%)	8 (29.6%)	
Non-Sexual Assault[3]	5 (11.6%)	2 (7.4%)	
Sexual assault[3]	5 (11.6%)	6 (22.2%)	
Accident	2 (4.7%)	0	
Natural Disaster	0	0	
Military	1 (2.3%)	0	
Witnessing Others die/seriously hurt	5 (11.6%)	1 (3.7%)	
Childhood abuse[3]	3 (8.0%)	4 (7.4%)	
Sudden, traumatic loss	7 (16.3%)	1 (3.7%)	
Life-threatening illness	3 (7.0%)	0	
Armed robbery[3]	1 (2.3%)	0	
Imprisonment	0	1 (3.7%)	
Other[4]	5 (11.6%)	4 (14.8%)	Interpersonal[3] vs. non-interpersonal traumas: $x^2(1)$ = 1.00, p = .32
TRAUMA CHARACTERISTICS	**M (SD)**		
Time since Trauma (years)	10.12 (10.18)	9.20 (11.19)	$t(67)$ = .35, p = .72

[1]Due to missing data, the sample sizes were: Trauma, n = 35, PTSD n = 30
[2]Medication use compares distribution of psychotropic, non-psychotropic and no medication use.
[3]Classified as interpersonal trauma types for the comparison of interpersonal vs. non-interpersonal trauma.
[4]Includes vicarious traumas as part of job, learning about a sexual assault, life threatening injuries

Recruitment and ethics

The study received NHS ethical approval from the South-Central Oxford C Research ethics committee (Ref: 14/SC/0198). The full recruitment procedure is described in Chapter 5. Traumatised control participants were recruited via adverts and participants with PTSD were recruited from participating NHS treatment clinics in London and Oxford. PTSD patients who attended Session 1 (Chapter 5) were asked if they would be happy to return for a second session at the end of their PTSD treatment, 3 months later, all agreed, and 7 later dropped out (see Figure 6.1). Trauma controls were also invited to a second research session after an equivalent time period (3 months) with no intervention. Thirty-one agreed, and 29 attended.

Measures

All measures are the same as in Chapter 5, and listed in brief below. See Chapter 5 for full descriptions of each measure.

Clinician Assessment

Clinician-administered PTSD Scale (CAPS) for DSM-5 (Weathers et al., 2013). The CAPS is a clinician-administered measure of PTSD diagnosis according to DSM-5 criteria (APA, 2013).

Symptom Measures

Life Events Checklist (LEC) (Foa et al., 1997). The LEC was administered to determine whether participants had experienced a Criterion A traumatic event, according to DSM-5 criteria (APA, 2013) (see Appendix E for scale).

Posttraumatic Diagnostic Scale (PDS) (Foa et al., 1997). The PDS is a validated self-report measure assessing the severity of DSM-5 specified PTSD symptoms (range: 0–60). A PDS sum score without the sleep item (PDSwos) was also computed for use in analyses (range: 0–57).

Beck Depression Inventory (BDI) (Beck et al., 1961). The BDI is a widely used 21-item questionnaire assessing the severity of depressive symptoms over the previous two weeks (range: 0-63).

Posttraumatic Cognitions Inventory (PTCI) (Foa, Ehlers, Clark, Tolin, & Orsillo, 1999b). The PTCI was used to assess excessively negative appraisals of the trauma and its consequences (range: 1–140); higher scores indicate more maladaptive appraisals.

Pre-Sleep Cognition Scale (PSCS) (Woodward et al., in prep; see Chapter 4). The PSCS measures the frequency of sleep-interfering pre-sleep cognitions during sleep onset (range: 0–63). The scale includes two sub-scales assessing insomnia related pre-sleep cognitions ($PSCS_{INSOM,}$ range: 0–36) and PTSD related pre-sleep cognitions ($PSCS_{PTSD,}$ range: 0-27) (see Appendix C for scale).

Subjective sleep measures

Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989). The PSQI was used to measure the overall severity of sleep disturbances in the previous month, and includes 7 sub-scales assessing different aspects of sleep dysfunction (sub-scales are scored from 0 to 3), which sum to a global PSQI score (range: 0-21). Higher scores indicate more severe sleep disturbances, and a global score of greater than 5 has been shown to

indicate clinically significant sleep disturbances (Buysse et al., 1989), and insomnia (Backhaus et al., 2002).

Pittsburgh Sleep Quality Index Addendum for PTSD (PSQIA) The PSQIA (Germain et al., 2005), Assesses the severity of PTSD related sleep disturbances over the past month (score range: 0-21).

Sleep Diary. The sleep diary was used to monitor participant's self-reported sleep over 7 days. Questions asked were used to calculate sleep duration (total sleep time: TST), sleep onset latency (SOL), number of awakenings after sleep (WASO no.) duration of wake after sleep (WASO min), sleep efficiency ((time asleep/time in bed) x 100), sleep quality (SQ; *'Overall how well did you sleep?'* rated from 0 '*not at all well*' to 100 '*extremely well*'). Additional questions were added to assess nightmare frequency (*'how many nightmares did you have in total last night')*, distress at nightmares (rated from 0 '*not at all*', to 100 '*extremely distressed*'), whether the nightmare was of or related to the trauma (yes/no), and pre-bed anxiety ('*how anxious are you about going to bed tonight?'* rated from 0 '*not at all*' to 100 '*extremely anxious*'). Nightmare frequency was calculated as the number of days nightmares were had on. See Appendix F for sleep diary instructions and items included in these analyses.

Objective sleep measures

Actigraphy. Actigraphy was used as a home-based objective measure of sleep and wake. Participants wore an actigraphy wristband (GeneACTIV; ActivInsights, Ltd., Kimbolton, UK) on their non-dominant wrist for seven days while completing the sleep diary (see Chapter 5).

Objective arousal measures

Heart-rate. Heart-rate was assessed over 24-hours, including during sleep, in patient's own homes, using a Polar RS800CX (Polar Electro Oy, Kempele, Finland; 1000 Hz) ambulatory heart-rate monitor. A 5-minute segment was selected from the recording during actual sleep (selected to be 2 hours after sleep onset, and confirmed against actigraphy and the sleep diary). Mean heart-rate and a frequency domain measure of HRV (LF/HF ratio: Higher values indicate greater sympathetic activation/ autonomic arousal) were calculated in MATLAB (version R2016a, The MathWorks, Inc., Natick, Massachusetts) and analysed (see Chapter 5).

Cortisol. Basal, diurnal variation (short daytime profile) of free cortisol was assessed. Participants collected their saliva samples at 8am, 4pm, and 10pm on the second measurement day at Session 1 and Session 2. Analysis of cortisol concentration (nmol/l) was carried out in duplicate, and the duplicate mean was used in the analysis.

Procedure

See Chapter 5 for full Session 1 procedure. Participants attending Session 1 were assessed for PTSD diagnosis with the CAPS, completed a questionnaire pack to assess self-reported sleep and PTSD symptoms, and had their baseline heart-rate measured for 2-minutes. They were then given their sleep diary, saliva sample pots to take home, and a heart-rate monitor (24 hours) and actigraphy wristband (7 days) to wear at home. Participants wore the heart-rate monitor for the first 24 hours (over the first night of sleep), collected the saliva samples on the second day, and wore the actigraphy band and recorded their sleep daily for 7 days after the session. PTSD patients awaiting treatment were invited back to a second session 3 months later, after receiving Cognitive Therapy for PTSD (Ehlers et al., 2005), which follows Ehlers and Clark's

(2000) cognitive model of PTSD. CT-PTSD (described more fully in Chapters 1, 2 and 3) is a trauma-focused psychological therapy for PTSD, delivered in 12-weekly sessions. Trauma controls were invited back after an equivalent time period (3 months) with no intervention. At the second session, the CAPS was repeated to assess PTSD diagnosis, followed by the same procedure and measurement week as in session 1 (see Chapter 5).

Data Analysis

Analyses were conducted in IBM SPSS statistics (version 22.0). Data was checked for assumptions of normality and homogeneity, and non-parametric tests were used where appropriate.

Question 1

To investigate treatment effects on subjective and objective sleep, arousal, and pre-sleep cognitive activity, groups with participants who attended both sessions (PTSD; n = 23; Trauma; n = 29) were compared on measures from Session 1 to Session 2. The PTSD patient post-treatment sample included those not recovered from PTSD at post-treatment (7 out of 23 patients). Recovery from PTSD (treatment responder) was defined as the absence of PTSD diagnosis on the CAPS at post-treatment.

To investigate treatment effects on subjective (PSQI, PSQIA, Sleep diary) and objective sleep measures (actigraphy), and pre-sleep cognitive activity ($PSCS_{INSOM}$, $PSCS_{PTSD}$), mixed ANOVAs were conducted comparing change in these measures, with between subjects factor 'group' (trauma, PTSD) and within subjects factor 'time' (Session 1, Session 2). Effect sizes (ES) are reported as partial $\eta 2$, with small ES $\geq$ 0.01; medium $\geq$ 0.06; and large $\geq$ 0.14, and significant interactions between group and time are reported

in the text. Significant group x time interactions were investigated with planned comparisons, using paired samples t-tests to compare variables from Session 1 to Session 2 within each group. Correlations between objective and subjective estimates of sleep duration examined consistency between measures. To investigate whether treatment affected insomnia and PTSD related cognitions differently, percentage change in $PSCS_{PTSD}$ and $PSCS_{INSOM}$ scores from Session 1 (pre-treatment) to Session 2 (post-treatment) was calculated for PTSD patients only (score change/Session 1 score x 100) and compared using paired t-tests.

To investigate treatment effects on hyperarousal, cortisol and HRV during sleep were compared between groups from Session 1 to 2. Due to small sample sizes, the LF/HF ratio (HRV) during sleep was investigated using a Wilcoxon signed rank test comparing LF/HF ratio at Session 1 and Session 2, within each group. Groups were also compared on mean cortisol, and the area under the measurement curve (8am, 4pm, 10pm) with respect to ground (AUCg; ground was set at zero), and with respect to increase (AUCi; with respect to baseline measurement, i.e. 8am) (see Fekedulegn et al., 2007 for formula). To examine treatment effects on the daytime profile of cortisol, a repeated measures ANOVA with within subjects factor 'time' (Session 1, Session 2), between subjects factor group (trauma, PTSD) compared groups on AUCi and AUCg, from Session 1 to Session 2. To examine treatment effects on mean cortisol, mixed ANOVAs compared groups from Session 1 to Session 2, with the between subjects factor 'group' (trauma, PTSD), and the within subjects factors 'sampling time' (8am, 4pm, 10pm) and 'time' (Session 1, Session 2). Demographic variables that differed between groups were entered as covariates into the analyses comparing groups on sleep (PSQI), cortisol, and LF/HF ratio, and were retained as covariates if they had a significant main effect or interaction.

Question 2

To investigate whether sleep disturbances persisted after PTSD recovery, the percentage of recovered PTSD patients reporting clinically significant sleep problems (PSQI global score > 5) at post-treatment (Session 2) was calculated and reported.

Question 3

The relationship between PTSD symptoms, pre-sleep cognitive activity, and sleep disturbance (PSQI global score) in those recovered from PTSD was examined using regression. Analyses were conducted at Session 2 with those who had recovered from PTSD (n = 16), combined with trauma survivors who were assessed as having had PTSD in the past (n = 9), in order to increase the sample size (final n = 25).

Question 4

To explore variables that may be associated with sleep disturbance improvements during treatment, change from Session 1 to Session 2 was calculated (Session 2 – Session 1 score) for sleep measures that showed significant change with treatment, and these were correlated with change in PTSD symptoms, depression symptoms, posttraumatic appraisals, and pre-sleep cognitive activity. To explore variables that may be associated with residual sleep problems at post-treatment, post-treatment subjective and objective sleep parameters (TST, SOL, WASO, SQ) were correlated with post-treatment depression (BDI), PTSD symptoms (PDSwos), posttraumatic cognitions (PTCI), pre-sleep cognitive activity (PSCS), and measures of arousal (cortisol, LF/HF ratio during sleep). Analyses were conducted with those who had recovered from PTSD at post-treatment (n = 16), in order to examine factors that may be associated with persistent sleep problems in the absence of PTSD diagnosis.

Question 5

To investigate whether the findings of Chapter 2 could be replicated, sleep duration (objective, subjective), sleep quality, and sleep disturbance severity (PSQI) at Session 1 were correlated with PTSD symptom severity at Session 2 (post-treatment). As in Chapter 2, analyses were conducted in the entire pre to post-treatment sample (n = 23), including those who had not recovered from PTSD at post-treatment.

Results

Demographic statistics

Demographic and test statistics are shown in Table 6.1.

The groups did not differ on age and gender distribution and medication use at baseline (see Table 6.1) and medication use did not change from Session 1 to Session 2 in either group (p > .05). There was no difference in trauma type (interpersonal versus non-interpersonal) between PTSD and trauma controls (see Table 6.1). The groups differed on ethnicity distribution, as the PTSD group had more people of ethnic minority than controls or trauma controls. Ethnicity was entered as a covariate into analyses, and did not significantly effect Session 1 to Session 2 changes in sleep disturbance (PSQI), PTSD symptom severity, LF/HF ratio, or cortisol (8am, 4pm, 10pm), p's > .05, and so ethnicity was included as a covariate in further analyses. The distribution of participants reporting physical health conditions also differed significantly, and was higher in the PTSD group. Physical health problems were entered as covariate into analyses, and did not significantly effect Session 1 to Session 2 changes in sleep disturbance, PTSD symptom severity, LF/HF ratio, or cortisol, p's > .05, and so physical health problems was not included as a covariate in further analyses.

PTSD symptom severity (PDS) was compared between trauma survivors with and without PTSD. People with PTSD had significantly higher PDS scores compared to trauma survivors without PTSD, $t(74) = 6.96$, $p < .001$**.** PTSD patients who did and did not drop out of treatment were comparable in age, PTSD symptom severity, depression severity, and sleep disturbance severity (PSQI) (Table 6.2).

Table 6.2. Baseline demographic information and test-statistics (Mann Whitney) comparing participants who attended both sessions, and those who dropped out after Session 1.

	Attended both sessions	**Dropped out**	**Test statistic**
	M (SD)	M (SD)	Mann-Whitney U, *p*
PTSD patients (*n*)	*n* = 23	*n* = 7	
Age (years)	33.00 (9.33)	37.71 (13.19)	41.00, *.33*
PDS	34.00 (10.49)	29.00 (13.34)	74.00, .30
BDI	21.71 (7.49)	24.14 (10.25)	37.5, .45
PSQI (global score)	10.12 (3.63)	10.29 (3.55)	55.00, 1.0
Trauma controls (*n*)	*n* = 29	*n* = 14	
Age (years)	31.82 (11.20)	33.38 (15.72)	231.50, .46
PDS	8.55 (7.31)	8.15 (6.04)	180.00, .55
BDI	7.45 (7.87)	9.54 (7.39)	177.00, .50
PSQI (global score)	5.31 (2.89)	5.57 (1.99)	180.00, .55

PDS = PTSD symptom severity, BDI = Beck depression inventory, PSQI = global sleep disturbance severity.

PTSD symptoms: change with treatment

Change in PTSD symptom severity (including sleep) was compared with a mixed repeated-measures ANOVA with the between subjects factor 'group' (trauma, PTSD), and within subjects factor 'time' (Session 1, Session 2). There was a significant main effect of time, $F(1, 41) = 51.17$, $p < .001$, group, $F(1, 41) = 52.47$, $p < .001$, and a significant group x time interaction, $F(1, 41) = 27.27$, $p < .001$. Paired t-tests showed that PTSD symptoms (PDS scores) significantly reduced from pre to post treatment for PTSD patients, $t(21) = 6.87$, $p < .001$ (Mean change = 17.09, SD= 11.67), and slightly reduced for trauma controls, $t(20) = 2.44$, $p = .03$ (Mean change = 2.67, SD = 5.01).

Post-treatment (Session 2) CAPS assessment showed that 16 out of 23 (69.57%) PTSD patients no longer met criteria for PTSD diagnosis after treatment, and none of the trauma controls met criteria for PTSD diagnosis.

Research Question 1: Does CT-PTSD lead to improvements in subjective and objective measures of sleep, pre-sleep cognitive activity and objective arousal?

Subjective Sleep

Pittsburgh Sleep Quality Index (PSQI)

Descriptive and full test-statistics are reported in Table 6.3. The mixed ANOVA showed a significant group x time interaction, $F(1, 48) = 5.92$, $p = .02$, $\eta 2 = .11$. Paired t-tests showed that for PTSD patients, sleep disturbance severity (PSQI global score) significantly decreased from Session 1 to Session 2 (Mean change = 2.64, SD = 4.88). Trauma survivors showed no significant change in PSQI global score from Session 1 to Session 2, suggesting that the PSQI changes in the PTSD group were due to treatment rather than time or the effects of repeating the research session (Figure 6.2, Table 6.3). Analysis of the PSQI sub-scales, showed significant group x time interactions for three out of seven PSQI sub-scales; daytime dysfunction, sleep onset latency, sleep quality (Table 6.3). Paired t-tests showed significant improvements on these three sub-scales for the PTSD group only, such that daytime dysfunction was lower, sleep onset latency was shorter and sleep quality was higher at Session 2. There was no significant group x time interaction for the sub-scales; sleep duration, sleep efficiency, sleep medication use, or sleep disturbance (which includes items such as; waking in the night, bad dreams, and feeling too hot/cold) (see Table 6.3). These results suggest that some self-reported sleep disturbances were improved with PTSD treatment.

Addendum for PSTD (PSQIA)

Descriptive and full test-statistics are reported in Table 6.3. An ANOVA was conducted on the PTSD-related sleep disturbances (PSQIA sum score), and showed a significant group x time interaction, $F(1, 48) = 4.69$, $p = .04$, partial $\eta 2 = .09$. Paired t-tests showed a significant reduction in PSQIA scores from Session 1 to Session 2 for PTSD patients and no significant changes for trauma controls (see Table 6.3). Further, the number of PTSD patients endorsing trauma-related nightmares in the past month on the PSQIA trauma-nightmare item (score > 0 on PSQIA *'memories or nightmares of the trauma'*) was 36.7% at post-treatment (Session 2), compared to 80% at pre-treatment (Session 1). These results suggest that PTSD related sleep disturbances were reduced with PTSD treatment.

Sleep Diary

Descriptive and full test-statistics are reported in Table 6.3. The mixed ANOVAs showed no significant group x time interactions for sleep onset latency, $F(1, 49) = .80$, $p = .38$, $\eta 2 = .02$, number of awakenings after sleep, $F(1, 49) = 1.9$, $p = .67$, $\eta 2 = .004$, wake after sleep duration, $F(1, 49) = 2.41$, $p = .13$, $\eta 2 = .05$, sleep duration, $F(1, 49) = .45$, $p = .50$, $\eta 2 = .01$, sleep quality, $F(1, 49) = 1.34$, $p = .25$, $\eta 2 = .03$, sleep efficiency, $F(1, 49) = 1.35$, $p = .25$, $\eta 2 = .03$, trauma nightmare frequency, $F(1, 49) = 1.41$, $p = .24$, $\eta 2 = .02$, and trauma-nightmare distress, $F(1, 7) = 1.38$, $p = .28$, $\eta 2 = 17$. There was a significant group x time interaction for pre-bed anxiety, $F(1, 49) = 15.27$, $p < .001$, $\eta 2 = 24$. Paired t-tests showed that PTSD patients reported a significant reduction in pre-bed anxiety with treatment, and trauma controls showed no change from Session 1 to Session 2 (see Table 6.3). These results show that, for PTSD patients, pre-bed anxiety is reduced with treatment, but there was no significant change with treatment on other subjective sleep parameters.

Table 6.3. Descriptive and test-statistics for each group, for participants who attended both Session 1 and Session 2.

	TRAUMA (*n* = 29)		**PTSD (*n* = 23)**		**TEST STATISTICS**			**TRAUMA**	**PTSD**
	SESSION 1	SESSION 2	SESSION 1	SESSION 2	TIME (F, *p*)	GROUP (F, *p*)	INTERACTION (F, *p*)	T-TEST t, *p*, (*d*)	T-TEST t, *p* (*d*)
	Mean (SD)								
SYMPTOMS AND APPRAISALS									
PDSwos	7.81 (6.92)	5.48 (7.93)	34.18 (11.01)	17.86 (12.63)					
BDI	7.31 (7.58)	7.00 (7.87)	22.11 (7.59)	12.00 (6.48)	24.15, < .001	26.19, < .001	21.36, < .001	.25, .80 (.04)	5.54, <.001 (1.43)
PTCI	72.14 (33.62)	63.71 (34.08)	127.42 (35.65)	79.11 (26.64)	28.42, < .001	20.01, < .001	14.40, <.001	1.44, .16 (.25)	4.99, <.001 (1.54)
PITTSBURGH SLEEP QUALITY INDEX									
PSQI (Global score)	5.21 (2.90)	5.14 (2.97)	11.00 (3.88)	8.36 (4.98)	6.6, .01	24.66, <.001	5.92, .02	.16, .88 (.02)	2.54, .02, (.59)
Sleep Quality	1.00 (.94)	1.07 (.86)	2.09 (0.75)	1.18 (0.85)	5.96, .02	9.66, .003	8.19, .01	-.33, .75 (.07)	3.58, .002 (1.14)
Sleep Onset Latency	1.14 (.84)	1.11 (.83)	2.36 (0.68)	1.84 (0.83)	10.11, .003	9.44, 004	8.02, .01	.25, .80 (.03)	3.75, .001 (.68)
Sleep Duration	.32 (.67)	.25 (.59)	1.24 (0.94)	0.81 (0.93)	5.88, .02	12.29, <.001	3.10, .09		
Sleep Efficiency	.46 (.79)	.39 (.63)	1.48 (1.21)	1.09 (1.37)	1.69, 20	12.03, .001	.82, .37		
Sleep Disturbances	1.43 (.63)	1.21 (.42)	1.82 (0.66)	1.68 (0.72)	5.42, .02	6.79, .01	.22, .64		
Daytime Dysfunction	.79 (.57)	1.00 (.72)	1.71 (0.78)	1.24 (0.89)	2.47, .12	8.08, 01	15.46, <.001	-2.71, .01 (.32)	2.69, .01 (.56)
Sleep Medication	.07 (.38)	.11 (.57)	0.71 (1.15)	0.57 (1.12)	.21, .65	5.30, .03	.57, .45		
PSQI-A (sum score)	3.14 (2.38)	2.39 (2.25)	8.48 (3.93)	5.76 (4.67)	14.00, <.001	4.5, .04	4.69, .04	1.97, .06 (.32)	2.88, .01 (.63)

SLEEP DIARY									
Sleep onset latency	18.21 (15.35)	17.84 (18.04)	31.20 (26.13)	26.11 (27.79)	1.07, .31	3.79, .057	.80, .38		
Sleep duration (TST)	7.09 (1.21)	7.27 (1.65)	6.49 (1.27)	6.91 (2.02)	2.78, .10	1.41, .24	.45, .50		
Sleep efficiency (%)	83.24 (11.00)	83.62 (13.60)	75.62 (15.63)	77.06 (22.53)	.35, .56	2.82, .10	1.35, .25,		
Wake after sleep (no.)	1.45 (0.95)	0.99 (0.75)	1.97 (1.50)	1.63 (1.44)	8.67, .01	3.80, .0	1.9, .67		
Wake after sleep (min.)	14.29 (14.96)	14.17 (23.21)	37.92 (46.82)	24.90 (25.09)	2.5, .12	6.09, .02	2.41, .13		
Sleep quality (0-100)	64.69 (17.05)	67.42 (17.16)	47.30 (13.96)	54.30 (17.31)	6.98, .01	12.62, .001	1.34, .25		
Trauma nightmare freq.[1]	.21 (.62)	.24 (.64)	.96 (1.26)	.74 (1.05)	.46, .50	.86, .005	1.41, .24		
Trauma nightmare distress (0-100)	66.67 (18.86)	75.00 (21.21)	37.00 (27.97)	38.82 (19.32)	.03, .87	3.36, .11	1.38, .28		
Pre-bed anxiety (0-100)	9.59 (13.28)	10.79 (16.80)	37.52 (23.63)	20.54 (19.12)	11.49, 001	16.99, <.001	15.27, <.001	-.61, .55 (.07)	3.63, .002 (.79)
ACTIGRAPHY									
Time in bed	7.72 (1.21)	7.37 (1.05)	7.15 (1.91)	8.38 (1.71)	3.18, .08	.30, .59	10.24, .003	1.34, .20 (.31)	-2.94, .01 (.68)
Sleep duration (TST)	7.23 (1.21)	6.87 (1.05)	5.93 (2.25)	7.55 (2.25)	5.73, .02	.47, .49	14.41, .001	1.33, .20 (.31)	-3.59, .002 (.72)
Sleep efficiency (%)	93.65%	93.22%	82.94%	90.10%					
PRE-SLEEP COGNITION SCALE (PSCS)									
PSCS (SUM)	11.21 (9.66)	9.25 (9.83)	31.14(17.24)	19.32 (17.34)					
PSCS$_{INSOM}$	9.18 (7.73)	7.32 (7.14)	20.00 (10.55)	12.95 (10.08)	18.07, <.001	12.98, .001	6.14, .02	1.57, .13 (.25)	3.86, .001 (.68)
PSCS$_{PTSD}$	2.04 (3.23)	1.92 (4.14)	11.14 (7.86)	6.36 (8.73)	8.52, .01	19.22, <.001	7.79, .01	.12, .90 (.03)	3.11, .005 (.58)

[1]*Trauma nightmare frequency refers to the number of days that nightmares were had, that were of or related to the trauma.*
Note. Test statistics are shown for main effect of time (session 1, session 2) and group (Trauma, PTSD), and paired t-test compare session 1 to 2 within each group.
(d) = effect size, where a small effect size = .20, medium = .50, and large = .80, according to Cohen (1992).

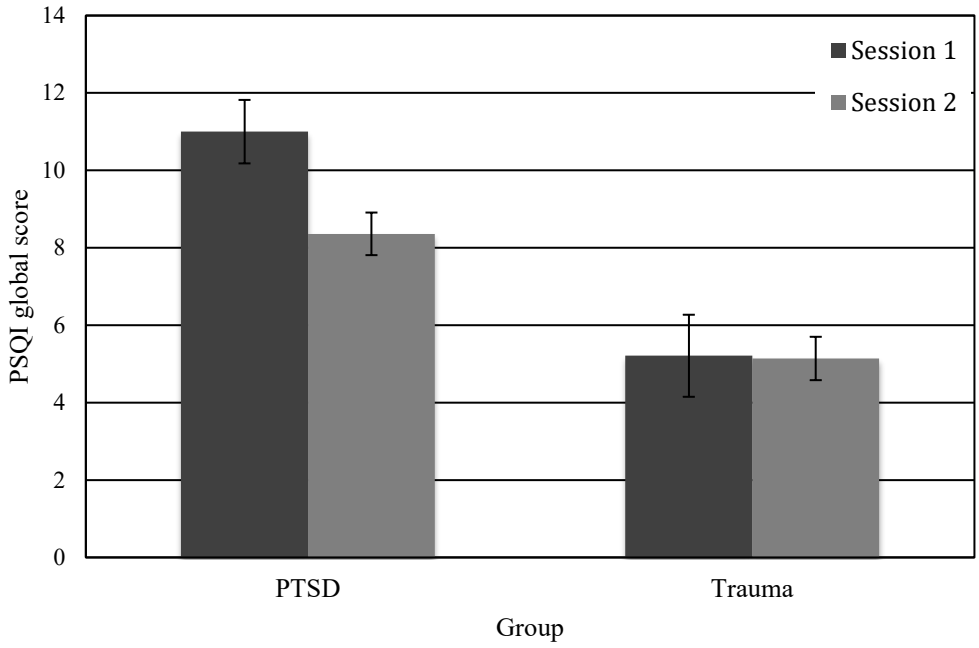


Figure 6.2. Mean PSQI global sum score (with standard error bars) for each group at Session 1 and Session 2. Note. Trauma *n* = 29, PTSD *n* = 23.

Objective Sleep: Actigraphy

Descriptive and full test-statistics are reported in Table 6.3. The ANOVA showed a significant group x time interaction for objective sleep duration, $F(1, 37) = 14.41$, $p = .001$, $\eta 2 = .28$, and time in bed, $F(1, 37) = 10.24$, $p = .003$, $\eta 2 = .21$. Paired t-tests showed that for PTSD patients, there was a significant increase of 90 minutes sleep duration from Session 1 to Session 2 (Mean change: 1.62 hours, SD = 2.13), and no significant change from Session 1 to 2 for trauma controls (see Table 6.3). These results show that in PTSD patients, objectively measured sleep duration increased with treatment.

At Session 1, mean subjective (diary) sleep duration was significantly correlated with mean objective total sleep time in both the trauma control group, $r = .63$, $p < .001$, and PTSD group, $r = .49$, $p = .007$. At Session 2 mean subjective sleep duration was

correlated for trauma controls, r = .52, p = .01, but was not correlated for PTSD patients at post-treatment, r = .01, p = .96.

Pre-Sleep Cognitive Activity

Descriptive and full test-statistics are reported in Table 6.3. For both insomnia-related ($PSCS_{INSOM}$) and PTSD-related ($PSCS_{PTSD}$) pre-sleep cognitive activity, mixed ANOVAs showed significant main effects of time, group and group x time interactions; $PSCS_{INSOM,}$ $F(1, 48) = 6.14$, $p = .02$, $\eta 2 = .11$ and $PSCS_{PTSD,}$ $F(1, 48) = 7.79$, $p = .01$, $\eta 2 = .14$ (interaction effect). Paired t-tests within the PTSD group showed a significant decrease in the $PSCS_{INSOM}$ and $PSCS_{PTSD}$ scores from pre to post treatment, whereas there were no changes for trauma controls (see Table 6.3). The percentage reduction with treatment in $PSCS_{PTSD}$ scores (Mean reduction = 52.13%, SD = 46.55) was significantly greater than for $PSCS_{INSOM}$ scores (Mean reduction = 31.53%, SD = 58.47), $t(20) = -2.90$, $p = .009$.

Objective Arousal: Heart-rate and heart-rate variability during sleep

Descriptive statistics are shown in Table 6.4. Of those who attended both sessions, 8 trauma controls had available data at both sessions, and 7 PTSD patients (all of whom had recovered from PTSD at post-treatment). The small sample sizes were due to exclusion of 3 trauma controls at baseline (for alcohol use before bed) and the remainder (18 trauma, 16 PTSD) had missing data due to over-night recording device failure or removal of the device overnight at one of the sessions.

As the sample sizes were too small for an ANOVA, a Wilcoxon signed-rank test was used to compare LF/HF ratio within each group from Session 1 to Session 2. There was

no significant change in LF/HF ratio for PTSD patients, T = 17.00, p = .51, or trauma controls T = 23.00, p = .48.

Table 6.4. Mean (standard deviation) for heart-rate and LF/HF ratio value during sleep for trauma controls and PTSD patients with data at Sessions 1 and Session 2.

	Trauma (n = 8)		**PTSD (n = 7)**	
	Session 1	Session 2	Session 1	Session 2
Heart rate				
Sleep	73.73 (10.61)	71.09 (6.54)	65.21 (13.71)	68.68 (11.32)
LF/HF				
Sleep	4.10 (0.45)	4.67 (1.81)	3.73 (0.35)	3.87 (0.29)

Objective Arousal: Cortisol

Mean cortisol (nmol/l) at Session 1 and Session 2 is shown in Figure 6.3 (PTSD) and Figure 6.4 (trauma controls). A total of 42 participants had data available at Session 1 and Session 2 (25 trauma controls, 17 PTSD patients). Two from each group were excluded for non-compliance with sampling times, and so the final sample size for analysis was 38 (23 Trauma, 15 PTSD).

The repeated measures ANCOVA showed a significant effect of 'sampling time', F(2, 68) = 18.61, p < .001, and no significant effect of 'time' (Session1, Session 2), F(1, 68) = 0.4, p = .85, 'group', F(1, 34) = .01, p = .95, group x time interaction, F(1, 68) = .69, p = .41, η2 = .02, and a trend towards a group x sampling time (quadratic) interaction, F(1, 68) = 3.50, p =.07. Overall this indicated no change in the daily rhythm of cortisol with treatment. Similarly, AUCg showed no significant effect of 'group', F(1, 35) = .70, p = .41, 'time', F(1, 35) = 1.31, p = .26, or 'group' x 'time' interaction, F(1, 35) = .70, p = .41, η2 = .02, and the same pattern was found for AUCi with no significant effect of group, F(1, 35) = 1.72, p = .20, time, F(1, 35) = .02, p = .91 or group x time interaction, F(1, 35) = .04, p = .98, η2 =.00.

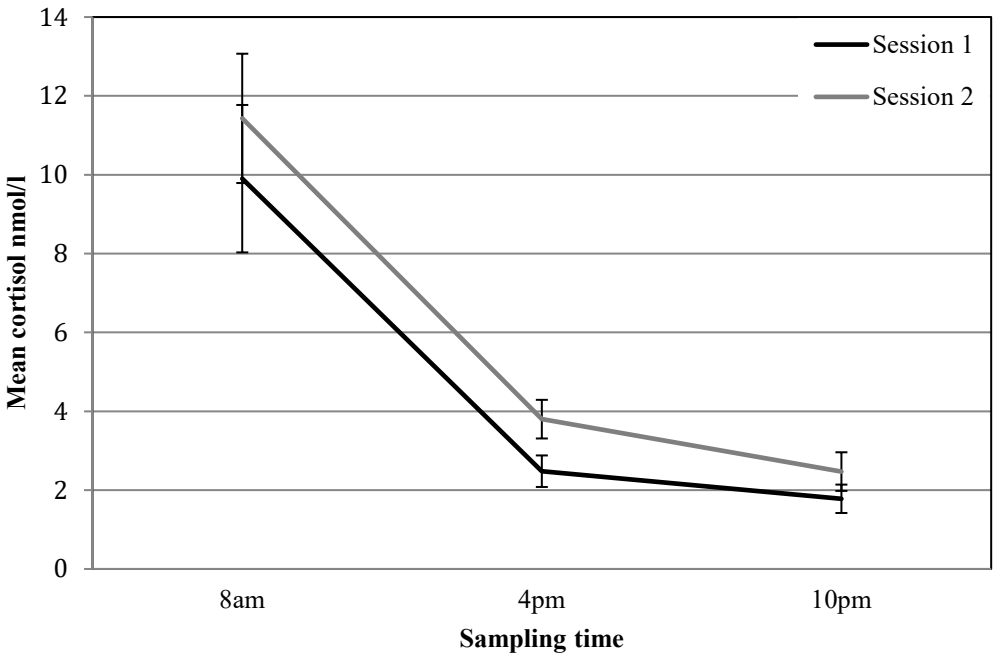


Figure 6.3. Mean cortisol (with standard error bars) at Session 1 and Session 2 (post-treatment), at 8am, 4pm and 10pm, for PTSD patients with cortisol data at both sessions (n = 15).

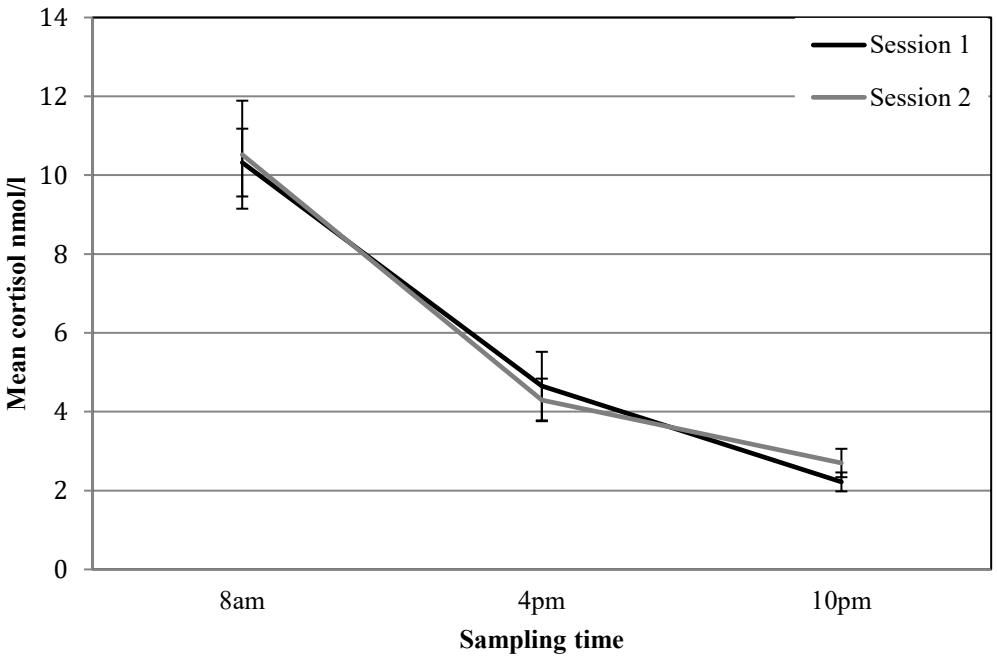


Figure 6.4. Mean cortisol (with standard error bars) at Session 1 and Session 2 (post-treatment), at 8am, 4pm and 10pm, for trauma controls with cortisol data at both sessions (n = 23).

Question 2: Do sleep problems persist after otherwise effective PTSD treatment, when other PTSD symptoms have resolved?

Of those who recovered from PTSD at post-treatment (n = 16), 14 (87.5%) had sleep problems at baseline according to PSQI global score (> 5), and of these, 50% (7/14)

continued to have clinically significant sleep problems at post-treatment. Of those who did not recover from PTSD at post-treatment (7 out of 23), and had sleep problems at baseline (6 out of 7), all 6 continued to have sleep problems at post-treatment (Figure 6.5). Exploratory analyses were conducted with PTSD treatment responders only (n = 16), comparing subjective sleep from pre to post-treatment. Results showed significant reductions in duration of wake after sleep, $t(14) = 2.52$, $p = .02$ (mean change: 24.83 mins, SD = 38.11), increases in sleep quality, $t(14) = -2.12$, $p = .04$ (mean change: 8.47, SD = 14.82), and sleep efficiency, $t(14) = -2.26$, $p = .04$ (mean change: 6.37, SD = 10.55). This suggests greater sleep improvements in people who responded to PTSD treatment.

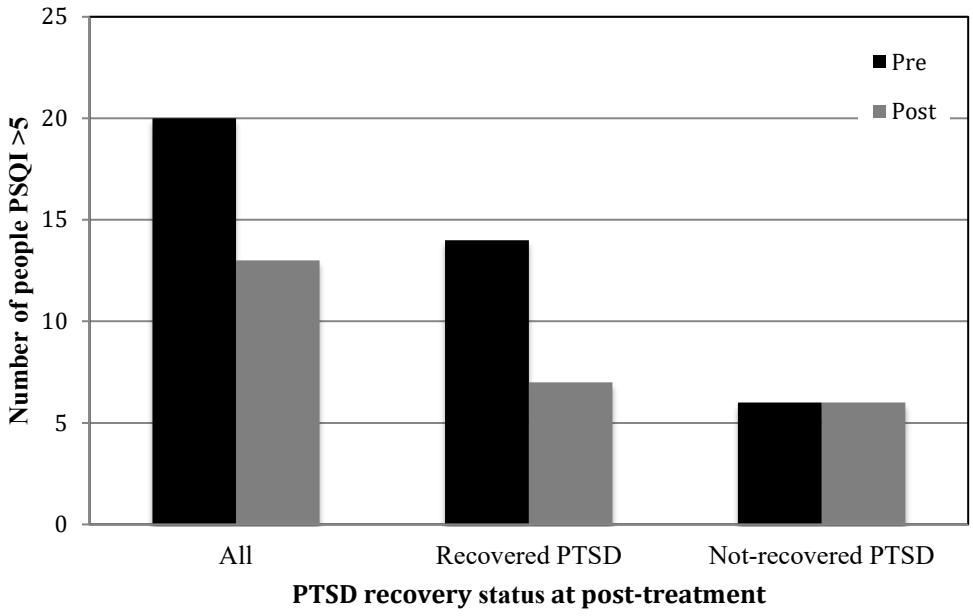


Figure 6.5. Number of PTSD patients with clinically significant sleep problems (PSQI global score >5) at pre and post-treatment (All), and by post-treatment PTSD recovery status (recovered/not recovered). All = those who attended both session 1 and 2 (n = 23).

Research Question 3: Does pre-sleep cognitive activity play a role in reported sleep problems after PTSD recovery?

Regression analysis was used to investigate the relationships between PTSD symptoms (excluding sleep; PDSwos), pre-sleep cognitive activity (PSCS) and subjective sleep disturbance severity (PSQI) in trauma survivors recovered from PTSD (n = 25). As in Chapter 5, the sum score for both sub-scales of the Pre-Sleep Cognition Scale was used to avoid violating multicollinearity assumptions. Simple regression showed that PTSD symptom severity (PDSwos) did not predict sleep disturbance severity, R^2 = .02, F(1, 23) =.40, p = .54, but pre-sleep cognitive activity (sum score) did, R^2 =.25, F(1, 23) =7.70, p = .01, beta = .50, accounting for 25.1% of the variance in PSQI (see Table 6.5). This suggests that the frequency of pre-sleep cognitive activity accounts for some of the variance in sleep disturbances in those recovered from PTSD.

Table 6.5. Regression results for trauma survivors recovered from PTSD (n = 25).

	b	**Standard Error**	**β**	***p***	**R^2**
Constant	5.35	.94		<.001	
PDSwos	.04	.07	.13	.54	.02
Constant	4.21	.80		<.001	
PSCSsum	.18	.06	.50	.01	.25

Research question 4: What other factors may be related to sleep changes with treatment and sleep problems after otherwise effective PTSD Treatment?

Correlating change in sleep with change in symptoms, cognitions and arousal

In PTSD patients (n = 23) mean change in sleep measures that had shown significant change with treatment (PSQI global, PSQIA, objective sleep duration, pre-bed anxiety) were correlated with change in PTSD symptoms (PDSwos), depression symptoms (BDI), posttraumatic appraisals (PTCI), and pre-sleep cognitive activity (PSCS) (Table 6.6). Reduction in PSQI global score was positively correlated with PDSwos reduction,

r = .44, p = .049, reduction in PTSD related ($PSCS_{PTSD}$), r = .59, p = .004, and insomnia related ($PSCS_{INSOM}$) pre-sleep cognitive activity, r = .51, p = .02, and reduction in depression symptoms (BDI), r = .48, p = .04. There was a trend that objective sleep duration increase was associated with a reduction in PDSwos, r = -.43, p = .07, but this was not significant. Pre-bed anxiety reductions were associated with reductions in depression (BDI), r = .56, p = .04. Reduction in PSQIA score was associated with reduction in the PDSwos, r = .52, p = .02, the $PSCS_{PTSD}$, r = .66, p = .001, and $PSCS_{INSOM}$, r = .53, p = .01. Full results are shown in Table 6.6.

Table 6.6. Pearson product moment correlations within PTSD patients (n = 23) of *change* scores with treatment.

	PDSwos	**BDI**	**PTCI**	**$PSCS_{INSOM}$**	**$PSCS_{PTSD}$**
PSQI (global)	.44*	.48*	.31	.51*	.59**
Objective TST	-.43	-.36	.04	-.20	-.01
Pre-bed anxiety	.33	.62**	.27	.10	.14
PSQIA	.52*	.41	.29	.53*	.66**

*Note. Significance indicated by * p <.05, ** p <.01 *** p <.001. Objective TST = sleep duration estimated from actigraphy. PSQIA = Pittsburgh Sleep Quality Index Addendum for PTSD sum score.*

Correlating post-treatment sleep, symptoms, cognitions and arousal

In PTSD patients recovered from PTSD at post-treatment (n = 16) the number of awakenings after sleep were significantly, positively correlated with PTSD symptom severity (PDSwos), r = .62, p = .02, depression severity (BDI), r =.60, p = .02), and PTSD-related pre-sleep cognitive activity ($PSCS_{PTSD}$), *rho* = .61, p = .02. Sleep quality was negatively associated with PDSwos, r = -.71, p = .004, depression symptoms, r = -.72, p = .004, PTSD-related pre-sleep cognitive activity, *rho* = -.67, p = .007, and cortisol at 4pm, r = -.61, p = .04 (see Table 6.7). These results suggest that worse sleep at post-treatment was associated with more severe PTSD and depression symptoms, more PTSD-related pre-sleep cognitive activity, and higher physiological arousal

Table 6.7. Pearson product moment correlations at Session 2 between each measure and sleep parameters in recovered PTSD patients (n = 16).

	Subjective TST	SOL	WASO no.	WASO mins	Sleep Qual	Objective TST
PDSwos	-.07	-.26	.62*	.11	-.71**	.22
BDI	-.02	-.35	.60*	.20	-.72**	.17
PTCI[1]	-.02	-.18	-.06	.03	-.42	.40
$PSCS_{INSOM}$	-.33	.12	.42	.28	-.45	-.23
$PSCS_{PTSD}$[1]	-.10	-.20	.61*	.32	-.67*	.08
HRV						
LF/HF ratio	.45	-.18	.04	-.53	-.28	.39
Cortisol(nmol/l)[2]						
8am	-.01	-.40	.46	-.19	-.05	-.21
4pm	-.33	.05	.18	.50	-.61*	-.17
10pm	-.29	.29	.003	-.23	.09	-.17
AUCg	-.19	-.24	.53	.13	-.30	-.29
AUCi	-.10	.40	-.40	.29	.09	.13

PDSwos = PDS sum score without the sleep item. Subjective TST = subjective (diary) sleep duration; SOL = subjective sleep onset latency (diary); WASO no. = subjective number of awakenings (diary); WASO mins = duration of awakenings (diary); Objective TST = mean objective sleep duration (actigraphy). [1] = Spearman's rank correlations.

Research Question 5: Does baseline sleep severity predict PTSD treatment outcome: replications of analyses from previous Chapters.

In the entire pre to post-treatment sample (n = 23), PSQI global score at baseline did not significantly correlate with PTSD symptom severity, excluding sleep (PDSwos) at end of treatment, r = -.05, p > .05, nor did retrospectively reported (PSQI) total sleep time, r = -.18, p > .05, average diary reported total sleep time, r = -.26, p > .05, retrospectively reported (PSQI) sleep quality, r = .06, p > .05, or diary reported sleep quality, r = -.35, p > .05. Objective total sleep time at baseline was also not correlated with PDSwos at post-treatment, r = -.17, p > .05. Correlations were checked, and were also not significant for the DSM-4 PDS items only, which was the version of the PDS used in

Chapters 2 and 3. This suggests that, as in Chapter 2, baseline sleep severity, duration and quality were not related to PTSD treatment outcome.

Discussion

Summary

This study aimed to further investigate the effects of Cognitive Therapy for PTSD (Ehlers et al., 2005) on objective and subjectively measured sleep, pre-sleep cognitive activity, and hyperarousal and to explore factors that may account for persistent sleep problems after otherwise effective treatment.

The results confirmed most of the hypotheses; 1) Subjective sleep, objectively measured sleep duration and pre-sleep cognitive activity (particularly PTSD related) improved with PTSD therapy. However, there was no change in cortisol and LF/HF ratio with treatment, contrary to the hypothesis. 2) At post-treatment, sleep problems were clinically significant for half of recovered PTSD patients; 3) In those recovered from PTSD, pre-sleep cognitive activity accounted for significant variance in sleep disturbance; 4) Sleep improvements with therapy were associated with improvements in PTSD, depression, and pre-sleep cognitive activity. In recovered PTSD patients, worse subjective sleep at post-treatment was associated with higher PTSD and depression symptoms, PTSD-related pre-sleep cognitive activity and lower afternoon cortisol. 5) The results supported the findings in Chapter 2 that baseline sleep duration and quality did not predict PTSD treatment outcome, and extended this to show that objective sleep duration also did not predict treatment outcome.

In sum, subjective and objective sleep was improved with CT-PTSD but remained residual for half of recovered patients, which was associated with sub-clinical PTSD and depression symptoms, higher pre-sleep cognitive activity and daytime arousal.

The effects of PTSD treatment on sleep, and residual sleep problems after treatment

The results replicate the findings from previous Chapters that CT-PTSD improves sleep, and add to the findings of Chapters 2, 3 by showing that sleep improvements with CT-PTSD are reflected in validated subjective sleep measures (PSQI) assessing the clinical significance of sleep problems. PTSD patients showed treatment improvements in subjective global sleep disturbance (PSQI global), and on the PSQI sub-scales; sleep onset latency, daytime dysfunction and sleep quality. These findings add to previous studies investigating the effects of CBT for PTSD on sleep, by showing that PTSD therapy improved objectively measured sleep duration (by 1 ½ hours in this study). This suggests that it is more than just the subjective experience of sleep that is improved with CT-PTSD. It is in contrast with previous lab-based studies which did not find objective sleep duration improvements in single night recordings after CBT for PTSD (Nishith et al., 2003), which could be explained by the differences in measurement environment. The results of this study provide some objective evidence of sleep improvements in the home environment in PTSD. This is in line with previous suggestions that PTSD patients sleep better in the laboratory than in their homes, where they may feel less safe (Woodward, Bliwise, Friedman, & Gusman, 1996a), and where their reported sleep difficulties occur.

However, it is important to note that despite improvements shown in actigraphic recordings of sleep duration, subjective sleep duration (diary) did not significantly

increase with treatment (although mean sleep duration showed a non-significant 25 minutes increase), in contrast with the results of Chapters 2 and 3, which showed significant sleep duration improvements of up to 1 hour with CT-PTSD. However, this is consistent with a previous study, which found improvements in sleep disturbance, but not sleep duration, after CBT for PTSD (Belleville et al., 2011). Furthermore, in the present study, subjective and objective sleep duration did not correlate at Session 2 for PTSD patients, but still correlated for trauma controls. This could indicate that PTSD patients under-reported sleep duration improvements with treatment, and that actual sleep duration improvements with treatment were greater than those perceived and reported by patients. Another possibility is that patients may still experience low quality sleep at post-treatment, consistent with lack of improvement in (diary) sleep quality in this study, which could affect their perception of their sleep duration estimates. This could be similar to sleep misperception commonly found in insomnia, where objective sleep duration estimates often do not match subjective reports. However, the results must be interpreted with caution, as actigraphy does not directly measure sleep, and is limited in detecting wake while in bed (Paquet et al., 2007). Therefore, greater objective sleep duration at post-treatment could also reflect longer time spent in bed rather than longer sleep duration, which could be due to reduced avoidance of the bed and sleep. Sleep changes with treatment need to be further investigated with home-based polysomnography, which directly measures sleep and wake.

Patients also reported fewer PTSD-related sleep disturbances and fewer patients endorsed trauma nightmares on the PSQIA after treatment. This is consistent with the findings of Chapter 2 that sleep improvements with CT-PTSD are associated with reductions in traumatic nightmares, which was proposed as one possible pathway for sleep improvements with PTSD treatment. However, diary-reported nightmare

frequency and distress did not improve with treatment, suggesting that in this study trauma-nightmares remained distressing when they occurred, and may be a residual problem for some patients. These findings are in contrast with the results of Chapter 2, which found significant reductions in clinician-assessed nightmares with CT-PTSD. There were also no reported improvements in diary reported sleep onset time, awakenings after sleep, or sleep duration and efficiency. Results of previous chapters have shown improvements in sleep quality and duration, which in this study were replicated in retrospective sleep measures (for sleep quality only), but not sleep diary measures. However, this difference could be accounted for by the PTSD treatment non-responders who made up a third of the post-treatment sample. This is supported by the exploratory analyses showing that subjective (diary) wake after sleep, sleep quality and sleep efficiency were improved with treatment in PTSD treatment responders. This shows that sleep improvements are greater in those who respond to PTSD treatment, consistent with the results of Chapter 3. Anxiety about going to bed was also reduced with treatment, consistent with the results of Chapter 2. As in Chapters 2 and 3, sleep problems were residual for half after otherwise effective PTSD treatment, when PTSD had remitted. This is also highly consistent with previous studies that have found residual sleep problems after psychotherapy for PTSD (Belleville et al., 2011; Galovski et al., 2009; Gutner et al., 2013; Zayfert & DeViva, 2004), and after effective CBT for PTSD (Zayfert & DeViva, 2004).

In sum, the results build on Chapters 2 and 3 by showing which aspects of sleep are improved with PTSD treatment, and showing that objective sleep duration increased with CT-PTSD. It also raises questions about whether PTSD patients may under-report sleep duration improvements with treatment, compared to objective estimates, however further research is required.

The effect of PTSD treatment on objective arousal

The results showed no group differences between trauma controls and PTSD, and no effect of PTSD treatment on the daily rhythm of cortisol or on overall cortisol release. In contrast to the findings of this study, Chapter 5 showed lower afternoon cortisol in PTSD compared to trauma controls, and some treatment studies have found increases in plasma cortisol with psychotherapy for PTSD (Olff et al., 2007), and increases in urinary cortisol and reductions in glucocorticoid sensitivity with effective PTSD therapy (Yehuda et al., 2014). However, Yehuda and colleagues (2014) did not find changes in salivary cortisol circadian rhythm, nor did van Liempt and colleagues (2013) similar to the present study. The findings of this study suggest that arousal is not reduced with PTSD therapy, however as group differences that were found in Chapter 5 between PTSD and trauma controls, with larger samples, were not found in this study, this may alternatively suggest that the sample size was too small, limiting interpretation of the results. This is confirmed by the post hoc power analysis which showed that the available cortisol sample size produced a power of 35% to detect a medium effect size, Similarly, there were no group differences or treatment effects on sympathetic activation (LF/HF ratio) during sleep. This result is difficult to interpret due to small sample sizes, and an underpowered analysis. Post hoc power analysis showed that the available heart rate sample size produced a power of 13% to detect a medium effect size. The findings could suggest that there was no reduction in night-time arousal with treatment. This is in contrast with a previous study that found a reduction in LF/HF ratio during sleep after psychotherapy for PTSD in a small sample of six treatment responders (Nishith et al., 2003). This study measured sleep and heart-rate in a laboratory setting over night (Nishith et al., 2003), in contrast to the ambulatory assessment of heart-rate used in the present study. This could possibly go towards

explaining the differences between the results. However, the findings of the present study must be interpreted cautiously due to very small sample sizes and underpowered analyses, and further research with larger samples is needed.

The role of pre-sleep cognitive activity

The results showed that pre-sleep cognitive activity (particularly PTSD related) reduced with treatment. There was a greater reduction of PTSD compared to insomnia-related pre-sleep cognitions with CT-PTSD, suggesting PTSD treatment has a more targeted effect on PTSD-related pre-sleep thought content than insomnia-related. Reductions in PTSD-related pre-sleep cognitive activity may indicate a mechanism of sleep improvement with PTSD therapy. This could occur via modification of trauma-related appraisals about threat and the need for vigilance, and reduced nightmares with CT-PTSD, leading to fewer PTSD specific pre-sleep cognitions, such as those about threat and fear of nightmares. The finding that reductions (with therapy) in PTSD related pre-sleep cognitive activity was associated with improvements in sleep disturbance, support this interpretation. Pre-sleep cognitive activity could be a target for improving sleep with PTSD therapy. The smaller reduction in insomnia related pre-sleep cognitions with PTSD treatment, indicates a smaller change in a factor known to maintain general insomnia (Harvey, 2002; Harvey & Espie, 2004). Persistent insomnia-related pre-sleep cognitive activity could plausibly contribute to persistent insomnia in the absence of PTSD symptoms. These change associations and treatment effects cannot inform about the direction of effects. However, in those recovered from PTSD, PTSD symptoms did not predict sleep disturbance severity but pre-sleep cognitive activity did. This suggests that, as in primary insomnia (Harvey, 2002), pre-sleep cognitive activity may contribute to sleep disturbances after PTSD recovery. This is consistent with suggestions that insomnia may develop into an independent problem in the absence of PTSD symptoms

(Krakow, Johnston, et al., 2001c), which could be maintained by perpetuating factors unrelated to PTSD symptomatology (Zayfert & DeViva, 2004), such as pre-sleep cognitive activity.

In sum, the results suggest that pre-sleep cognitive activity is associated with disturbed sleep in PTSD, and reductions in pre-sleep cognitive activity (particularly PTSD related), is associated with reductions in sleep disturbances. The findings further suggest that pre-sleep cognitions may play a role in maintaining sleep problems in those recovered from PTSD.

Symptom changes associated with sleep improvements

Subjective sleep improvements were associated with PTSD symptom improvements, consistent with the results of Chapter 3. Global sleep disturbance (PSQI) reductions were also associated with reductions in pre-sleep cognitive activity of both insomnia and PTSD-related content, although more strongly correlated with PTSD-related pre-sleep cognitions. As discussed previously, this could suggest that PTSD-related pre-sleep cognitions are more specifically affected by CBT for PTSD, and improvements are associated with sleep improvements. Sleep disturbance (PSQI) improvements were also associated with depression symptom reduction, which is consistent with a recent study showing corresponding improvements in depression symptoms as sleep and PTSD symptoms improved with psychotherapy for PTSD (Galovski et al., 2016). Interestingly, in the present study, posttraumatic appraisal change was not associated with improvements in sleep disturbances or objective sleep time. In contrast, Chapter 2 found that change in trauma appraisals predicted subsequent sleep changes. It is possible that session-to-session changes in appraisals predict subsequent sleep duration improvements (Chapter 2), but that the overall amount of change in appraisals is not

associated, which could account for the differences in findings between this study and Chapter 2. Alternatively, sample sizes in the present study were too small to detect associations, compared to the sample size of around 200 in Chapter 3. Overall the results suggest that sleep improvements with PTSD treatment were associated with reductions in PTSD, depression, and pre-sleep cognitive activity (both insomnia and PTSD related).

Possible explanations for persistent sleep problems after PTSD therapy

In PTSD treatment responders, at post-treatment, more subjective awakenings after sleep and lower sleep quality were associated with more severe PTSD and depression symptoms, and more PTSD-related pre-sleep cognitive activity. Even though patients no longer met criteria for PTSD, this suggests that sub-clinical psychopathology symptoms could contribute to disturbed sleep after PTSD treatment. The association between PTSD-related pre-sleep cognitive activity with more awakenings and lower sleep quality, may suggest that in those recovered from PTSD, pre-sleep cognitions that are trauma or threat related are more likely to be associated with worse sleep than thoughts about sleep and the consequences of poor sleep (insomnia related). Associations between low sleep quality and low mood and PTSD symptoms are consistent with studies showing low sleep quality in both PTSD (Cox & Olatunji, 2016) and depression (Riemann et al., 2001). Lower sleep quality at post-treatment was also associated with lower afternoon cortisol (4pm). The association between low afternoon cortisol with poor sleep quality is consistent with previous studies linking low daytime cortisol with worse sleep (Backhaus et al., 2004), and associating night-time HPA-axis activation with more awakenings, and lower perceived sleep depth in PTSD (van Liempt, Arends, Cluitmans, Westenberg, Kahn, & Vermetten, 2013a). Low afternoon cortisol in the present study could reflect night-time awakening, which has been shown

to lead to attenuated cortisol when experimentally manipulated (Spath-Schwalbe, Gofferje, Kern, Born, & Fehm, 1991), although these were not directly associated in the present study, and results must be interpreted cautiously due to the sample size. However, issues with multiple testing (correlations between measures) may also have led to inflation of the error rate, leading to some associations becoming significant. Therefore significant associations should be interpreted cautiously, and the results should be viewed more as interesting, possible associations, that should be investigated with further research targeting specific associations of interest. Post-treatment sleep was not associated with sympathetic activation during sleep (LF/HF ratio). This could suggest that the ANS and sleep are not associated in PTSD, which has been suggested in two recent studies which also did not find an associations in PTSD between heart-rate and sleep quality (van Liempt, Arends, Cluitmans, Westenberg, Kahn, & Vermetten, 2013a), or between HRV and sleep duration (Kobayashi et al., 2014). However, the small sample size limits the conclusions that can be drawn, and further investigation is required with adequately powered analyses.

Overall, the results point to an association between residual sleep disturbances after effective PTSD therapy with insomnia related maintenance factors, such as hyperarousal (cortisol) and PTSD-related pre-sleep cognitive activity, although due to small sample sizes, hyperarousal results must be interpreted with caution. Pre-sleep cognitive activity is targeted in CBT for insomnia (CBT-I), a highly effective sleep treatment (Mitchell et al., 2012) shown to improve insomnia in PTSD (Talbot, 2014). Pre-sleep cognitions may be a clear target for additional intervention to further improve sleep in PTSD therapy.

Limitations, strengths and future research

The study has a number of limitations. First, as recruitment targets were not met, analyses were mostly underpowered, and so results must be interpreted with appropriate caution. Second, available heart-rate data was limited at pre and post-treatment, resulting in small sample sizes that limited the conclusions that can be drawn from these results, as analyses were underpowered. Studies point to the importance of ambulatory home-based assessments of sleep disturbances in PTSD, highlighting discrepancies found between laboratory assessments of objective sleep (Germain et al., 2006) and autonomic arousal (Kobayashi, Lavela, Bell, & Mellman, 2016a), compared to those conducted in patients own homes. For example, Kobayashi and colleagues (2014) found increased sympathetic activation during sleep in PTSD patients compared to trauma controls when heart-rate was assessed at home using an ambulatory heart-rate device, and sleep were assessed with actigraphy. However, in a more recent study they did not find an overall increased in autonomic arousal when sleep and heart-rate was assessed over two nights in a laboratory, rather they found that autonomic arousal was increased during early stages of non-rapid eye movement (NREM) sleep, compared to trauma controls (Kobayashi, Lavela, Bell, & Mellman, 2016a). This highlights the importance of assessing sleep and associated disturbances in patients own environments, during normal activity and where the reported difficulties are occurring. However, lab-based assessments enable greater control over confounding variables, such as alcohol and drug use, which required the exclusion of a number of participants in the present study. Further, in the present study a large amount of data was lost due to either device failure or participants removing or disconnecting the device overnight, which could have been better monitored in a lab setting. In sum, ambulatory assessment provides an inexpensive, typically unobtrusive means of objective assessment in the home and during a patient's normal activity. However, difficulties can arise, and ideally it should

be combined with laboratory assessments where possible to also assess these variables under tighter experimental control. The addition of home-based polysomnography would also be a great asset to studies investigating PTSD treatment effects on sleep, as it would enable the assessment of actual sleep, and also sleep stages and treatment effects on the duration of sleep stages. Third, the sample size was under-powered to detect group differences in cortisol levels with treatment, and patient reports were relied upon to confirm compliance with sampling times and guidelines, and so it is possible that unreported non-compliance could have influenced the saliva samples. Fourth, as noted in Chapter 5, proximity of the sample to waking influences morning cortisol levels (Edwards, Evans, Hucklebridge, & Clow, 2001; Kudielka & Kirschbaum, 2003), and as samples were collected at set-times rather than natural wake-time, this could have affected the results. Fifth, the study did not include a waitlist comparison, and so PTSD treatment changes could not be compared against a group waiting for treatment. Future studies should aim to include waitlist groups to better assess the affects of PTSD treatment on sleep, arousal and pre-sleep cognitive activity. Future research should also aim to use larger sample sizes to ensure adequately powered analyses when investigating treatment effects on sleep, heart-rate and cortisol. Finally, future studies should also combine controlled laboratory and home-based saliva sampling methods to control possible confounding variables, and collect cortisol samples upon natural awakening. Finally, as noted, there may have been issues with multiple testing inflating the error rate generally in this study, which could have led to some results becoming incorrectly significant by chance. Results should be interpreted with appropriate caution. While this study provided some interesting initial information on possible factors associated with sleep improvements and persistent sleep problems after PTSD therapy, it is a preliminary study. Future research should therefore aim to investigate

specific explanations of persistent sleep problems, such as arousal, rather than testing multiple possibilities.

The strengths of the study are that it adds to a very small number of studies investigating the effects of CBT for PTSD on sleep (Belleville et al., 2011; Lommen et al., 2015; Nishith et al., 2003; Zayfert & DeViva, 2004), and provides the first study to confirm objective, home-based sleep improvements with psychotherapy for PTSD. It provides novel findings of the effects of CBT for PTSD on pre-sleep cognitive activity, in line with suggestions that studies investigating insomnia should also investigate the role of pre-sleep cognitive activity and changes with treatment (Harvey, 2002), and that studies should combine multiple measures to fully capture the experience of insomnia (Kohn & Espie, 2005). It further contributes to questions raised in the literature about possible explanations for persistent sleep problems after PTSD therapy. Future research should aim to further investigate the role of persistent arousal and pre-sleep cognitive activity in maintaining sleep problems after PTSD therapy.

Conclusion

In sum, the results showed that subjective sleep and objective sleep duration, and pre-sleep cognitive activity are improved with CT-PTSD. However, consistent with previous research (Zayfert & DeViva, 2004), and Chapters 2 and 3, sleep problems remained residual for half of patients, after otherwise effective PTSD treatment. The results suggest that persistent sleep problems after PTSD treatment could be related to factors known to maintain primary insomnia, such as hyperarousal and pre-sleep cognitive activity. The results further suggest that pre-sleep cognitive activity predicts sleep disturbances in those recovered from PTSD, suggesting that it may contribute to sleep disturbances in trauma survivors after PTSD recovery. The study findings

highlight possible additional targets for intervention to further improve comorbid sleep problems in PTSD therapy, and suggest interesting areas for further research.

Chapter 7: General discussion

Overview

This thesis aimed to investigate the effects of Cognitive Therapy for PTSD (CT-PTSD; Ehlers et al., 2005) on sleep disturbances, to identify aspects of PTSD therapy and associated symptom changes that may promote sleep improvements with PTSD therapy, and to explore reasons for residual sleep problems after PTSD therapy. Five key research questions were investigated

1) Does Cognitive Therapy for PTSD improve sleep disturbances?
2) Do sleep disturbances interfere with the efficacy of psychotherapy for PTSD?
3) How might sleep improvements occur with PTSD therapy?
4) Do factors known to perpetuate insomnia also contribute to sleep problems in PTSD?
5) What may account for persistent sleep problems after otherwise effective PTSD therapy?

Five studies were conducted to investigate these research questions. This discussion will briefly summarise the key findings of the thesis in line with each research question, and then discuss the potential theoretical and clinical implications of the results. Limitations and future directions for further research will then be discussed.

Summary of findings and conclusions

Research question 1 (*Does Cognitive Therapy for PTSD improve sleep disturbances)* was addressed with the studies presented in Chapters 2, 3 and 6. The results of Chapters 2 and 3 showed that CT-PTSD led to improvements in subjective sleep duration (up to 1 hour), subjective sleep quality, nightmares and insomnia symptoms. These results were

found both from an RCT (compared to waitlist), and from an audit of treatment outcomes in routine clinical care. Sleep improvements in both studies were maintained at six-months and one-year follow-up. Chapter 6 built on these findings by including sleep measures recommended for the standardised assessment of sleep (Buysse et al., 2006), to assess PTSD patients before and after therapy. The results showed that both subjective sleep and objectively measured sleep duration (1.5 hour increase) improved with CT-PTSD. Overall sleep disturbances (PSQI) and PTSD-related sleep disturbances (PSQIA), including trauma nightmares, were significantly improved with CT-PTSD, with a medium effect size on sleep disturbances (PSQI). Subjective sleep duration and quality did not significantly improve in this smaller sample. Chapters 2, 3 and 6 all found that sleep problems were residual after CT-PTSD. In each treatment study, insomnia was residual at post-treatment for approximately half of patients (Chapter 3: 43%, Chapter 2: 38%) including those recovered from PTSD (Chapter 6: 50%). In sum, the results showed that both subjective and objective sleep improved, and these gains were maintained for up to one year with CT-PTSD. However, for up to half of patients, sleep disturbances remained residual and clinically significant after PTSD treatment. These results are consistent with findings from previous studies, which have shown that sleep improves but sleep disturbances remain residual after PTSD therapy (Belleville et al., 2011; Galovski et al., 2009; 2016; Gutner et al., 2013; Nishith et al., 2003; Zayfert & DeViva, 2004). The findings of this thesis add to the nine studies to date that have investigated the effects of first-line treatments for PTSD on sleep problems (Belleville et al., 2011; Galovski et al., 2009; 2016; Gutner et al., 2013; Levrier et al., 2016; Lommen et al., 2015; Nishith et al., 2003; Raboni, 2006; Zayfert & DeViva, 2004). The results build on these findings by showing that sleep improvements are reflected in objective, home-based measures of sleep, which is a novel addition to the literature, and adds to findings of objective sleep improvements in laboratory settings (Nishith et al.,

2003; Raboni, 2006). This suggests that more than just the perception of sleep is improved in PTSD. Residual sleep disturbances suggest that for some people, sleep disturbances may have evolved into a independent problem (Krakow, Germain, et al., 2001a), maintained by factors unrelated to PTSD symptomatology (Zayfert & DeViva, 2004), which may require additional sleep-focused interventions, such as CBT for insomnia (CBT-I).

Research question 2 *(Do sleep disturbances interfere with the efficacy of psychotherapy for PTSD?)* was addressed with the studies presented in Chapters 2, 3 and 6. Chapter 2 showed that in an RCT, lower subjective sleep duration at pre-treatment did not predict worse PTSD treatment outcome. However, Chapter 3 showed that lower subjective sleep duration at pre-treatment predicted slower PTSD symptom response over treatment, and lower subjective sleep quality at pre-treatment predicted slower PTSD symptom reduction only in those who had comorbid major depression. Sleep duration/quality at the end of treatment did not predict PTSD symptom severity at 1-year follow-up. Chapter 6 replicated the findings of Chapter 2, showing that pre-treatment subjective sleep duration, quality and disturbances did not predict PTSD symptom severity at the end of treatment. Chapter 6 extended the findings of Chapter 2 by showing that pre-treatment objective sleep duration also did not predict PTSD symptom severity at post-treatment. These findings are generally consistent with previous studies, which have found no strong evidence that sleep interferes with overall PTSD treatment efficacy (Levrier et al., 2016). However, low pre-treatment sleep duration and sleep quality (with depression) may lead to slower response to treatment, consistent with a previous study (Lommen et al., 2015). Sleep severity could slow down the response to PTSD treatment by impacting processes important in therapy, such as learning and memory (Yoo et al., 2007), and fear extinction learning (Kleim, et al.,

2013b; Pace-Schott et al., 2012; Pace-Schott, Germain, & Milad, 2015a; Spoormaker et al., 2011; Spoormaker & Montgomery, 2008). Overall, the findings of Chapters 2 and 6 suggest that PTSD therapy is efficacious in the presence of sleep disturbances, consistent with previous studies (Gutner et al., 2013). However, pre-treatment sleep severity may impact the speed of response to therapy, which raises some clinical implications.

Research question 3 *(How might sleep improvements occur with PTSD therapy?)* was addressed with the studies presented in Chapters 2, 3 and 6. In Chapter 2 subjective sleep improved more with trauma-focused psychotherapy for PTSD (CT-PTSD), compared to non-trauma-focused therapy. Subjective sleep improved faster when CT-PTSD was delivered intensively in seven days. These results suggest sleep improvements were due to specific effects of the trauma-focused intervention. Subjective sleep duration improved by 40 minutes after memory-updating in CT-PTSD, compared to no intervention. Greater nightmare and hyperarousal reductions were associated with more improvement in sleep duration with CT-PTSD. Chapter 3 built on Chapter 2, showing that subjective sleep (duration and quality) changed simultaneously with PTSD symptoms during CT-PTSD. Change in posttraumatic appraisals and flashback-quality each predicted improvements in sleep duration, suggesting they may be mechanisms of sleep change with PTSD treatment. Appraisal change and flashback-quality did not predict change in sleep quality, suggesting that other treatment mechanisms may influence sleep quality changes. Hyperarousal was proposed as one possibility. Chapter 6 showed that sleep improvements with therapy were associated with reductions in PTSD and depression symptoms, and PTSD-related and insomnia-related pre-sleep cognitive activity.

In sum, these findings suggest that trauma-focused therapy leads to greater sleep improvements than non-trauma-focused therapy, possibly due to updating trauma memories, and that sleep improvements occur with CT-PTSD via change in trauma appraisals, flashback-quality of intrusions, and are associated with nightmare, arousal and pre-bed anxiety reductions. This is in line with the theory that CT-PTSD reduces PTSD symptoms via a modification of dysfunctional trauma appraisals and trauma memory qualities (Ehlers et al., 2005). It is a novel finding that change in pre-sleep cognitions was associated with sleep changes in PTSD treatment. It suggests that reduction in pre-sleep cognitive activity may be a mechanism of sleep improvement with trauma-focused psychotherapy for PTSD. Specifically targeting these pre-sleep cognitions, may also serve to additionally enhance sleep improvements with PTSD therapy.

Research question 4 *(Do factors known to perpetuate insomnia also contribute to sleep problems in PTSD?)* was addressed by the studies presented in Chapters 4, 5 and 6. In Chapter 4, a measure of PTSD and insomnia-related pre-sleep cognitive activity was developed and validated. People with PTSD reported both insomnia-related and PTSD-related cognitions in the pre-sleep period, both of which were associated with worse subjective sleep and higher reported pre-sleep physiological and cognitive arousal. Frequency of insomnia related pre-sleep cognitive activity was similar between insomnia, depression and PTSD, but PTSD-related cognitions were specific to PTSD. Sleep hygiene and pre-sleep behaviours related to PTSD were not associated with worse sleep, suggesting they may not play an important role in sleep disturbances in PTSD. Chapter 5 showed that people with PTSD had higher objective autonomic arousal during sleep, and lower cortisol. Higher heart rate in PTSD was associated with worse sleep, and lower cortisol was associated with more PTSD-related pre-sleep cognitive

activity. Further, pre-sleep cognitive activity mediated the relationship between PTSD symptoms and sleep disturbances. These findings suggest that factors contributing to insomnia without a mental health problem, such as pre-sleep cognitive activity (Harvey, 2002), and physiological arousal (Bonnet & Arand, 2010; Espie et al., 2006; Riemann et al., 2010), may also contribute to sleep disturbances in PTSD. These results are consistent with preliminary (untested) theories of sleep disturbances in PTSD that worry and hypervigilance to danger (Galovski et al., 2016), and hyperarousal (Germain, 2013; Sinha, 2016) may contribute to disturbed sleep in PTSD. It also suggests that pre-sleep cognitions may be more important than pre-sleep behaviours in disturbed sleep in PTSD, however this should be interpreted cautiously as the Pre-Sleep Behaviour Scale had weak psychometric properties. The findings add to literature on the nature of insomnia in PTSD, and so may inform targets for intervention, such as reducing pre-sleep cognitions.

Research question 5 *(What may account for persistent sleep problems after otherwise effective PTSD therapy?)* was addressed in Chapter 6. Half of recovered PTSD patients still had residual sleep problems after CT-PTSD. These persistent sleep problems were associated with more severe PTSD and depression symptoms, more frequent PTSD-related pre-sleep cognitions, and lower afternoon cortisol (higher physiological arousal). Finally, in people recovered from PTSD, pre-sleep cognitive activity predicted sleep disturbance severity, but PTSD symptom severity was not related, suggesting pre-sleep cognitive activity may contribute to insomnia in the absence of PTSD symptoms. These findings suggest that hyperarousal and pre-sleep cognitive activity, may be related to persistent sleep problems after PTSD treatment, highlighting these as possible additional targets for intervention. This is consistent with theories that insomnia may persist after PTSD treatment due to perpetuating factors other than PTSD symptoms

(Zayfert & DeViva, 2004), but this study does suggest that sleep problems were also related to sub-clinical psychopathology (depression and PTSD symptoms). It is further consistent with evidence from the insomnia literature that pre-sleep cognitive activity (see Harvey, 2002) and hyperarousal (Bonnet & Arand, 2010; Riemann et al., 2010) disturb sleep.

Theoretical implications

The results have a number of theoretical implications. The simultaneous improvement of sleep and PTSD symptoms with therapy support suggestions of a vicious cycle where sleep and PTSD may maintain and exacerbate each other (Babson & Feldner, 2010). In Chapter 3, appraisal change predicted subsequent sleep change, but appraisal change was not predicted by prior sleep improvement. This suggests that modifying maladaptive appraisals about the trauma and its consequences, such as appraisals about threat, can have a subsequent beneficial impact on sleep. It further suggests that while sleep is important for processes involved in therapy, such as learning and memory, and fear extinction learning (Kleim, et al., 2013b; Pace-Schott et al., 2012; Pace-Schott, Germain, & Milad, 2015a; Spoormaker et al., 2011; Spoormaker & Montgomery, 2008; Yoo et al., 2007), sleep deprivation in PTSD may not be severe enough to impact these processes. This is consistent with studies showing that PTSD treatment gains were not augmented with sleep-directed hypnosis before PTSD therapy (Galovski et al., 2016). The overall finding that sleep was improved when PTSD symptoms were targeted in PTSD therapy illustrates the maintenance of sleep problems by PTSD symptoms (in part). The persistence of sleep problems after PTSD therapy, particularly in the absence of PTSD symptoms, are in line with suggestions that sleep problems are more than just a consequence or secondary symptom of PTSD, as this would be expected to resolve with effective PTSD treatment (Spoormaker & Montgomery, 2008). The findings also

suggest that pre-sleep cognitive activity and physiological hyperarousal, which are known to perpetuate insomnia without a mental health problem (e.g., Espie et al., 2006; Harvey, 2002; see also Riemann et al., 2010), may contribute to sleep disturbances in PTSD. This is consistent with preliminary, but untested, theories of sleep disturbances in PTSD (e.g., Sinha, 2016). In fact, the findings showed that PTSD symptoms affected sleep disturbances in part via pre-sleep cognitive activity (Chapter 5), which may add to theories of sleep disturbance in PTSD. In people with PTSD, reported interference from pre-sleep cognitions that were both PTSD-related (such as worrying about vulnerability while asleep), and insomnia-related (such as worry about the consequences of poor sleep) while trying to fall asleep, is consistent with suggestions that similarities may underlie insomnia with and without a mental health problem (Kohn & Espie, 2005), and also that differences may exist between insomnia alone and comorbid with PTSD (Ulmer et al., 2011). Harvey (2002) proposed that daytime processes also maintain insomnia, such as inadequate emotional processing during the day, which may rebound at night fuelling pre-sleep cognitive activity. A similar process may occur in PTSD where known strategies to deal with intrusive re-experiencing during the day, such as avoidance and suppression of unprocessed trauma memories and thoughts about the trauma (see Ehlers & Clark, 2000), may rebound at night, particularly during the pre-sleep and wake after sleep periods, when options for cognitive distraction are likely to be lower, fuelling PTSD related pre-sleep cognitive activity. Finally, the prediction of sleep disturbance by pre-sleep cognitive activity, but not PTSD symptoms, suggest that for some, insomnia may become (or have become) an independent problem, maintained by factors other than PTSD symptoms (Krakow, Germain, et al., 2001a; Zayfert & DeViva, 2004). In sum, the findings of this thesis may have some theoretical implications for understanding the relationship between sleep disturbances in PTSD,

and could help to inform theoretical models of sleep and PTSD. It also adds to evidence of PTSD treatment effects on sleep.

Clinical implications

The results have a number of clinical implications. Clinically the findings suggest that PTSD can be successfully treated, with very large effect sizes (Chapter 2: d = 2.53) in the presence of sleep disturbances. This suggests that sleep impairment should not deter clinicians from delivering trauma-focused psychological therapy, if the patient is willing. However, slower improvements in those with very low sleep duration, or poor sleep quality and depression, suggest that it would be important to assess sleep disturbances at the start of treatment. This would help identify those who may benefit from a sleep-focused intervention prior to trauma-focused work. This may be particularly important for cases where slow treatment gains may negatively impact PTSD treatment engagement. The results also do not preclude the possibility that sleep treatment, such as CBT-I before PTSD treatment may enhance treatment gains, however this was not investigated in this thesis. The results highlight components of trauma-focused therapy, which may best promote sleep improvements. Memory-updating, and changing trauma appraisals in particular appear to be important for sleep improvements in PTSD therapy. Therefore, asking patients about posttraumatic appraisals that include appraisals about threat and the need for vigilance at night or during sleep may help to improve sleep further in PTSD therapy. Pre-sleep cognitions both PTSD-related, and about sleep and its consequences, are related to sleep disturbances in PTSD. Asking patients about pre-sleep thought content and appraisals relating to poor sleep may be an additional area for intervention in PTSD therapy, which may further enhance sleep improvements. This is supported by studies showing that CBT-I, which includes modification of appraisals about sleep and its consequences, leads to sleep

improvements in people with PTSD (Talbot, 2014). As studies before this have shown, residual post-treatment sleep problems are common, emphasising the importance of assessing sleep disturbances at the end of PTSD treatment. This would help to identify those who may benefit from additional, sleep-focused interventions after PTSD therapy. Finally, as described in Chapter 1, a recent meta-analysis showed that sleep-focused treatments improved sleep disturbances with large effect sizes, and PTSD symptoms with a medium effect size (see Ho et al., 2016). Similarly, the findings of this thesis showed that trauma-focused therapy (CT-PTSD) improved PTSD symptoms with a large effect size, and sleep disturbances (PSQI) with a medium effect size in Chapter 6, and sleep quality and insomnia were improved with large effect sizes in Chapter 2 and 3. Large effects on both sleep and PTSD symptoms have been found when sleep-focused therapy, nightmare treatment and aspects of CBT for PTSD have been combined (Ulmer et al., 2011). One possible implication is that sleep-focused therapies could be an alternative for when a patient is not yet ready to engage in trauma-focused work, but that for patients ready to engage in trauma-focused therapy, it is likely to be efficacious for PTSD symptoms and to resolve sleep problems for half of patients. This further underlines the importance of assessing sleep difficulties at the end of trauma-focused treatments, to determine whether a sleep-focused intervention is required for some people. However, studies have not directly compared trauma-focused and sleep-focused treatments, therefore further research is required to directly compare the efficacy and acceptability of these therapies. Further research should also investigate whether PTSD treatment effects on sleep are enhanced if a sleep-focused intervention, or aspects of sleep-focused treatments such as from CBT for insomnia, is included.

Limitations and future directions

This thesis has a number of limitations. Firstly, the first two studies of treatment effects (Chapters 2 and 3) used only subjective measures, and did not include measures that are recommended for the assessment of sleep (Buysse et al., 2006) or objective measures. Therefore the studies can only provide initial evidence about the effects of PTSD therapy on sleep. The studies in Chapters 5 and 6 included actigraphy, an objective measure of sleep. The primary benefit of actigraphy is that it has high ecological validity, as it enables the measurement of objective sleep in participant's own homes. This is particularly important for PTSD, as it is thought patients may feel safer and sleep better in laboratories than at home, and so home-based assessment methods are more likely to detect actual sleep abnormalities (Germain, 2006; Herbst et al., 2010; Woodward, Bliwise, Friedman, & Gusman, 1996a). However, actigraphy is limited in that it does not directly measure sleep, and is limited in detecting wake after sleep (Paquet et al., 2007), which is a common disturbance in PTSD (Germain & Nielsen, 2003; Straus et al., 2015). Therefore, while suggestive that objective sleep duration improves with CT-PTSD, future treatment studies should include home-based polysomnography to confirm this. Secondly, measurement difficulties were encountered with the objective assessment of autonomic arousal (heart-rate), resulting in small sample sizes and underpowered analyses, particularly for the treatment study reported in Chapter 6. There was no effect of treatment on sympathetic activation, however the analysis was underpowered. It is unclear if this finding would have remained with larger sample sizes. Ambulatory assessment of heart-rate has similar benefits to actigraphy, as it enables assessment in an individual's home environment, during normal activity. Thus, ecological validity is higher than when assessing heart-rate in an overnight laboratory recording, where PTSD patients may feel safer and calmer. However, weaknesses include the lack of experimental control of variables that could influence

recordings (such as alcohol and drugs), and reliance on participant compliance and reporting to check for possible confounding influences. In the future, the combination of ambulatory and laboratory assessment may be useful. In addition, small sample sizes for the heart-rate measure meant that contributing factors to residual sleep disturbances at post-treatment could not be modelled to include autonomic arousal. Further research should aim to collect data from larger sample sizes at pre and post PTSD treatment, on measures of physiological hyperarousal, pre-sleep cognitive activity and sleep, and model the relative contribution of these influences to residual sleep problems after PTSD treatment. This would help to further elucidate why sleep problems persist after PTSD treatment, highlighting targets for intervention. Thirdly, pre-existing sleep problems were not assessed in any of the studies. Sleep problems before and after a trauma have been shown to predict PTSD development (Gehrman et al., 2013; Mellman et al., 2002). Therefore it is possible that those with sleep problems pre-existing PTSD development or trauma exposure, may have been more likely to have residual sleep problems after PTSD treatment. Future research should aim to assess whether sleep disturbances may have pre-dated PTSD development, and whether this may account for some variance in residual sleep problems. Thirdly, in Chapter 6, the PTSD patient sample that attended both pre and post treatment assessment was small, limiting conclusions that could be drawn. In addition to addressing these limitations, future studies should further investigate the relationships between pre-sleep cognitive activity and sleep problems in PTSD, hyperarousal and sleep in PTSD, and relationships between pre-sleep cognitive activity and hyperarousal in PTSD. This could be done by including insomnia and pre-sleep cognition measures in PTSD treatment studies, to evaluate change with treatment. Experimental designs could also investigate the effects of analogue trauma on pre-sleep cognitive activity, nocturnal physiological arousal, and sleep. Recent studies have begun exploring the effects of sleep deprivation on response

to analogue trauma, (Kleim, Wysokowsky, Schmid, Seifritz, & Rasch, 2016; Porcheret, Holmes, Goodwin, Foster, & Wulff, 2015), which may also be a useful paradigm for exploring these relationships further. For example, experimental manipulation of pre-sleep cognitions or arousal after analogue trauma (such as a trauma film) could enable investigation of the causal effect of cognitions and arousal on sleep impairment after trauma.

Conclusions

To summarise, this thesis showed that sleep improved with Cognitive Therapy for PTSD, but remained residual for up to half of patients. Worse sleep interfered with the rate of recovery from PTSD during treatment, particularly for those who were depressed. Updating the trauma memory, and a trauma-focused therapy, promoted sleep improvements in PTSD therapy. Modifying maladaptive trauma appraisals, and reducing the intensity of re-experiencing symptoms may be mechanisms of sleep improvement with trauma-focused therapy. Reductions in nightmares, self-reported hyperarousal, PTSD symptoms, depression, and pre-sleep cognitive activity related to sleep improvements with CT-PTSD. Physiological hyperarousal and pre-sleep cognitive activity were associated with sleep disturbance severity in PTSD, and pre-sleep cognitive activity mediated the relationship between PTSD symptoms and sleep disturbances. This suggests that perpetuating factors known to maintain insomnia without a comorbid mental health problem may also be relevant for sleep impairment in PTSD. Residual sleep problems after PTSD therapy were associated with sub-clinical PTSD symptoms, depression and PTSD-related pre-sleep cognitive activity, and pre-sleep cognitive activity predicted sleep disturbances after PTSD recovery. The relationship between pre-sleep cognitive activity and sleep problems in PTSD, suggest that pre-sleep cognitive activity may be a promising target for intervention. This could help to further improve sleep problems with PTSD therapy, and considering PTSD-

related pre-sleep cognitions in sleep-focused therapy for PTSD could be beneficial. It is hoped that this thesis will have implications for clinical practice, and contribute to understanding the relationship between sleep and PTSD, and the nature and maintenance of sleep problems in PTSD and after PTSD treatment.

References

Adam, K., Tomeny, M., & Oswald, I. (1986). Physiological and psychological differences between good and poor sleepers. *Journal of Psychiatric Research*, *20*(4), 301–316.

Aerni, A., Traber, R., & Hock, C. (2004). Low-dose cortisol for symptoms of posttraumatic stress disorder. *American Journal of Psychiatry*, *161*(8), 1488–1490. http://doi.org/10.1176/appi.ajp.161.8.1488

American Academy of Sleep Medicine. (2005). *The international classification of sleep disorders: diagnostic and coding manual*. American Acad. of Sleep Medicine.

American Psychiatric Association. (2003). APA (2000). *Diagnostic and statistical manual of mental disorders*, *4*.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC:

Ancoli-Israel, S., Cole, R., Alessi, C., & Chambers, M. (2003). The role of actigraphy in the study of sleep and circadian rhythms. American Academy of Sleep Medicine Review Paper. *Sleep*.

Ansfield, M. E., Wegner, D. M., & Bowser, R. (1996). Ironic effects of sleep urgency. *Behaviour Research and Therapy*, *34*(7), 523–531.

Argyropoulos, S. V., Hicks, J. A., Nash, J. R., Bell, C. J., Rich, A. S., Nutt, D. J., & Wilson, S. J. (2003). Correlation of subjective and objective sleep measurements at different stages of the treatment of depression. *Psychiatry Research*, *120*(2), 179–190. http://doi.org/10.1016/S0165-1781(03)00187-2

Armitage, R., Trivedi, M., Hoffmann, R., & Rush, A. J. (1997). Relationship between objective and subjective sleep measures in depressed patients and healthy controls. *Depression and Anxiety*, *5*(2), 97–102. http://doi.org/10.1002/(SICI)1520-6394(1997)5:2<97::AID-DA6>3.0.CO;2-2

Babson, K. A., & Feldner, M. T. (2010). Temporal relations between sleep problems and both traumatic event exposure and PTSD: A critical review of the empirical literature. *Journal of Anxiety Disorders*, *24*(1), 1–15. http://doi.org/10.1016/j.janxdis.2009.08.002

Babson, K. A., Badour, C. L., Feldner, M. T., & Bunaciu, L. (2012). The Relationship of Sleep Quality and PTSD to Anxious Reactivity from Idiographic Traumatic Event Script-Driven Imagery. *Journal of Traumatic Stress*, *25*(5), 503–510. http://doi.org/10.1002/jts.21739

Backhaus, J., Junghanns, K., & Hohagen, F. (2004). Sleep disturbances are correlated with decreased morning awakening salivary cortisol. *Psychoneuroendocrinology*, *29*(9), 1184–1191. http://doi.org/10.1016/j.psyneuen.2004.01.010

Backhaus, J., Junghanns, K., Broocks, A., Riemann, D., & Hohagen, F. (2002). Test–retest reliability and validity of the Pittsburgh Sleep Quality Index in primary insomnia. *Journal of Psychosomatic Research*, *53*(3), 737–740. http://doi.org/10.1016/S0022-3999(02)00330-6

Baron, R. M., & Kenny, D. A. (1986). The moderator–mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of personality and social psychology*, *51*(6), 1173.

Bastien, C. H. (2011). Insomnia: Neurophysiological and NeuropsychologicalApproaches. *Neuropsychology Review*, *21*(1), 22–40. http://doi.org/10.1007/s11065-011-9160-3

Bastien, C. H., Vallieres, A., & Morin, C. M. (2001). Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep Medicine*. http://doi.org/10.1016/S1389-9457(00)00065-4

Beck, A. T., Ward, C. H., Mendelson, M., Mock, J., & Erbaugh, J. (1961). An Inventory for Measuing Depression. *Archives of General Psychiatry*, *4*, 53–63.
Belleville, G., Guay, S., & Marchand, A. (2009). Impact of Sleep Disturbances on PTSD Symptoms and Perceived Health. *The Journal of Nervous and Mental Disease*, *197*(2), 126–132. http://doi.org/10.1097/NMD.0b013e3181961d8e
Belleville, G., Guay, S., & Marchand, A. (2011). Persistence of sleep disturbances following cognitive-behavior therapy for posttraumatic stress disorder. *Journal of Psychosomatic Research*, *70*(4), 318–327. http://doi.org/10.1016/j.jpsychores.2010.09.022
Blake, D. D., & Gomez, M. H. (1998). A scale for assessing sleep hygiene: preliminary data. *Psychological Reports*, *83*(3 Pt 2), 1175–1178. http://doi.org/10.2466/pr0.1998.83.3f.1175
Blake, D. D., Weathers, F. W., Nagy, L. M., Kaloupek, D. G., Gusman, F. D., Charney, D. S., & Keane, T. M. (1995). The Development of a Clinician Administered PTSD Scale. *Journal of Traumatic Stress*, *8*(1), 75–90. http://doi.org/10.1007/BF02105408
Bonnet, M. H., & Arand, D. L. (1997a). Heart rate variability-sleep stage, time of night and arousal. *Electroencephalography and Clinical …*, *102*(5), 390–396. http://doi.org/10.1016/S0921-884X(96)96070-1
Bonnet, M. H., & Arand, D. L. (1997b). Hyperarousal and insomnia. *Sleep Medicine Reviews*, *1*(2), 97–108. http://doi.org/10.1016/S1087-0792(97)90012-5
Bonnet, M. H., & Arand, D. L. (2010). Hyperarousal and insomnia: State of the science. *Sleep Medicine Reviews*, *14*(1), 9–15. http://doi.org/10.1016/j.smrv.2009.05.002
Bootzin, R. R., & Perlis, M. L. (1992). Nonpharmacologic treatments of insomnia. *The Journal of Clinical Psychiatry*, *53 Suppl*, 37–41.
Borkovec, T. D., Lane, T. W., & VanOot, P. H. (1981). Phenomenology of sleep among insomniacs and good sleepers: wakefulness experience when cortically asleep. *Journal of Abnormal Psychology*, *90*(6), 607–609.
Brewin, C. R., Dalgleish, T., & Joseph, S. (1996). A dual representation theory of posttraumatic stress disorder. *Psychological Review*, *103*(4), 670–686. http://doi.org/10.1037/0033-295X.103.4.670
Brown, F. C., Buboltz, W. C., Jr, & Soper, B. (2002). Relationship of Sleep Hygiene Awareness, Sleep Hygiene Practices, and Sleep Quality in University Students. *Behavioral Medicine*, *28*(1), 33–38. http://doi.org/10.1080/08964280209596396
Buijs, R. M., van Eden, C. G., Goncharuk, V. D., & Kalsbeek, A. (2003). The biological clock tunes the organs of the body: timing by hormones and the autonomic nervous system. *The Journal of Endocrinology*, *177*(1), 17–26.
Burgess, H. J., Trinder, J., Kim, Y., & Luke, D. (1997). Sleep and circadian influences on cardiac autonomic nervous system activity. *The American Journal of Physiology*, *273*(4 Pt 2), H1761–8.
Buysse, D. J., Ancoli-Israel, S., Edinger, J. D., Lichstein, K. L., & Morin, C. M. (2006). Recommendations for a standard research assessment of insomnia. *Sleep*, *29*(9), 1155–1173.
Buysse, D. J., Reynolds, C. F. 3., Kupfer, D. J., Thorpy, M. J., Bixler, E., Manfredi, R., et al. (1994). Clinical diagnoses in 216 insomnia patients using the International Classification of Sleep Disorders (ICSD), DSM-IV and ICD-10 categories: a report from the APA/NIMH DSM-IV Field Trial. *Sleep*, *17*(7), 630–637.
Buysse, D. J., Reynolds, C. F., III, Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh sleep quality index: A new instrument for psychiatric practice and research. *Psychiatry Research*, *28*(2), 193–213. http://doi.org/10.1016/0165-1781(89)90047-4

Calhoun, P. S., Wiley, M., Dennis, M. F., Means, M. K., Edinger, J. D., & Beckham, J. C. (2007). Objective evidence of sleep disturbance in women with posttraumatic stress disorder. *Journal of Traumatic Stress*, *20*(6), 1009–1018. http://doi.org/10.1002/jts.20255

Carney, C. E., Buysse, D. J., Ancoli-Israel, S., Edinger, J. D., Krystal, A. D., Lichstein, K. L., & Morin, C. M. (2012). The Consensus Sleep Diary: Standardizing Prospective Sleep Self-Monitoring. *Sleep*, 1–16. http://doi.org/10.5665/sleep.1642

Casement, M. D., & Swanson, L. M. (2012). A meta-analysis of imagery rehearsal for post-trauma nightmares: Effects on nightmare frequency, sleep quality, and posttraumatic stress. *Clinical Psychology Review*, *32*(6), 566–574. http://doi.org/10.1016/j.cpr.2012.06.002

Cattell, R. B. (1966). The Scree Test For The Number Of Factors. *Multivariate Behavioral Research*, *1*(2), 245–276. http://doi.org/10.1207/s15327906mbr0102_10

Chapotot, F., Buguet, A., Gronfier, C., & Brandenberger, G. (2001). Hypothalamo-pituitary-adrenal axis activity is related to the level of central arousal: effect of sleep deprivation on the association of high-frequency waking electroencephalogram with cortisol release. *Neuroendocrinology*, *73*(5), 312–321.

Cheek, R. E., Shaver, J. L. F., & Lentz, M. J. (2004). Variations in sleep hygiene practices of women with and without insomnia. *Research in Nursing & Health*, *27*(4), 225–236. http://doi.org/10.1002/nur.20025

Cohen, J. (1992). A power primer. *Psychological bulletin*, *112*(1), 155.

Cohen, D. J., Begley, A., Alman, J. J., Cashmere, D. J., Pietrone, R. N., Seres, R. J., & Germain, A. (2013). Quantitative electroencephalography during rapid eye movement (REM) and non-REM sleep in combat-exposed veterans with and without post-traumatic stress disorder. *Journal of Sleep Research*, *22*(1), 76–82. http://doi.org/10.1111/j.1365-2869.2012.01040.x

Cooper, N. A., & Clum, G. A. (1989). Imaginal Flooding as a Supplementary Tretament for PTSD in Combat Veterans: A Controlled Study. *Behavior Therapy*, *20*(3), 381–391. http://doi.org/10.1016/S0005-7894(89)80057-7

Cox, R. C., & Olatunji, B. O. (2016). A systematic review of sleep disturbance in anxiety and related disorders. *Journal of Anxiety Disorders*, *37*, 1–26. http://doi.org/10.1016/j.janxdis.2015.12.001

Dagan, Y., Zinger, Y., & Lavie, P. (1997). Actigraphic sleep monitoring in posttraumatic stress disorder (PTSD) patients. *Journal of Psychosomatic Research*, *42*(6), 577–581. http://doi.org/10.1016/S0022-3999(97)00013-5

Davis, J. L., & Wright, D. C. (2007). Randomized clinical trial for treatment of chronic nightmares in trauma-exposed adults. *Journal of Traumatic Stress*, *20*(2), 123–133. http://doi.org/10.1002/jts.20199

Davis, J. L., Byrd, P., Rhudy, J. L., & Wright, D. C. (2007). Characteristics of chronic nightmares in a trauma-exposed treatment-seeking sample. *Dreaming*, *17*(4), 187–198. http://doi.org/10.1037/1053-0797.17.4.187

Davis, J. L., Rhudy, J. L., Pruiksma, K. E., Byrd, P., Williams, A. E., McCabe, K. M., & Bartley, E. J. (2011). Physiological Predictors of Response to Exposure, Relaxation, and Rescripting Therapy for Chronic Nightmares in a Randomized Clinical Trial. *Journal of Clinical Sleep Medicine*, 1–10. http://doi.org/10.5664/jcsm.1466

de Kloet, C. S., Vermetten, E., Heijnen, C. J., Geuze, E., Lentjes, E. G. W. M., & Westenberg, H. G. M. (2007). Enhanced cortisol suppression in response to dexamethasone administration in traumatized veterans with and without posttraumatic stress disorder. *Psychoneuroendocrinology*, *32*(3), 215–226. http://doi.org/10.1016/j.psyneuen.2006.12.009

De Kloet, E. R., Sutanto, W., Rots, N., van Haarst, A., van den Berg, D., Oitzl, M., et al. (1991). Plasticity and function of brain corticosteroid receptors during aging. *Acta Endocrinologica*, *125*, 65–72.

DeViva, J. C., Zayfert, C., & Mellman, T. A. (2004). Factors associated with insomnia among civilians seeking treatment for PTSD: an exploratory study. *Behavioral Sleep Medicine*, *2*(3), 162–176. http://doi.org/10.1207/s15402010bsm0203_5

DeViva, J. C., Zayfert, C., Pigeon, W. R., & Mellman, T. A. (2005). Treatment of residual insomnia after CBT for PTSD: case studies. *Journal of Traumatic Stress*, *18*(2), 155–159. http://doi.org/10.1002/jts.20015

Duffy, M., Gillespie, K., & Clark, D. M. (2007). Post-traumatic stress disorder in the context of terrorism and other civil conflict in Northern Ireland: randomised controlled trial. *BMJ (Clinical Research Ed.)*, *334*(7604), 1147. http://doi.org/10.1136/bmj.39021.846852.BE

Dunmore, E., Clark, D. M., & Ehlers, A. (2001). A prospective investigation of the role of cognitive factors in persistent Posttraumatic Stress Disorder (PTSD) after physical or sexual assault. *Behaviour Research and Therapy*, *39*(9), 1063–1084. http://doi.org/10.1016/S0005-7967(00)00088-7

Edinger, J. D., Wohlgemuth, W. K., Radtke, R. A., Marsh, G. R., & Quillian, R. E. (2001). Cognitive behavioral therapy for treatment of chronic primary insomnia: a randomized controlled trial. *Jama*, *285*(14), 1856–1864.

Edwards, S., Evans, P., Hucklebridge, F., & Clow, A. (2001). Association between time of awakening and diurnal cortisol secretory activity. *Psychoneuroendocrinology*, *26*(6), 613–622.

Ehlers, A., & Clark, D. M. (2000). A cognitive model of posttraumatic stress disorder. *Behaviour Research and Therapy*, *38*(4), 319–345. http://doi.org/10.1016/S0005-7967(99)00123-0

Ehlers, A., Clark, D. M., Hackmann, A., McManus, F., & Fennell, M. (2005). Cognitive therapy for post-traumatic stress disorder: development and evaluation. *Behaviour Research and Therapy*, *43*(4), 413–431. http://doi.org/10.1016/j.brat.2004.03.006

Ehlers, A., Hackmann, A., Grey, N., Wild, J., & Liness, S. (2014). A randomized controlled trial of 7-day intensive and standard weekly cognitive therapy for PTSD and emotion-focused supportive therapy. *American Journal of Psychiatry*, *171*(3), 294–304. http://doi.org/10.1176/appi.ajp.2013.13040552

Ehring, T., Ehlers, A., & Glucksman, E. (2008a). Do cognitive models help in predicting the severity of posttraumatic stress disorder, phobia, and depression after motor vehicle accidents? A prospective longitudinal study. *Journal of Consulting and Clinical Psychology*, *76*(2), 219–230. http://doi.org/10.1037/0022-006X.76.2.219

Ehring, T., Ehlers, A., Cleare, A. J., & Glucksman, E. (2008b). Do acute psychological and psychobiological responses to trauma predict subsequent symptom severities of PTSD and depression? *Psychiatry Research*, *161*(1), 67–75. http://doi.org/10.1016/j.psychres.2007.08.014

Ehring, T., Kleim, B., Clark, D. M., Foa, E. B., & Ehlers, A. (2007). Screening for Posttraumatic Stress Disorder. *The Journal of Nervous and Mental Disease*, *195*(12), 1004–1012. http://doi.org/10.1097/NMD.0b013e31815c1999

Engdahl, B. E., Eberly, R. E., Hurwitz, T. D., & Mahowald, M. W. (2000). Sleep in a community sample of elderly war veterans with and without posttraumatic stress disorder. *Biological Psychiatry*, *28*, 1. http://doi.org/10.1016/S0924-9338(13)76519-2

Engström, E., Ottosson, E., & Wohlfart, B. (2012). Comparison of heart rate measured by Polar RS400 and ECG, validity and repeatability. *Advances in Physiotherapy*,

14(3), 115–122. http://doi.org/10.3109/14038196.2012.694118
Espie, C. A. (1999). Cognitive behaviour therapy as the treatment of choice for primary insomnia. *Sleep Medicine Reviews*, *3*(2), 97–99.
Espie, C. A. (2002). Insomnia: conceptual issues in the development, persistence, and treatment of sleep disorder in adults. *Annual Review of Psychology*, *53*(1), 215–243. http://doi.org/10.1146/annurev.psych.53.100901.135243
Espie, C. A. (2007). Understanding insomnia through cognitive modelling. *Sleep Medicine*, *8*, S3–S8. http://doi.org/10.1016/S1389-9457(08)70002-9
Espie, C. A., Broomfield, N. M., MacMahon, K. M. A., Macphee, L. M., & Taylor, L. M. (2006). The attention–intention–effort pathway in the development of psychophysiologic insomnia: A theoretical review. *Sleep Medicine Reviews*, *10*(4), 215–245. http://doi.org/10.1016/j.smrv.2006.03.002
Espie, C. A., Kyle, S. D., Miller, C. B., Ong, J., Hames, P., & Fleming, L. (2014). Attribution, cognition and psychopathology in persistent insomnia disorder: outcome and mediation analysis from a randomized placebo-controlled trial of online cognitive behavioural therapy. *Sleep Medicine*, *15*(8), 913–917. http://doi.org/10.1016/j.sleep.2014.03.001
Espie, C. A., Lindsay, W. R., Brooks, D. N., Hood, E. M., & Turvey, T. (1989). A controlled comparative investigation of psychological treatments for chronic sleep-onset insomnia. *Behaviour Research and Therapy*, *27*(1), 79–88.
Fekedulegn, D. B., Andrew, M. E., Burchfiel, C. M., Violanti, J. M., Hartley, T. A., Charles, L. E., & Miller, D. B. (2007). Area Under the Curve and Other Summary Indicators of Repeated Waking Cortisol Measurements. *Psychosomatic Medicine*, *69*(7), 651–659. http://doi.org/10.1097/PSY.0b013e31814c405c
First, M. B., Gibbon, M., Spitzer, R. L., & Williams, J. B. (1996). User's guide for the structured clinical interview for DSM-IV axis I Disorders—Research version. *New York: Biometrics Research Department, New York State Psychiatric Institute*.
Foa, E. B., Cashman, L., Jaycox, L., & Perry, K. (1997). The validation of a self-report measure of posttraumatic stress disorder: The Posttraumatic Diagnostic Scale. *Psychological Assessment*, *9*(4), 445–451. http://doi.org/10.1037/1040-3590.9.4.445
Foa, E. B., Ehlers, A., Clark, D. M., Tolin, D. F., & Orsillo, S. M. (1999a). The Posttraumatic Cognitions Inventory (PTCI): Development and Validation. *Psychological Assessment*, *11*(3), 303–314.
Foa, E. B., Ehlers, A., Clark, D. M., Tolin, D. F., & Orsillo, S. M. (1999b). The Posttraumatic Cognitions Inventory (PTCI): Development and validation., *11*(3), 303–314. http://doi.org/10.1037//1040-3590.11.3.303
Galea, S., Resnick, H., Ahern, J., Gold, J., Bucuvalas, M., Kilpatrick, D., et al. (2002). Posttraumatic stress disorder in Manhattan, New York City, after the September 11th terrorist attacks. *Journal of Urban Health : Bulletin of the New York Academy of Medicine*, *79*(3), 340–353. http://doi.org/10.1093/jurban/79.3.340
Galovski, T. E., Harik, J. M., Blain, L. M., Elwood, L., Gloth, C., & Fletcher, T. D. (2016). Augmenting cognitive processing therapy to improve sleep impairment in PTSD: A randomized controlled trial. *Journal of Consulting and Clinical Psychology*, *84*(2), 167–177. http://doi.org/10.1037/ccp0000059
Galovski, T. E., Monson, C., Bruce, S. E., & Resick, P. A. (2009). Does cognitive-behavioral therapy for PTSD improve perceived health and sleep impairment? *Journal of Traumatic Stress*, *22*(3), 197–204. http://doi.org/10.1002/jts.20418
Gehrman, P., Seelig, A. D., Jacobson, I. G., & Boyko, E. J. (2013). Predeployment sleep duration and insomnia symptoms as risk factors for new-onset mental health disorders following military deployment. http://doi.org/10.5665/sleep.2798

Gellis, L. A., Gehrman, P. R., & Mavandadi, S. (2010). Predictors of sleep disturbances in Operation Iraqi Freedom/Operation Enduring Freedom veterans reporting a trauma. *Military Medicine.* http://doi.org/10.2307/41061710?ref=search-gateway:ec80c61e0c4260f46010e8647817de94

Gellis, Les, & Lichstein, K. L. (2009). Sleep Hygiene Practices of Good and Poor Sleepers in the United States: An Internet-Based Study. *Behavior Therapy*, *40*(1), 1–9. http://doi.org/10.1016/j.beth.2008.02.001

Gerardi, M., Rothbaum, B. O., Astin, M. C., & Kelley, M. (2010). Cortisol Response Following Exposure Treatment for PTSD in Rape Victims. *Journal of Aggression, Maltreatment & Trauma*, *19*(4), 349–356. http://doi.org/10.1080/10926771003781297

Germain, A. (2006). Ecological Study of Sleep Disruption in PTSD: A Pilot Study. *Annals of the New York Academy of Sciences*, *1071*(1), 438–441. http://doi.org/10.1196/annals.1364.038

Germain, A. (2013). Sleep disturbances as the hallmark of PTSD: where are we now? *American Journal of Psychiatry*, *170*(4), 372–382. http://doi.org/10.1176/appi.ajp.2012.12040432

Germain, Ann, Buysse, D. J., Katherine Shear, M., fayyad, R., & Austin, C. (2004). Clinical Correlates of poor sleep quality in posttraumatic stress disorder. *Journal of Traumatic Stress*, 1–8. http://doi.org/10.1007/~10960-004-57%-6

Germain, Ann, Hall, M., Krakow, B., Katherine Shear, M., & Buysse, D. J. (2005). A brief Sleep Scale for Posttraumatic Stress Disorder: Pittsburgh Sleep Quality Index Addendum for PTSD. *Journal of Anxiety Disorders*, *19*(2), 233–244. http://doi.org/10.1016/j.janxdis.2004.02.001

Germain, Anne, & Nielsen, T. A. (2003). Sleep pathophysiology in posttraumatic stress disorder and idiopathic nightmare sufferers. *Biological Psychiatry*, *54*(10), 1092–1098. http://doi.org/10.1016/S0006-3223(03)00071-4

Germain, Anne, Buysse, D. J., & Nofzinger, E. (2008). Sleep-specific mechanisms underlying posttraumatic stress disorder: Integrative review and neurobiological hypotheses. *Sleep Medicine Reviews*, *12*(3), 185–195. http://doi.org/10.1016/j.smrv.2007.09.003

Germain, Anne, Hall, M., Shear, M. K., Nofzinger, E. A., & Buysse, D. J. (2006). Sleep disruption in PTSD: A pilot study with home-based polysomnography. *Sleep and Biological Rhythms*, *4*(3), 286–289. http://doi.org/10.1111/j.1479-8425.2006.00230.x

Germain, Anne, Shear, M. K., Hall, M., & Buysse, D. J. (2007). Effects of a brief behavioral treatment for PTSD-related sleep disturbances: A pilot study. *Behaviour Research and Therapy*, *45*(3), 627–632. http://doi.org/10.1016/j.brat.2006.04.009

Glaubman, H., Mikulincer, M., Porat, A., Wasserman, O., & Birger, M. (1990). Sleep of chronic post-traumatic patients. *Journal of Traumatic Stress*, *3*(2), 255–263. http://doi.org/10.1002/jts.2490030207

Goldstein, A. N., & Walker, M. P. (2014). The Role of Sleep in Emotional Brain Function. *Annual Review of Clinical Psychology*, *10*(1), 679–708. http://doi.org/10.1146/annurev-clinpsy-032813-153716

Gross, R. T., & Borkovec, T. D. (1982). Effects of a cognitive intrusion manipulation on the sleep-onset latency of good sleepers. *Behavior Therapy*, *13*(1), 112–116. http://doi.org/10.1016/S0005-7894(82)80054-3

Gutner, C. A., Casement, M. D., Gilbert, K. S., & Resick, P. A. (2013). Change in sleep symptoms across cognititve processing therapy and prolonged exposure: a longitudinal perspective. *Behaviour Research and Therapy*, *51*(12), 817–822. http://doi.org/10.1016/j.brat.2013.09.008

Habukawa, M., Uchimura, N., Maeda, M., Kotorii, N., & Maeda, H. (2007). Sleep Findings in Young Adult Patients with Posttraumatic Stress Disorder. *Biological Psychiatry*, *62*(10), 1179–1182. http://doi.org/10.1016/j.biopsych.2007.01.007

Halligan, S. L., Michael, T., Clark, D. M., & Ehlers, A. (2003). Posttraumatic stress disorder following assault: the role of cognitive processing, trauma memory, and appraisals. *Journal of Consulting and Clinical Psychology*, *71*(3), 419–431.

Harvey, A. G. (2002). A cognitive model of insomnia. *Behaviour Research and Therapy*, *40*(8), 869–893. http://doi.org/10.1016/S0005-7967(01)00061-4

Harvey, A. G. (2003). The Attempted Suppression of Presleep Cognitive Activity in Insomnia. *Cognitive Therapy and Research*, *27*(6), 593–602. http://doi.org/10.1023/A:1026322310019

Harvey, A. G. (2010). Pre-sleep cognitive activity: A comparison of sleep-onset insomniacs and good sleepers, 1–12.

Harvey, A. G., & Harvey, A. G. (2000). Sleep hygiene and sleep-onset insomnia. *The Journal of Nervous and Mental Disease*.

Harvey, A. G., & Payne, S. (2002). The management of unwanted pre-sleep thoughts in insomnia: distraction with imagery versus general distraction. *Behaviour Research and Therapy*, *40*(3), 267–277. http://doi.org/10.1016/S0005-7967(01)00012-2

Harvey, A. G., Tang, N. K. Y., & Browning, L. (2005). Cognitive approaches to insomnia. *Clinical Psychology Review*, *25*(5), 593–611. http://doi.org/10.1016/j.cpr.2005.04.005

Harvey, K. J., & Espie, C. A. (2004). Development and preliminary validation of the Glasgow Content of Thoughts Inventory (GCTI): A new measure for the assessment of pre-sleep cognitive activity, 1–12.

Herbst, E., Metzler, T. J., Lenoci, M., Mccaslin, S. E., Inslicht, S., Marmar, C. R., & Neylan, T. C. (2010). Adaptation effects to sleep studies in participants with and without chronic posttraumatic stress disorder. *Psychophysiology*, no–no. http://doi.org/10.1111/j.1469-8986.2010.01030.x

Herman, J. P., Ostrander, M. M., Mueller, N. K., & Figueiredo, H. (2005). Limbic system mechanisms of stress regulation: hypothalamo-pituitary-adrenocortical axis. *Progress in Neuropsychopharmacology & Biological Psychiatry*, *29*(8), 1201–1213. http://doi.org/10.1016/j.pnpbp.2005.08.006

Hirshkowitz, M., Whiton, K., Albert, S. M., Alessi, C., Bruni, O., DonCarlos, L., et al. (2015). National Sleep Foundation's sleep time duration recommendations: methodology and results summary. *Sleep Health*, *1*(1), 40–43. http://doi.org/10.1016/j.sleh.2014.12.010

Ho, F. Y.-Y., Chan, C. S., & Tang, K. N.-S. (2016). Cognitive-behavioral therapy for sleep disturbances in treating posttraumatic stress disorder symptoms: A meta-analysis of randomized controlled trials. *Clinical Psychology Review*, *43*(C), 90–102. http://doi.org/10.1016/j.cpr.2015.09.005

Holland, P., & Lewis, P. A. (2007). Emotional memory: selective enhancement by sleep. *Current Biology*, *17*(5), R179–R181. http://doi.org/10.1016/j.cub.2006.12.033

Hurwitz, T. D., Mahowald, M. W., Kuskowski, M., & Engdahl, B. E. (1998). Polysomnographic sleep is not clinically impaired in vietnam combat veterans with chronic posttraumatic stress disorder. *Biological Psychiatry*, *44*(10), 1066–1073. http://doi.org/10.1016/S0006-3223(98)00089-4

Jefferson, C. D., Drake, C. L., Scofield, H. M., Myers, E., McClure, T., Roehrs, T., & Roth, T. (2005). Sleep hygiene practices in a population-based sample of insomniacs. *Sleep*, *28*(5), 611–615.

Kazarian, S. S., Howe, M. G., Merskey, H., & Deinum, E. J. (1978). Insomnia: anxiety,

sleep-incompatible behaviors and depression. *Journal of Clinical Psychology*, *34*(4), 865–869.
Keenan, D. M., Roelfsema, F., & Veldhuis, J. D. (2004). Endogenous ACTH concentration-dependent drive of pulsatile cortisol secretion in the human. *American Journal of Physiology. Endocrinology and Metabolism*, *287*(4), E652–61.
Kellner, R., Singh, G., & Irigoyen-Rascon, F. (1991). Rehearsal in the Treatment of Recurring Nightmares in Post-Traumatic Stress Disorders and Panic Disorder: Case Histories. *Annals of Clinical Psychiatry*, *3*(1), 67–71. http://doi.org/10.3109/10401239109147970
Kessler, R. C., Chiu, W. T., Demler, O., & Walters, E. E. (2005). Prevalence, Severity, and Comorbidity of 12-Month DSM-IV Disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry*, *62*(6), 617. http://doi.org/10.1001/archpsyc.62.6.617
Kilpatrick, D. G., Resnick, H. S., Milanak, M. E., Miller, M. W., Keyes, K. M., & Friedman, M. J. (2013). National Estimates of Exposure to Traumatic Events and PTSD Prevalence Using DSM-IVand DSM-5Criteria. *Journal of Traumatic Stress*, *26*(5), 537–547. http://doi.org/10.1002/jts.21848
Klaassens, E. R., Giltay, E. J., van Veen, T., Veen, G., & Zitman, F. G. (2010). Trauma exposure in relation to basal salivary cortisol and the hormone response to the dexamethasone/CRH test in male railway employees without lifetime psychopathology. *Psychoneuroendocrinology*, *35*(6), 878–886. http://doi.org/10.1016/j.psyneuen.2009.11.012
Klassens, E. R., Giltay, E. J., Cuijpers, P., van Veen, T., & Zitman, F. G. (2012). Adulthood trauma and HPA-axis functioning in healthy subjects and PTSD patients: A meta-analysis. *Psychoneuroendocrinology*, *37*, 317–331. http://doi.org/10.1016/j.psyneuen.2011.07.003
Kleim, B., Grey, N., Wild, J., Nussbeck, F. W., Stott, R., Hackmann, A., et al. (2013a). Cognitive change predicts symptom reduction with cognitive therapy for posttraumatic stress disorder. *Journal of Consulting and Clinical Psychology*, *81*(3), 383–393. http://doi.org/10.1037/a0031290
Kleim, B., Wilhelm, F. H., Temp, L., Margraf, J., Wiederhold, B. K., & Rasch, B. (2013b). Sleep enhances exposure therapy. *Psychological Medicine*, 1–9. http://doi.org/10.1017/S0033291713001748
Kleim, B., Wysokowsky, J., Schmid, N., Seifritz, E., & Rasch, B. (2016). Effect of sleep after experimental trauma on intrusive memories. *Sleep*, *39*(12), 2125–2132.
Klein, E., Koren, D., Arnon, I., & Lavie, P. (2003). Sleep complaints are not corroborated by objective sleep measures in post-traumatic stress disorder: a 1-year prospective study in survivors of motor vehicle crashes. *Journal of Sleep Research*, 1–7.
Kline, R. B. (2010). Principles and practice of structural equation modeling. 2011. *New York: Guilford Press Google Scholar*.
Kobayashi, I., Boarts, J. M., & Delahanty, D. L. (2007). Polysomnographically measured sleep abnormalities in PTSD: A meta-analytic review. *Psychophysiology*, *44*(4), 660–669. http://doi.org/10.1111/j.1469-8986.2007.537.x
Kobayashi, I., Huntley, E., Lavela, J., & Mellman, T. A. (2012). Subjectively and Objectively Measured Sleep With and Without Posttraumatic Stress Disorder and Trauma Exposure. *Sleep*. http://doi.org/10.5665/sleep.1960
Kobayashi, I., Lavela, J., & Mellman, T. A. (2014). Nocturnal autonomic balance and sleep in PTSD and resilience. *Journal of Traumatic Stress*, *27*(6), 712–716. http://doi.org/10.1002/jts.21973
Kobayashi, I., Lavela, J., Bell, K., & Mellman, T. A. (2016a). The impact of

posttraumatic stress disorder versus resilience on nocturnal autonomic nervous system activity as functions of sleep stage and time of sleep. *Physiology & Behavior*, *164*(Part A), 11–18. http://doi.org/10.1016/j.physbeh.2016.05.005

Kobayashi, I., Mellman, T. A., Altaee, D., Howell, M. K., & Lavela, J. (2016b). Sleep and Processing of Trauma Memories. *Journal of Traumatic Stress*, *29*(6), 568–571. http://doi.org/10.1002/jts.22137

Koffel, E., Polusny, M. A., Arbisi, P. A., & Erbes, C. R. (2013). Journal of Anxiety Disorders. *Journal of Anxiety Disorders*, *27*(5), 512–519. http://doi.org/10.1016/j.janxdis.2013.07.003

Kohn, L., & Espie, C. A. (2005). Sensitivity and Specificity of Measures of the Insomnia Experience: a ComparativeStudy of Psychophysiologic Insomnia, Insomnia Associated with Mental Disorder and Good Sleepers. *Sleep*, *28*(1), 104–112.

Koren, D., Arnon, I., Lavie, P., & Klein, E. (2002). Sleep complaints as early predictors of posttraumatic stress disorder: a 1-year prospective study of injured survivors of motor vehicle accidents. *American Journal of Psychiatry, 159 (5), 855 - 857.*

Krakow, B., Germain, A., Warner, T. D., Schrader, R., Koss, M., Hollifield, M., et al. (2001a). The Relationship of Sleep Quality and Posttraumatic Stress to Potential Sleep Disorders in Sexual Assault Survivors with Nightmares, Insomnia, and PTSD. *Journal of Traumatic Stress*, *14*(4), 647–665. http://doi.org/10.1023/A:1013029819358

Krakow, B., Hollifield, M., Johnston, L., Koss, M., Schrader, R., Warner, T. D., et al. (2001b). Imagery Rehearsal Therapy for Chronic Nightmares in Sexual Assault Survivors With Posttraumatic Stress Disorder: A Randomized Controlled Trial. *Jama*, *286*(5), 537–545. http://doi.org/10.1001/jama.286.5.537

Krakow, B., Johnston, L., Melendrez, D., Hollifield, M., Warner, T. D., Chavez-Kennedy, D., & Herlan, M. J. (2001c). An Open-Label Trial of Evidence-Based Cognitive Behavior Therapy for Nightmares and Insomnia in Crime Victims With PTSD. *American Journal of Psychiatry*, *158*(12), 2043–2047. http://doi.org/10.1176/appi.ajp.158.12.2043

Krakow, B., Tandberg, D., Scriggins, L., & Barey, M. (1995). A Controlled Comparison of Self-Rated Sleep Complaints in Acute and Chronic Nightmare Sufferers. *The Journal of Nervous and Mental Disease*, *183*(10), 623.

Kroenke, K., Spitzer, R. L., & Williams, J. B. W. (2001). The PHQ-9: Validity of a brief depression severity measure. *Journal of General Internal Medicine*, *16*(9), 606–613. http://doi.org/10.1046/j.1525-1497.2001.016009606.x

Kudielka, B. M., & Kirschbaum, C. (2003). Awakening cortisol responses are influenced by health status and awakening time but not by menstrual cycle phase. *Psychoneuroendocrinology*, *28*(1), 35–47.

Kuisk, L. A., Bertelson, A. D., & Walsh, J. K. (1989). Presleep cognitive hyperarousal and affect as factors in objective and subjective insomnia. *Perceptual and Motor Skills*.

Lack, P., & Rotert, M. (1986). Knowledge and practice of sleep hygeine techniques in insomniacs and good sleepers, 1–4.

Lacks, P., & Morin, C. M. (1992). Recent advances in the assessment and treatment of insomnia. *Journal of Consulting and Clinical Psychology*, *60*(4), 586–594.

Lahiri, M. K., Kannankeril, P. J., & Goldberger, J. J. (2008). Assessment of Autonomic Function in Cardiovascular Disease. *Journal of the American College of Cardiology*, *51*(18), 1725–1733. http://doi.org/10.1016/j.jacc.2008.01.038

Lamarche, C. H., & Ogilvie, R. D. (1997). Electrophysiological changes during the sleep onset period of psychophysiological insomniacs, psychiatric insomniacs, and

normal sleepers. *Sleep*, *20*(9), 724–733.
Lamarche, L. J., & Koninck, J. D. (2007). Sleep Disturbance in Adults With Posttraumatic Stress Disorder. *The Journal of Clinical Psychiatry*, *68*(08), 1257–1270. http://doi.org/10.4088/JCP.v68n0813
Lehrner, A., Daskalakis, N., & Yehuda, R. (2016). Cortisol and the Hypothalamic–Pituitary–Adrenal Axis in PTSD (pp. 265–290). Hoboken, NJ, USA: John Wiley & Sons, Inc. http://doi.org/10.1002/9781118356142.ch11
Leskin, G. A., Woodward, S. H., & Young, H. E. (2002). Effects of comorbid diagnoses on sleep disturbance in PTSD. *Journal of Psychiatric Research*, *36*(6), 449–452. http://doi.org/10.1016/S0022-3956(02)00025-0
Levine, A., Zagoory-Sharon, O., Feldman, R., Lewis, J. G., & Weller, A. (2007). Measuring cortisol in human psychobiological studies. *Physiology & Behavior*, *90*(1), 43–53. http://doi.org/10.1016/j.physbeh.2006.08.025
Levrier, K., Marchand, A., Belleville, G., Dominic, B.-P., & Guay, S. (2016). Nightmare Frequency, Nightmare Distress and the Efficiency of Trauma-Focused Cognitive Behavioral Therapy for Post-Traumatic Stress Disorder. *Archives of Trauma Research*, *5*(3), 1–6. http://doi.org/10.5812/atr.33051
Lewis, V., Creamer, M., & Failla, S. (2009). Is poor sleep in veterans a function of post-traumatic stress disorder? *Military Medicine*, *174*(9), 948–951. http://doi.org/10.7205/MILMED-D-04-0208
Lichstein, K. L., & Rosenthal, T. L. (1980). Insomniacs' perceptions of cognitive versus somatic determinants of sleep disturbance. *Journal of Abnormal Psychology*, *89*(1), 105–107.
Lindert, te, B. H. W., & Van Someren, E. J. W. (2014). Sleep Estimates Using Microelectromechanical Systems (MEMS). *Sleep*. http://doi.org/10.5665/sleep.2648
Lipinska, M., Timol, R., Kaminer, D., & Thomas, K. G. F. (2014). Disrupted rapid eye movement sleep predicts poor declarative memory performance in post-traumatic stress disorder. *Journal of Sleep Research*, *23*(3), 311–319. http://doi.org/10.1111/jsr.12122
Lommen, M. J. J., Grey, N., Clark, D. M., Wild, J., Stott, R., & Ehlers, A. (2015). Sleep and Treatment Outcome in Posttraumatic Stress Disorder: Results From an Effectiveness Study. *Depression and Anxiety*. http://doi.org/10.1002/da.22420
Lundh, L.-G., & Broman, J.-E. (2000). Insomnia as an interaction between sleep-interfering and sleep-interpreting processes. *Journal of Psychosomatic Research*, *49*(5), 299–310. http://doi.org/10.1016/S0022-3999(00)00150-1
MacGregor, K. L., Funderburk, J. S., Pigeon, W., & Maisto, S. A. (2011). Evaluation of the PHQ-9 Item 3 as a Screen for Sleep Disturbance in Primary Care. *Journal of General Internal Medicine*, *27*(3), 339–344. http://doi.org/10.1007/s11606-011-1884-5
Marcks, B. A., Weisberg, R. B., Edelen, M. O., & Keller, M. B. (2010). The relationship between sleep disturbance and the course of anxiety disorders in primary care patients. *Bipolar Disorders and Quality of Life: the Impact of Attention Deficit/Hyperactivity Disorder and Substance Abuse in Euthymic Patients*, *178*(3), 487–492. http://doi.org/10.1016/j.psychres.2009.07.004
Margolies, S. O., Rybarczyk, B., Vrana, S. R., Leszczyszyn, D. J., & Lynch, J. (2013). Efficacy of a Cognitive-Behavioral Treatment for Insomnia and Nightmares in Afghanistan and Iraq Veterans With PTSD. *Journal of Clinical Psychology*, n/a–n/a. http://doi.org/10.1002/jclp.21970
Mastin, D. F., Bryson, J., & Corwyn, R. (2006). Assessment of Sleep Hygiene Using the Sleep Hygiene Index. *Journal of Behavioral Medicine*, *29*(3), 223–227. http://doi.org/10.1007/s10865-006-9047-6

Matsunaga, M. (2015). How to factor-analyze your data right: do's, don'ts, and how-to's. *International Journal of Psychological Research*, *3*(1), 97–110. http://doi.org/10.21500/20112084.854

McCrae, C. S., Rowe, M. A., Dautovich, N. D., Lichstein, K. L., Durrence, H. H., Riedel, B. W., et al. (2006). Sleep hygiene practices in two community dwelling samples of older adults. *Sleep*, *29*(12), 1551–1560.

McLay, R. N., Klam, W. P., & Volkert, S. L. (2010). Insomnia is the most commonly reported symptom and predicts other symptoms of post-traumatic stress disorder in US service members returning from military …. *Military Medicine*, *175*(10), 759–762. http://doi.org/10.7205/MILMED-D-10-00193

McMillen, J. C., North, C. S., & Smith, E. M. (2000). What parts of PTSD are normal: intrusion, avoidance, or arousal? Data from the Northridge, California, earthquake. *Journal of Traumatic Stress*, *13*(1), 57–75. http://doi.org/10.1023/A:1007768830246

Meerlo, P., Sgoifo, A., & Suchecki, D. (2008). Restricted and disrupted sleep: Effects on autonomic function, neuroendocrine stress systems and stress responsivity. *Sleep Medicine Reviews*, *12*(3), 197–210. http://doi.org/10.1016/j.smrv.2007.07.007

Meewisse, M. L., Reitsma, J. B., De Vries, G. J., Gersons, B. P. R., & Olff, M. (2007). Cortisol and post-traumatic stress disorder in adults: Systematic review and meta-analysis. *The British Journal of Psychiatry*, *191*(5), 387–392. http://doi.org/10.1192/bjp.bp.106.024877

Mellman, T. A., & Kulick-Bell, R. (1995). Sleep events among veterans with combat-related posttraumatic stress disorder. *The American Journal …*.

Mellman, T. A., Bustamante, V., Fins, A. I., Pigeon, W. R., & Nolan, B. (2002). REM Sleep and the Early Development of Posttraumatic Stress Disorder. *American Journal of …*, *159*, 1696–1701.

Mellman, T. A., Knorr, B. R., Pigeon, W. R., & Leiter, J. C. (2004). Heart rate variability during sleep and the early development of posttraumatic stress disorder. *Biological Psychiatry*, *55*(9), 953–956. http://doi.org/10.1016/j.biopsych.2003.12.018

Mellman, T. A., Kobayashi, I., Lavela, J., Wilson, B., & Hall Brown, T. S. (2014). A Relationship between REM Sleep Measures and the Duration of Posttraumatic Stress Disorder in a Young Adult Urban Minority Population. *Sleep*, 1–6. http://doi.org/10.5665/sleep.3922

Mellman, T. A., Kumar, A., Kulick-Bell, R., Kumar, M., & Nolan, B. (1995). Nocturnal/daytime urine noradrenergic measures and sleep in combat-related PTSD. *Biological Psychiatry*, *38*(3), 174–179. http://doi.org/10.1016/0006-3223(94)00238-X

Mellman, T. A., Pigeon, W. R., Nowell, P. D., & Nolan, B. (2007). Relationships between REM sleep findings and PTSD symptoms during the early aftermath of trauma. *Journal of Traumatic Stress*, *20*(5), 893–901. http://doi.org/10.1002/jts.20246

Michael, T., Ehlers, A., Halligan, S. L., & Clark, D. M. (2005). Unwanted memories of assault: what intrusion characteristics are associated with PTSD? *Behaviour Research and Therapy*, *43*(5), 613–628. http://doi.org/10.1016/j.brat.2004.04.006

Mitchell, M. D., Gehrman, P., Perlis, M., & Umscheid, C. A. (2012). Comparative effectiveness of cognitive behavioral therapy for insomnia: a systematic review. *BMC Family Practice*, *13*(1), 1–1. http://doi.org/10.1186/1471-2296-13-40

Morin, C. M., Belleville, G., Bélanger, L., & Ivers, H. (2011). The Insomnia Severity Index: psychometric indicators to detect insomnia cases and evaluate treatment response. *Sleep*.

Morin, C. M., Blais, F., & Savard, J. (2002). Are changes in beliefs and attitudes about sleep related to sleep improvements in the treatment of insomnia? *Behaviour Research and Therapy*, *40*(7), 741–752.
Morin, C. M., Culbert, J. P., & Schwartz, S. M. (1994). Nonpharmacological interventions for insomnia: a meta-analysis of treatment efficacy. *American Journal of Psychiatry*, *151*(8), 1172–1180. http://doi.org/10.1176/ajp.151.8.1172
Morin, C., Bootzin, R., Espie, C., Edinger, J., & Buysse, D. J. (2006). Psychological and behavioural treatment of insomnia: Update of the recent Evidence (1998 - 2004). *Sleep*, *29*(11), 1398–1414.
Nappi, C. M., Drummond, S. P. A., & Hall, J. M. H. (2012). Neuropharmacology. *Neuropharmacology*, *62*(2), 576–585. http://doi.org/10.1016/j.neuropharm.2011.02.029
Neylan, T. C., Lenoci, M., Maglione, M. L., Rosenlicht, N. Z., Metzler, T. J., Otte, C., et al. (2003). Delta sleep response to metyrapone in post-traumatic stress disorder. *Neuropsychopharmacology*, *28*(9), 1666–1676.
Nicassio, P. M., Mendlowitz, D. R., & Fussell, J. J. (1985). The phenomenology of the pre-sleep state: the development of the pre-sleep arousal scale. *Behaviour Research and …*, *23*(3), 263–271. http://doi.org/10.1016/0005-7967(85)90004-X
Nishida, M., Pearsall, J., Buckner, R. L., & Walker, M. P. (2009). REM Sleep, Prefrontal Theta, and the Consolidation of Human Emotional Memory. *Cerebral Cortex*, *19*(5), 1158–1166. http://doi.org/10.1093/cercor/bhn155
Nishith, P., Duntley, S. P., Domitrovich, P. P., Uhles, M. L., Cook, B. J., & Stein, P. K. (2003). Effect of Cognitive Behavioral Therapy on Heart Rate Variability During REM Sleep in Female Rape Victims with PTSD. *Journal of Traumatic Stress*, *16*(3), 247–250. http://doi.org/10.1023/A:1023791906879
Nunnally, *J. C.,* & Bernstein, I. H. (1994). Psychometric theory (3rd ed.). New. York; McGraw-Hill.
Ohayon, M. M. (2011). Epidemiological overview of sleep disorders in the general population. *Sleep Medicine Research (SMR)*, *2*(1), 1–9. http://doi.org/10.17241/smr.2011.2.1.1
Ohayon, M. M., & Shapiro, C. M. (2000). Sleep disturbances and psychiatric disorders associated with posttraumatic stress disorder in the general population. *Comprehensive Psychiatry*, *41*(6), 469–478. http://doi.org/10.1053/comp.2000.16568
Olff, M., de Vries, G.-J., Guzelcan, Y., Assies, J., & Gersons, B. P. R. (2007). Changes in cortisol and DHEA plasma levels after psychotherapy for PTSD. *Psychoneuroendocrinology*, *32*, 619–626. http://doi.org/10.1016/j.psyneuen.2007.04.001
Olff, M., Guzelcan, Y., de Vries, G.-J., Assies, J., & Gersons, B. P. R. (2006). HPA- and HPT-axis alterations in chronic posttraumatic stress disorder. *Psychoneuroendocrinology*, *31*(10), 1220–1230. http://doi.org/10.1016/j.psyneuen.2006.09.003
Olff, M., Langeland, W., & Gersons, B. P. R. (2005). Effects of appraisal and coping on the neuroendocrine response to extreme stress. *Neuroscience & Biobehavioral Reviews*, *29*(3), 457–467. http://doi.org/10.1016/j.neubiorev.2004.12.006
Open Science Collaboration. (2015). Estimating the reproducibility of psychological science. *Science*, *349*(6251), aac4716–aac4716. http://doi.org/10.1126/science.aac4716
Otte, C., Lenoci, M., Metzler, T., Yehuda, R., Marmar, C. R., & Neylan, T. C. (2005). Hypothalamic–Pituitary–Adrenal Axis Activity and Sleep in Posttraumatic Stress Disorder. *Neuropsychopharmacology*, *30*(6), 1173–1180.

http://doi.org/10.1038/sj.npp.1300676
Pace-Schott, E. F., Germain, A., & Milad, M. R. (2015a). Effects of sleep on memory for conditioned fear and fear extinction. *Psychological Bulletin*, *141*(4), 835–857. http://doi.org/10.1037/bul0000014
Pace-Schott, E. F., Germain, A., & Milad, M. R. (2015b). Sleep and REM sleep disturbance in the pathophysiology of PTSD: the role of extinction memory. *Biology of Mood & Anxiety Disorders*, *5*(1), 268–19. http://doi.org/10.1186/s13587-015-0018-9
Pace-Schott, E. F., Milad, M. R., Orr, S. P., & Rauch, S. L. (2009). Sleep promotes generalization of extinction of conditioned fear. *Sleep*.
Pace-Schott, E. F., Verga, P. W., Bennett, T. S., & Spencer, R. M. C. (2012). Sleep promotes consolidation and generalization of extinction learning in simulated exposure therapy for spider fear. *Journal of Psychiatric Research*, *46*(8), 1036–1044. http://doi.org/10.1016/j.jpsychires.2012.04.015
Paquet, J., Kawinska, A., & Carrier, J. (2007). Wake detection capacity of actigraphy during sleep. *Sleep*.
Perlis, ML., Giles, D., Bootzin, R., & Wyatt, J. K. (1997). Psychophysiological insomnia: the behavioural model and a neurocognitive perspective. *Journal of Sleep Research*, 1–10.
Perlis, M. L., Smith, M. T., Andrews, P. J., Orff, H., & Giles, D. E. (2001). Beta/Gamma EEG activity in patients with primary and secondary insomnia and good sleeper controls. *Sleep*, *24*(1), 110–117.
Philbert, J., Pichat, P., Beeské, S., Decobert, M., Belzung, C., & Griebel, G. (2011). Acute inescapable stress exposure induces long-term sleep disturbances and avoidance behavior: A mouse model of post-traumatic stress disorder (PTSD). *Behavioural Brain Research*, *221*(1), 149–154. http://doi.org/10.1016/j.bbr.2011.02.039
Pietrzak, R. H., Morgan, C. A., III, & Southwick, S. M. (2010). Sleep quality in treatment-seeking veterans of Operations Enduring Freedom and Iraqi Freedom: The role of cognitive coping strategies and unit cohesion. *Journal of Psychosomatic Research*, *69*(5), 441–448. http://doi.org/10.1016/j.jpsychores.2010.07.002
Porcheret, K., Holmes, E. A., Goodwin, G. M., Foster, R. G., & Wulff, K. (2015). Psychological Effect of an Analogue Traumatic Event Reduced by Sleep Deprivation. *Sleep*, *38*(07), 1017–1025. http://doi.org/10.5665/sleep.4802
Pruessner, J. C., Wolf, O. T., & Hellhammer, D. H. (1997). Free cortisol levels after awakening: a reliable biological marker for the assessment of adrenocortical activity. *Life Sciences*, *61*(26), 2539–2549. http://doi.org/10.1016/s0024-3205(97)01008-4
Pruiksma, K. E., Taylor, D. J., Ruggero, C., Boals, A., Davis, J. L., Cranston, C., et al. (2016). A Psychometric Study of the Fear of Sleep Inventory-Short Form (FoSI-SF). *Journal of Clinical Sleep Medicine*, 1–8. http://doi.org/10.5664/jcsm.3710
Raboni, M. R. (2006). Treatment of PTSD by Eye Movement Desensitization Reprocessing (EMDR) Improves Sleep Quality, Quality of life, and Perception of Stress. *Annals of the New York Academy of Sciences*, *1071*(1), 508–513. http://doi.org/10.1196/annals.1364.054
Rasmusson, A. M., Vythilingam, M., & Morgan, C. A. 3. (2003). The neuroendocrinology of posttraumatic stress disorder: new directions. *CNS Spectr*, *8*(9), 651–6– 665–7.
Ree, M. J., Harvey, A. G., Blake, R., Tang, N. K. Y., & Shawe-Taylor, M. (2005). Attempts to control unwanted thoughts in the night: development of the thought control questionnaire-insomnia revised (TCQI-R). *Behaviour Research and*

Therapy, *43*(8), 985–998. http://doi.org/10.1016/j.brat.2004.07.003
Riad-Fahmy, D., Read, G. F., Gaskell, S. J., Dyas, J., & Hindawi, R. (1979). A simple, direct radioimmunoassay for plasma cortisol, featuring a 125I radioligand and a solid-phase separation technique. *Clinical Chemistry*, *25*(5), 665-668.
Riemann, D., & Perlis, M. L. (2009). The treatments of chronic insomnia: A review of benzodiazepine receptor agonists and psychological and behavioral therapies. *Sleep Medicine Reviews*, *13*(3), 205–214. http://doi.org/10.1016/j.smrv.2008.06.001
Riemann, D., Berger, M., & Voderholzer, U. (2001). Sleep and depression—results from psychobiological studies: an overview. *Biological Psychology*, *57*(1-3), 67–103. http://doi.org/10.1016/s0301-0511(01)00090-4
Riemann, D., Spiegelhalder, K., Feige, B., Voderholzer, U., Berger, M., Perlis, M., & Nissen, C. (2010). The hyperarousal model of insomnia: A review of the concept and its evidence. *Sleep Medicine Reviews*, *14*(1), 19–31. http://doi.org/10.1016/j.smrv.2009.04.002
Rohleder, N., Nater, U. M., Wolf, J. M., Ehlert, U., & Kirschbaum, C. (2004). Psychosocial stress-induced activation of salivary alpha-amylase: an indicator of sympathetic activity? *Annals of the New York Academy of Sciences*, *1032*(1), 258–263. http://doi.org/10.1196/annals.1314.033
Saper, C. B., Scammell, T. E., & Lu, J. (2005). Hypothalamic regulation of sleep and circadian rhythms. *Nature*, *437*(7063), 1257–1263. http://doi.org/10.1038/nature04284
Schnyder, U., Ehlers, A., Elbert, T., Foa, E. B., Gersons, B. P. R., Resick, P. A., et al. (2017). Psychotherapies for PTSD: what do they have in common? *European Journal of Psychotraumatology*, *6*(1), 28186–10. http://doi.org/10.3402/ejpt.v6.28186
Seth, J., & Brown, L. M. (1978). A simple radioimmunoassay for plasma cortisol. *Clinica Chimica Acta*, *86*(1), 109-120.
Sforza, E., Chapotot, F., Lavoie, S., Roche, F., Pigeau, R., & Buguet, A. (2004). Heart rate activation during spontaneous arousals from sleep: effect of sleep deprivation. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology*, *115*(11), 2442–2451. http://doi.org/10.1016/j.clinph.2004.06.002
Sherin, J. E., & Nemeroff, C. B. (2011). Post-traumatic stress disorder: the neurobiological impact of psychological trauma. *Dialogues Clin Neurosci*.
Silvestri, A. J. (2005). REM sleep deprivation affects extinction of cued but not contextual fear conditioning. *Physiology & Behavior*, *84*(3), 343–349. http://doi.org/10.1016/j.physbeh.2004.11.011
Sinha, S. S. (2016). Trauma-induced insomnia: A novel model for trauma and sleep research. *Sleep Medicine Reviews*, *25*(C), 74–83. http://doi.org/10.1016/j.smrv.2015.01.008
Smith, P., Yule, W., Perrin, S., Tranah, T., Dalgleish, T., & Clark, D. M. (2007). Cognitive-Behavioral Therapy for PTSD in Children and Adolescents: A Preliminary Randomized Controlled Trial. *Journal of the American Academy of Child & Adolescent Psychiatry*, *46*(8), 1051–1061. http://doi.org/10.1097/CHI.0b013e318067e288
Soehner, A. M., Kaplan, K. A., & Harvey, A. G. (2014). Prevalence and clinical correlates of co-occurring insomnia and hypersomnia symptoms in depression. *Journal of Affective Disorders*, *167*, 93–97. http://doi.org/10.1016/j.jad.2014.05.060
Spath-Schwalbe, E., Gofferje, M., Kern, W., Born, J., & Fehm, H. L. (1991). Sleep disruption alters nocturnal ACTH and cortisol secretory patterns. *Biological Psychiatry*, *29*(6), 575–584.

Spiegelhalder, K., Fuchs, L., Ladwig, J., Kyle, S. D., Nissen, C., Voderholzer, U., et al. (2011). Heart rate and heart rate variability in subjectively reported insomnia. *Journal of Sleep Research*, *20*(1pt2), 137–145. http://doi.org/10.1111/j.1365-2869.2010.00863.x

Spitzer, R. L., & Kroenke, K. (2006). A brief measure for assessing generalized anxiety disorder: the GAD-7. *Archives of Internal …*. http://doi.org/10.1001/archinte.166.10.1092

Spoormaker, V. I. (2008). A cognitive model of recurrent nightmares.

Spoormaker, V. I., & Montgomery, P. (2008). Disturbed sleep in post-traumatic stress disorder: Secondary symptom or core feature? *Sleep Medicine Reviews*, *12*(3), 169–184. http://doi.org/10.1016/j.smrv.2007.08.008

Spoormaker, V. I., Schröter, M. S., Andrade, K. C., Dresler, M., Kiem, S. A., Goya-Maldonado, R., et al. (2011). Effects of rapid eye movement sleep deprivation on fear extinction recall and prediction error signaling. *Human Brain Mapping*, *33*(10), 2362–2376. http://doi.org/10.1002/hbm.21369

Spoormaker, V. I., Sturm, A., Andrade, K. C., Schröter, M. S., Goya-Maldonado, R., Holsboer, F., et al. (2010). Journal of Psychiatric Research. *Journal of Psychiatric Research*, *44*(16), 1121–1128. http://doi.org/10.1016/j.jpsychires.2010.04.017

Steiger, A. (2007). Neurochemical regulation of sleep. *Journal of Psychiatric Research*, *41*(7), 537–552. http://doi.org/10.1016/j.jpsychires.2006.04.007

Stewart, S. H., Mitchell, T. L., Wright, K. D., & Loba, P. (2004). The relations of PTSD symptoms to alcohol use and coping drinking in volunteers who responded to the Swissair Flight 111 airline disaster. *Journal of Anxiety Disorders*, *18*(1), 51–68.

Straus, L. D., Drummond, S. P. A., Nappi, C. M., Jenkins, M. M., & Norman, S. B. (2015). Sleep Variability in Military-Related PTSD: A Comparison to Primary Insomnia and Healthy Controls. *Journal of Traumatic Stress*, *28*(1), 8–16. http://doi.org/10.1002/jts.21982

Şalcıoğlu, E., Başoğlu, M., & Livanou, M. (2007). Effects of live exposure on symptoms of posttraumatic stress disorder: The role of reduced behavioral avoidance in improvement. *Behaviour Research and Therapy*, *45*(10), 2268–2279. http://doi.org/10.1016/j.brat.2007.04.012

Talbot, L. S. (2014). Cognitive Behavioral Therapy for Insomnia in Posttraumatic Stress Disorder:A Randomized Controlled Trial, 1–15. http://doi.org/10.5665/sleep.3408

Tan, G., Dao, T. K., Farmer, L., Sutherland, R. J., & Gevirtz, R. (2011). Heart Rate Variability (HRV) and Posttraumatic Stress Disorder (PTSD): A Pilot Study. *Applied Psychophysiology and Biofeedback*, *36*(1), 27–35. http://doi.org/10.1007/s10484-010-9141-y

Tarrier, N., Sommerfield, C., Pilgrim, H., & Faragher, B. (2000). Factors associated with outcome of cognitive-behavioural treatment of chronic post-traumatic stress disorder. *Behaviour Research and Therapy*, *38*(2), 191–202.

Tiemeier, H., Pelzer, E., Jonck, L., Moller, H.-J., & Rao, M. L. (2002). Plasma catecholamines and selective slow wave sleep deprivation. *Neuropsychobiology*, *45*(2), 81–86.

Tsao, J. C. I., & Craske, M. G. (2003). Fear of loss of vigilance: development and preliminary validation of a self-report instrument. *Depression and Anxiety*, *18*(4), 177–186. http://doi.org/10.1002/da.10074

Tsigos, C., & Chrousos, G. P. (2002). Hypothalamic–pituitary–adrenal axis, neuroendocrine factors and stress. *Journal of Psychosomatic Research*, *53*(4), 865–871. http://doi.org/10.1016/S0022-3999(02)00429-4

Ulmer, C. S., Calhoun, P. S., Edinger, J. D., Wagner, H. R., & Beckham, J. C. (2009).

Sleep disturbance and baroreceptor sensitivity in women with posttraumatic stress disorder. *Journal of Traumatic Stress*, n/a–n/a. http://doi.org/10.1002/jts.20464
Ulmer, C. S., Edinger, J. D., & Calhoun, P. S. (2011). A multi component cognitive-behavioral intervention for sleep disturbance in veterans with PTSD: a pilot study. *J Clin Sleep Med*.
van der Kloet, D. V. H. (2014). Self-reported sleep disturbances in patients with dissociative identity disorder and post-traumatic stress disorder and how they relate to cognitive failures and fantasy proneness, 1–5. http://doi.org/10.3389/fpsyt.2014.00019/abstract
van der Kolk, B., Blitz, R., Burr, W., Sherry, S., & Hartmann, E. (1984). Nightmares and trauma: a comparison of nightmares after combat with lifelong nightmares in veterans. *American Journal of Psychiatry*, *141*(2), 187–190. http://doi.org/10.1176/ajp.141.2.187
van Liempt, S. (2012). Sleep disturbances and PTSD: a perpetual circle? *European Journal of Psychotraumatology*, *3*(0), 291–9. http://doi.org/10.3402/ejpt.v3i0.19142
van Liempt, S., Arends, J., Cluitmans, P. J. M., Westenberg, H. G. M., Kahn, R. S., & Vermetten, E. (2013a). Sympathetic activity and hypothalamo-pituitary–adrenal axis activity during sleep in post-traumatic stress disorder: A study assessing polysomnography with simultaneous blood sampling. *Psychoneuroendocrinology*, *38*(1), 155–165. http://doi.org/10.1016/j.psyneuen.2012.05.015
van Liempt, S., van Zuiden, M., Westenberg, H., Super, A., & Vermetten, E. (2013b). Impact Of Impaired Sleep On The Development Of Ptsd Symptoms In Combat Veterans: A Prospective Longitudinal Cohort Study. *Depression and Anxiety*, *30*(5), 469–474. http://doi.org/10.1002/da.22054
van Mill, J. G., Hoogendijk, W. J. G., Vogelzangs, N., van Dyck, R., & Penninx, B. W. J. H. (2010). Insomnia and Sleep Duration in a Large Cohort of Patients With Major Depressive Disorder and Anxiety Disorders. *The Journal of Clinical Psychiatry*, *71*(03), 239–246. http://doi.org/10.4088/JCP.09m05218gry
van Zuiden, M., Kavelaars, A., Geuze, E., Olff, M., & Heijnen, C. J. (2013). Predicting PTSD: Pre-existing vulnerabilities in glucocorticoid-signaling and implications for preventive interventions. *Brain, Behavior, and Immunity*, *30*, 12–21. http://doi.org/10.1016/j.bbi.2012.08.015
Varela, E., Koustouki, V., Davos, C. H., & Eleni, K. (2008). Psychological consequences among adults following the 1999 earthquake in Athens, Greece. *Disasters*, *32*(2), 280–291. http://doi.org/10.1111/j.1467-7717.2008.01039.x
Wagner, U., Hallschmid, M., Rasch, B., & Born, J. (2006). Brief sleep after learning keeps emotional memories alive for years. *Biological Psychiatry*, *60*(7), 788–790. http://doi.org/10.1016/j.biopsych.2006.03.061
Walker, M. P. (2009). The role of slow wave sleep in memory processing. *Journal of Clinical Sleep Medicine*.
Walker, M. P., & van der Helm, E. (2009). Overnight therapy? The role of sleep in emotional brain processing. *Psychological Bulletin*, *135*(5), 731–748. http://doi.org/10.1037/a0016570
Watts, F. N., Coyle, K., & East, M. P. (1994). The contribution of worry to insomnia. *The British Journal of Clinical Psychology*, *33 (Pt 2)*, 211–220.
Weathers, F. W., Blake, D. D., Schnurr, P. P., Kaloupek, D. G., Marx, B. P., & Keane, T. M. (2013). Clinician-administered PTSD scale for DSM-5. *Interview Available From the National Center for PTSD at Www.Ptsd.Va.Gov*, *13*(3), 132–156. http://doi.org/10.1002/da.1029
Weibel, L., Follenius, M., Spiegel, K., Ehrhart, J., & Brandenberger, G. (1995). Comparative effect of night and daytime sleep on the 24-hour cortisol secretory

profile. *Sleep*, *18*(7), 549–556.
Weippert, M., Kumar, M., Kreuzfeld, S., Arndt, D., Rieger, A., & Stoll, R. (2010). Comparison of three mobile devices for measuring R–R intervals and heart rate variability: Polar S810i, Suunto t6 and an ambulatory ECG system. *European Journal of Applied Physiology*, *109*(4), 779–786. http://doi.org/10.1007/s00421-010-1415-9
Weitzman, E. D., Fukushima, D., Nogeire, C., Roffwarg, H., Gallagher, T. F., & Hellman, L. (1971). Twenty-four hour pattern of the episodic secretion of cortisol in normal subjects. *The Journal of Clinical Endocrinology and Metabolism*, *33*(1), 14–22. http://doi.org/10.1210/jcem-33-1-14
Wessa, M., Rohleder, N., Kirschbaum, C., & Flor, H. (2006). Altered cortisol awakening response in posttraumatic stress disorder. *Psychoneuroendocrinology*, *31*(2), 209–215. http://doi.org/10.1016/j.psyneuen.2005.06.010
Wicklow, A., & Espie, C. A. (2000). Intrusive thoughts and their relationship to actigraphic measurement of sleep: towards a cognitive model of insomnia. *Behaviour Research and Therapy*, *38*, 679–693.
Wittmann, L., Schredl, M., & Kramer, M. (2007). Dreaming in Posttraumatic Stress Disorder: A Critical Review of Phenomenology, Psychophysiology and Treatment. *Psychotherapy and Psychosomatics*, *76*(1), 25–39. http://doi.org/10.1159/000096362
Woodward, S. H., Arsenault, N. J., Murray, C., & Bliwise, D. L. (2000). Laboratory sleep correlates of nightmare complaint in PTSD inpatients. *Biological Psychiatry*, *48*(11), 1081–1087. http://doi.org/10.1016/S0006-3223(00)00917-3
Woodward, S. H., Arsenault, N. J., Voelker, K., Nguyen, T., Lynch, J., Skultety, K., et al. (2009). Autonomic Activation During Sleep in Posttraumatic Stress Disorder and Panic: A Mattress Actigraphic Study. *Biological Psychiatry*, *66*(1), 41–46. http://doi.org/10.1016/j.biopsych.2009.01.005
Woodward, S. H., Bliwise, D. L., Friedman, M. J., & Gusman, D. F. (1996a). Subjective versus objective sleep in Vietnam combat veterans hospitalized for PTSD. *Journal of Traumatic Stress*, *9*(1), 137–143. http://doi.org/10.1002/jts.2490090112
Woodward, S. H., Friedman, M. J., & Bliwise, D. L. (1996b). Sleep and depression in combat-related PTSD inpatients. *Biological Psychiatry*, *39*(3), 182–192. http://doi.org/10.1016/0006-3223(95)00104-2
Wright, K. M., Britt, T. W., Bliese, P. D., Adler, A. B., Picchioni, D., & Moore, D. (2011). Insomnia as predictor versus outcome of PTSD and depression among Iraq combat veterans. *Journal of Clinical Psychology*, *67*(12), 1240–1258. http://doi.org/10.1002/jclp.20845
Wuyts, J., De Valck, E., Vandekerckhove, M., Pattyn, N., Bulckaert, A., Berckmans, D., et al. (2012). The influence of pre-sleep cognitive arousal on sleep onset processes. *International Journal of Psychophysiology*, *83*(1), 8–15. http://doi.org/10.1016/j.ijpsycho.2011.09.016
Yehuda, R. (2006). Advances in Understanding Neuroendocrine Alterations in PTSD and Their Therapeutic Implications. *Annals of the New York Academy of Sciences*, *1071*(1), 137–166. http://doi.org/10.1196/annals.1364.012
Yehuda, R. (2009). Status of Glucocorticoid Alterations in Post-traumatic Stress Disorder. *Annals of the New York Academy of Sciences*, *1179*(1), 56–69. http://doi.org/10.1111/j.1749-6632.2009.04979.x
Yehuda, R., Boisoneau, D., Mason, J. W., & Giller, E. L. (1993). Glucocorticoid Receptor Number and Cortisol Excretion in Mood, Anxiety, and Psychotic Disorders. *Biological Psychiatry*, *34*, 18–25.

Yehuda, R., Pratchett, L. C., Elmes, M. W., Lehrner, A., Daskalakis, N. P., Koch, E., et al. (2014). Glucocorticoid-related predictors and correlates of post-traumatic stress disorder treatment response in combat veterans. *Interface Focus*, *4*(5), 20140048–20140048. http://doi.org/10.1098/rsfs.2014.0048

Yehuda, R., Southwick, S. M., Nussbaum, G., Wahby, V., Giller, E. L. J., & Mason, J. W. (1990). Low urinary cortisol excretion in patients with posttraumatic stress disorder. *The Journal of Nervous and Mental Disease*, *178*(6), 366–369.

Yehuda, R., Teicher, M. H., Trestman, R. L., Levengood, R. A., & Siever, L. J. (1996). Cortisol regulation in posttraumatic stress disorder and major depression: A chronobiological analysis. *Biological Psychiatry*, *40*(2), 79–88. http://doi.org/10.1016/0006-3223(95)00451-3

Yoo, S.-S., Hu, P. T., Gujar, N., Jolesz, F. A., & Walker, M. P. (2007). A deficit in the ability to form new human memories without sleep. *Nature Neuroscience*, *10*(3), 385–392. http://doi.org/10.1038/nn1851

Young, E. A., & Breslau, N. (2004). Saliva Cortisol in Posttraumatic Stress Disorder: A Community Epidemiologic Study. *Biological Psychiatry*, 205–209. http://doi.org/10.1016/j.biopsych.2004.05.011

Zayfert, C., & DeViva, J. C. (2004). Residual Insomnia Following Cognitive Behavioral Therapy for PTSD, 1–5.

Zhong, X., Hilton, H. J., Gates, G. J., Jelic, S., Stern, Y., Bartels, M. N., et al. (2005). Increased sympathetic and decreased parasympathetic cardiovascular modulation in normal humans with acute sleep deprivation. *Journal of Applied Physiology (Bethesda, Md. : 1985)*, *98*(6), 2024–2032. http://doi.org/10.1152/japplphysiol.00620.2004