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DOCTOR OF PHILOSOPHY
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Associations between Sleep and Cognitive-Affective Functioning in Posttraumatic Stress Disorder

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Declaration

I hereby declare that this dissertation is my own unaided work, both in concept and execution. To the best of my knowledge and belief this dissertation contains no material written by another person, except where due acknowledgement has been made in the text. Neither the substance nor any part of the above thesis has been submitted in the past, or is being, or is to be submitted for a degree at this University or at any other university, except where the methods reported in this dissertation overlap with other projects coming from our laboratory (e.g. the configuration of electrodes used in the polysomnographic studies).

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Signed by candidate

Malgorzata Lipinska

_16.12.2016_____

Date

"Sleep will do much to cure irritability of temper, peevishness, uneasiness. It will build up and make strong a weary body. It will do much to cure dyspepsia, particularly that variety known as nervous dyspepsia. It will relieve the languor and prostration felt by consumptives. It will cure hypochondria. It will cure neuralgia. It will cure a broken spirit. It will cure sorrow. Indeed, we might make a long list of nervous maladies that sleep will cure."

~ from a newspaper: Sonoma Democrat, Number 5, 6 November 1869

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"a person is a person through other people."

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Abbreviations

AIDS	Acquired immune deficiency syndrome
ANOVA	Analysis of variance
ANS	Autonomic nervous system
BDI-II	Beck Depression Inventory – Second Edition
CAPS	Clinician Administered PTSD Scale
ECG	Electrocardiograph
EEG	Electroencephalograph
EMG	Electromyograph
EOG	Electrooculograph
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders – Forth Edition Text Revision
GLM	General linear model
GC	Gas chromatography
HC	Healthy control
HIV	Human immunodeficiency virus
HR	Heart rate
IAPS	International Affective Picture System
ICG	Impedance cardiograph
IEG	Immediate early gene
LM	Logical Memory
LTD	Long-term depression
LTP	Long-term potentiation
LVET	Left ventricular ejection time
MS	Mass spectrometry
MINI	MINI International Neuropsychiatric Interview
MANOVA	Multivariate analysis of variance
NREM 1	Non-rapid eye movement sleep stage 1
NREM 2	Non-rapid eye movement sleep stage 2
NREM 1/SWS	NREM1 percentage and SWS percentage composite

PEP	Pre-ejection period
PGO	Ponto-geniculo-occipital
PIQ	Performance IQ
PSG	Polysomnography/polysomnographic
PSQI	Pittsburgh Sleep Quality Index
PTSD	Posttraumatic stress disorder
REM	Rapid eye movement
REM → NREM1/W	REM arousals leading to NREM1 or wake
SCL	Skin conductance level
SM	Story Memory
SWS	Slow wave sleep
TE	Trauma-exposed non-PTSD
UCT	University of Cape Town
VU-AMS	Vrije Universiteit Ambulatory Monitoring System
WASI PIQ	Wechsler Abbreviated Scale of Intelligence Performance IQ score
WASO	The number of minutes spent awake after sleep onset
WL	Word List
WMS-III	Wechsler Memory Scale – Third Edition
WRAML-II	Wide Range Assessment of Memory and Learning

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Abstract

The current research tested the proposition that the sleep disruption characteristic of posttraumatic stress disorder (PTSD) has discrete, predictable, and significant effects on the processing of neutral declarative memory, emotional memory, and emotional reactivity. Research spanning multiple neuroscientific literatures demonstrates that healthy, uninterrupted sleep is critical for memory consolidation and emotional regulation, and that PTSD-diagnosed individuals experience sleep disruption, memory deficits, and emotional dysregulation. To test whether these behavioral, cognitive, and affective characteristics of PTSD are meaningfully related, I recruited three groups of participants: PTSD (n = 21), trauma-exposed non-PTSD (TE; n = 19), and healthy controls (HC; n = 20). Each participant was assessed before and after an 8-hour period of sleep and an 8-hour period of waking activity. The assessment featured measures of neutral declarative memory (learning of stimuli before the delay, and a free recall task afterward), emotional memory (exposure to highly-arousing negatively valenced, highly-arousing positively valenced, and low arousing neutral pictures before the delay, and a recognition task afterward), and emotional reactivity (physiological responses to the emotional pictures, both before and after the delay). The results are presented under the headings of four investigations. Investigation 1, which focused on objective and subjective sleep quality, suggested that PTSD-diagnosed participants had decreased sleep depth in comparison to HC participants, but presented with no other evidence of objective sleep disruption. Furthermore, PTSD-diagnosed participants reported better subjective sleep quality in the sleep laboratory than in their home environment, an effect not observed in TE and HC participants. Investigation 2, which focused on neutral declarative memory, suggested that after a sleep-filled, but not wake-filled, delay, PTSD-diagnosed participants retained less neutral declarative information than TE and HC participants. Furthermore, increased fragmentation of rapid eye movement (REM) sleep

in PTSD-diagnosed individuals was a significant predictor of post-sleep memory retention deficits. In contrast, Investigations 3 and 4 suggested no significant between-group differences in emotional memory or emotional reactivity. However, Investigation 3 suggested that, after a sleep-filled delay, pictures of all valence and arousal categories were recognized equally accurately by all participants. In contrast, after a wake-filled delay all participants had higher recognition accuracy for negative pictures. Furthermore, Investigation 4 suggested that a sleep-filled delay attenuated emotional reactivity to pictures of all arousal and valence categories, whereas a wake-filled delay was associated with a rise in emotional reactivity across the day. Together, these results suggest that fairly small sleep disruptions (specific to REM-related changes) in PTSD-diagnosed individuals will affect retention of neutral declarative information, but will have no significant effects on the processing of, or reactivity toward, arousing and valenced stimuli. Overall, these findings allow the conclusion that, in PTSD, the co-occurrence of sleep and neutral declarative memory difficulties is not accidental – that is, these two symptom clusters are meaningfully related. Furthermore, the results demonstrate that a reasonable, not necessarily perfect, night of sleep in PTSD is associated with intact functioning within certain cognitive and affective domains. The research bolsters the neuroscientific view of sleep as a critical biological process linked integrally to psychological well-being.

CHAPTER ONE: INTRODUCTION

Healthy sleep plays a vital role in the processing of newly acquired neutral and emotional memories, and in regulating emotional functioning (Feld & Diekelmann, 2015; Goldstein & Walker, 2014). Individuals diagnosed with posttraumatic stress disorder (PTSD) do not, typically, experience healthy sleep, with disruptions at both rapid eye movement (REM) and non-rapid eye movement (NREM) stages (Kobayashi, Boarts, & Delahanty, 2007). Furthermore, from a clinical neuropsychological perspective, the diagnosis of PTSD is also associated with marked neutral and emotional memory impairment, and with disrupted emotional regulation (Fitzgerald et al., 2016; Johnsen & Asbjornsen, 2008).

Few empirical studies have, however, explored possible associations between disrupted sleep, deficits in neutral and emotional memory, and disrupted emotional regulation in PTSD. This dissertation describes four investigations that set out to examine those associations, and to test the general proposition that disrupted sleep is a critical mechanism underlying impairment of both neutral and emotional memory, as well as emotional dysregulation, in PTSD. To provide context with regard to these proposed investigations, I will first review research on sleep patterns in PTSD-diagnosed individuals. I will then proceed to review research on neutral declarative memory processing during sleep in healthy individuals, and I will describe characteristics of impairments related to both sleep and neutral declarative memory in PTSD-diagnosed individuals. Second, I will review models of emotional memory processing during sleep in healthy individuals, and I will describe characteristics of impairments related to both sleep and emotional memory in PTSD-diagnosed individuals. Third, I will examine theories related to emotional regulation during sleep in healthy individuals, and characterize impairments related to both sleep and emotional regulation in PTSD-diagnosed individuals.

Hence, the primary focus of this study is on the relationship between sleep disruption and aspects of memory and emotional functioning in PTSD. More broadly, however, this dissertation seeks to provide evidence bolstering the neuroscientific view of sleep as a critical biological process linked integrally to cognitive and emotional well-being.

CHAPTER TWO: LITERATURE REVIEW

Disrupted Sleep in PTSD

PTSD-diagnosed individuals give subjective reports of difficulties with sleep onset and maintenance (Chakravorty et al., 2014; Giosan et al., 2015; Werner, Griffin, & Galovski, 2016). These sleep difficulties, based on their frequency and prognostic value, form part of the diagnostic criteria for PTSD (A.P.A., 2013; Gehrman, Harb, Cook, Barilla, & Ross, 2015; Koren, Arnon, Lavie, & Klein, 2002; Taylor et al., 2014). Regarding objective polysomnographic measures of sleep, there is a fair amount of disagreement about what constitutes disordered sleep in PTSD, as different studies have found contradicting results. Some studies report gross sleep architecture disruptions, such as increased sleep latency (amount of time taken to fall asleep), sleep efficiency (percentage of time spent asleep versus time in bed), number of awakenings, and amount of time spent awake after sleep onset (Capaldi, Guerrero, & Killgore, 2011; Mellman, Kulick-Bell, Ashlock, & Nolan, 1995b; Mellman, Kumar, Kulick-Bell, Kumar, & Nolan, 1995; Mellman, Nolan, Hebding, Kulick-Bell, & Dominguez, 1997). However, these reports are not consistent across studies, with some research reporting none of these abnormalities (Engdahl, Eberly, Hurwitz, Mahowald, & Blake, 2000; Hurwitz, Mahowald, Kuskowski, & Engdahl, 1998; Klein, Koren, Arnon, & Lavie, 2002).Other studies report sleep-stage specific disruptions, such as decreases in REM and slow-wave sleep (SWS) percentage (Fuller, Waters, & Scott, 1994; Glaubman, Miculincer, Porat, Wasserman, & Birger, 1990; Hefez, Metz, & Lavie, 1987; Kramer & Kinney, 1988; Lavie, Hefez, Halperin, & Enoch, 1979; Mellman, Kobayashi, Lavela, Wilson, & Hall Brown, 2014; Yetkin, Aydin, & Ozgen, 2010), while others do not (Mellman, David, Kulick-Bell, Hebding, & Nolan, 1995; Mellman, Kulick-Bell, Ashlock, & Nolan, 1995a; Mellman et al., 1997). Furthermore, some studies show that PTSD-diagnosed individuals experience abnormalities in other polysomnographic variables such

as REM density (the number of eye movements within a REM period) and REM latency (the amount of time taken to reach the first REM period; Dow, Kelsoe, & Gillin, 1996; Mellman et al., 2014; Mellman, Kumar, et al., 1995; Yetkin et al., 2010).

One useful source of summary information in this regard is a meta-analysis by Kobayashi et al. (2007). That quantitative review of 20 studies controlled for inconsistencies across potentially moderating individual-level variables such as age, sex, time since trauma, comorbid psychiatric disorders, and substance abuse. Analyses revealed that, relative to sleep in individuals without PTSD, sleep in PTSD-diagnosed individuals is characterized by increased stage 1 sleep (light sleep), increased REM density, and decreased SWS.

In contrast to studies examining gross sleep architecture, several authors have taken a more nuanced approach to understanding sleep disruption in PTSD-diagnosed individuals. For example, instead of examining overall sleep architecture, Mellman and colleagues (2002) investigated REM fragmentation only. They found that fragmented REM sleep directly after a traumatic event predicted the development of PTSD. Similarly, Breslau and colleagues (2004) found that the main difference between PTSD-diagnosed individuals and controls was fragmented REM sleep. Furthermore, a recent study found that REM sleep was decreased and fragmented with longer REM latency for those participants with a recent diagnosis of PTSD compared to those with a long-standing diagnosis (Mellman et al., 2014). That is to say, participants with long-standing PTSD tended to have unchanged or increased REM sleep with shorter REM latency. These results suggest that PTSD duration is an important factor to consider when characterizing the presentation of sleep disruption within the disorder.

Standing alongside these findings regarding disrupted REM sleep in PTSD are other studies suggesting that, in PTSD-diagnosed individuals, SWS is fragmented during the first half of the night. For example van Liempt, Vermetten, Lentjes, Arends, & Westenberg (2011) found that war veterans diagnosed with PTSD experienced more awakenings during the SWS-rich first

half of the night rich in comparison with trauma-exposed individuals and healthy controls. However, findings of this nature are reported with less frequency than those related to REM fragmentation.

Taken together, and even in the face of some inconsistencies, these results suggest that PTSD is associated with objective sleep abnormalities, at both SWS and REM stages. Different research groups, often operating from different research perspectives, have investigated possible mechanisms underlying these sleep disruptions. One proposed mechanism suggests that increased hyperarousal, represented by increased autonomic activity at night, disrupts normal sleep architecture in PTSD-diagnosed individuals. For example, one study showed that, in PTSD-diagnosed individuals, a metabolite of noradrenaline (a marker of increased autonomic activation) was elevated, but only during the night (Mellman, Kumar, et al., 1995). In healthy individuals, noradrenergic activity during SWS is lower than during waking hours, and is absent during REM sleep (Pace-Schott & Hobson, 2002). The study also showed that concentrations of the metabolite (3-methoxy-4-hydroxyphenylglycol (MHPG)) were negatively correlated with total sleep time – that is, the higher the levels of MHPG, the less participants slept. Kobayashi and colleagues (2014) found that parasympathetic activity, associated with calmness, sleep, and digestion, was lower in PTSD-diagnosed individuals in comparison with trauma-exposed individuals during sleep. Parasympathetic activity was measured by heart rate variability. Furthermore there was no association between heart rate variability measures and sleep duration in PTSD-diagnosed individuals, while in contrast trauma-exposed participants showed a strong association between these two variables. These results suggest that at night (a) autonomic arousal is elevated in PTSD since activity of the parasympathetic branch of the ANS promoting calmness is lower in PTSD and (b) that the ANS is also dysregulated in this clinical population. Finally, a polysomnographic study in our laboratory showed that in comparison to PTSD-diagnosed individuals without prominent hyperarousal symptoms and healthy controls, PTSD-

diagnosed individuals with prominent hyperarousal symptoms experienced severe sleep disruption (van Wyk, Thomas, Solms, & Lipinska, 2016).

Together, these findings suggest that increased autonomic activity at night, represented by noradrenergic markers, heart rate variability, and subjective hyperarousal reports, may serve as a mechanism explaining the characteristic sleep disruption present in PTSD.

Healthy Sleep Enhances Consolidation of Neutral Declarative Memories

The term *memory* encompasses a broad array of neurobiological processes. These processes might be classed as serving different memory systems, such that each system has a distinct underlying neurobiology. Perhaps the most prominent distinction can be made between short-term memory systems (one of which is working memory) and long-term memory systems. The latter systems are typically divided into declarative and non-declarative components. Declarative components of memory are primarily sub-served by hippocampal and neocortical structures, while non-declarative aspects are sub-served by the amygdala, striatum, basal ganglia, and cerebellum (Squire & Dede, 2015). For a comprehensive understanding of memory classifications and underlying biology, please see recent reviews by Korte and Schmitz (2016) and Squire and Dede (2015). In this review, I focus on declarative memory for neutral (i.e., non-emotional) material, and then on emotional memory, as they both relate to sleep-dependent consolidation processes.

Sleep-related neutral declarative consolidation. Memory traces can evolve from unstable initial representations (formed at the encoding stage, where a representation of an experience is registered in the brain) to fully-fledged and stable images and narratives that may persist for years (Paller & Wagner, 2002; Schacter & Wagner, 1999). The process of memory consolidation is responsible for this evolution; it ensures that the initial representation is resistant to decay (forgetting), and it may even be responsible for enhancing the strength of memory traces (Robertson, Pascual-Leone, & Miall, 2004; Walker & Stickgold, 2005). In healthy

individuals experiencing uninterrupted sleep, consolidation of neutral declarative memories appears to occur throughout the night (Feld & Diekelmann, 2015; Gais, Lucas, & Born, 2006). In fact, it appears that the successive progression of sleep stages, from early-night, slow-wave-rich sleep to late-night, REM-rich sleep, promotes memory consolidation (Gais et al., 2007; Stickgold, 2005; Walker, 2009).

Consolidation during SWS. Two different theoretical models have, from a neurophysiological basis, attempted to explain how declarative memory consolidation occurs during SWS. The *active system consolidation theory*, incorporating findings from both the animal (Sirota & Buzsaki, 2005; Sirota, Csicsvari, Buhl, & Buzsaki, 2003; Stickgold, 2005; Stickgold & Walker, 2005) and human (Frankland & Bontempi, 2005; Marshall & Born, 2007; Takashima et al., 2006) literatures, suggests that the same brain regions and functional connective systems active during encoding in wakefulness are reactivated during sleep. Specifically, this theory posits that memory traces encoded initially in both the hippocampus (a central region of the brain associated with memory processing) and neocortex are reactivated during subsequent episodes of SWS. During those stages of sleep, slow electrophysiological oscillations generated by the neocortex drive repeated reactivations of memory traces in the hippocampus. The up-state (represented as the peak of the wave formation on EEG recordings) of these slow oscillations synchronizes with sharp-wave ripple from hippocampal- and thalamic-driven spindles (Klinzing et al., 2016; Wei, Krishnan, & Bazhenov, 2016). This synchronization promotes the formation of ripple-spindle events, which in turn promote effective transfer of reactivated memory traces from the hippocampus to neocortical structures (Maingret, Girardeau, Todorova, Goutierre, & Zugaro, 2016). Hence, the initially unstable and relatively weak memory traces based in the hippocampus are incorporated increasingly strongly into pre-existing networks of knowledge stored in neocortical circuits. During later waking activation, these memory traces are therefore less reliant on hippocampal activation (Gais et al., 2007).

Various empirical studies support this theoretical framework. Healthy participants asked to encode word pairs and then recall them later perform better when the delay is filled with the SWS-rich first half of the night than when it is filled with the REM-rich second half of the night, or with normal waking activity (Gais & Born, 2004; Plihal & Born, 1997, 1999). Additionally, when waves specific to SWS (i.e., very slow cortical oscillations of < 1 Hz) are induced in the prefrontal cortex (PFC) using direct current stimulation, participants in the stimulation condition have greater word-pair retention than no-stimulation controls (Barham, Enticott, Conduit, & Lum, 2016; Marshall, Helgadottir, Molle, & Born, 2006).

Some authors have questioned the active role that sleep plays in memory consolidation, arguing that paradigms that examine consolidation effects over either 12 hours of waking or 12 hours containing sleep are confounded by the fact that there is no interference during the sleep period. This counter-argument posits that sleep may passively consolidate information, because this information is not susceptible to interference as it is during waking when many other events occur during the interval period. However, Payne and colleagues (2012) demonstrated that over a 24-hour period containing equal amounts of sleep and waking in both conditions, only those individuals who slept shortly after encoding had better memory performance on subsequent retest 24 hours later. This result suggests an active component to sleep-dependent consolidation, as both groups experienced the same amount of wake time.

In contrast to the active system consolidation theory, the *synaptic homeostasis theory* (Tononi & Cirelli, 2003, 2006, 2014) suggests that the slow oscillations during SWS act to decrease, rather than increase, neural connections or synaptic strength. Specifically, this theory posits that, during waking, learning, and memory processes act to increase synaptic strength. During sleep synaptic connections are downscaled. Downscaling occurs in such a manner as to eliminate weakly potentiated synapses, leaving strongly potentiated synapses. This process has two important consequences. Firstly it ensures that memory circuits do not become saturated. A

state of saturation would, the theory posits, leave these circuits unable to encode information successfully the next day. Secondly the elimination of weakly potentiated synapses ensures better recall of relevant information.

Recent studies focusing on biological markers of synaptic strength such as long-term potentiation (LTP) and long-term depression (LTD) have provided some support for this theory. LTP is one key mechanism explaining long-lasting synaptic strengthening in neural networks; LTD, in contrast, is a process that selectively weakens specific synaptic connections over a period of hours, thus clearing them of old memory traces and allowing the potentiation of new traces (Kandel, 2001). Glutametergic AMPA receptors containing the subunit GluR1 appear to play an important role in mediating LTP and LTD processes (Malenka & Bear, 2004). Vyazovskiy and colleagues (2008), studying the rat hippocampus and cortex, showed that, during wakefulness, the levels of GluR1 containing AMPARs was high; during sleep, however, they were low. Further, changes in the expression of this receptor were consistent with LTP during the day and with LTD during the night. Importantly, changes in slow-wave activity in the rat brain during sleep were associated with changes in synaptic efficacy, further supporting the hypothesis that SWS is associated with LTD, and therefore with synaptic downscaling.

Are these two different models of the neurophysiological mechanisms underlying memory consolidation during SWS sleep compatible with one another? On the face of it, they are not: The active system consolidation model suggests a strengthening of synaptic connections, and therefore of memory traces, whereas the synaptic homeostasis theory suggests an overall decrease in synaptic connections. Nonetheless, several authors (e.g., Diekelmann & Born, 2010; Walker, 2009) have suggested that these models are in fact complementary, and that together they may explain discrete aspects of the consolidation process during SWS sleep. That is to say, the processes can operate simultaneously: While active system consolidation may strengthen memory traces and integrate them into wider and pre-existing networks of information, synaptic

downscaling may eliminate superfluous neural connections and refresh synaptic potential for encoding. Furthermore, and with specific regard to memory consolidation, one hypothesis (Walker, 2009) suggests that these processes work together to improve signal-to-noise ratio: When superfluous neural connections are eliminated, the connections that remain have greater overall strength, thus ensuring optimal consolidation. Exactly how these processes may work alongside each other remains an active area of investigation.

Consolidation during REM. There is evidence for two distinct memory consolidation processes, each based on discrete electrophysiological events, during REM. The first process involves ponto-geniculo-occipital (PGO) waves. In rats, PGO density during REM increases following learning (Datta, Li, & Auerbach, 2008; Ulloor & Datta, 2005). This increase is associated with post-sleep task performance improvements. Furthermore, PGO waves are associated with the expression of immediate early genes (IEGs), which are expressed during LTP in REM sleep. This expression results in long-term synaptic strengthening in the brain (Datta, Li, & Auerbach, 2008; Ravassard et al., 2016). Following learning, IEG activity is localized to brain regions that were involved in the acquisition of new material (Ribeiro et al., 2002; Ribeiro et al., 2007; Ulloor & Datta, 2005). A recent study also demonstrated that if REM sleep is selectively deprived after learning in rats, both memory consolidation and LTP are impaired (Ravassard et al., 2016).

A second electrophysiological process that promotes memory consolidation during REM is expression of the theta rhythm (Boyce, Glasgow, Williams, & Adamantidis, 2016; Diekelmann & Born, 2010). During waking, theta activity occurs during encoding of hippocampal-dependent memories (Buzsaki, 2002). During sleep, there is evidence of neuronal re-play, associated with theta activity, of this encoded information in the hippocampus (Louie & Wilson, 2001; Poe, Nitz, McNaughton, & Barnes, 2000). Furthermore, in mice, silencing of REM-specific theta rhythms only (i.e., leaving intact those rhythms during other stages of sleep)

selectively impairs consolidation of a number of memory systems, including that of neutral information related to novel object place recognition (Boyce et al., 2016). In humans, theta activity during REM increases after the learning of word pairs before sleep (Fogel, Smith, & Cote, 2007).

Current research shows that theta rhythm and PGO waves are related, in that PGO waves are phase-locked to theta rhythm (Reinoso-Suarez, de Andres, Rodrigo-Angulo, & Garzon, 2001). In animal models, eliciting theta waves during REM sleep in the medial septum entrains PGO waves to the theta rhythm. In humans, PGO waves are impossible to measure given current technology because they occur in medial centers of the brain and are not easily detected via surface EEG (Hutchison & Rathore, 2015). Hence, the relationship between theta rhythm and PGO waves, and their distinct or overlapping contribution to memory consolidation, remains unclear in humans.

In summary, these theoretical frameworks and empirical data help explain why the healthy progression of sleep stages over the night results in optimal memory consolidation. During early-night SWS, relevant memory traces are selected (by the strength of their potentiation at synapses; weak connections are eliminated) and integrated into pre-existing networks of knowledge. During REM sleep, these traces are strengthened so that they form long-lasting representations in the brain.

Neutral Declarative Memory and Sleep in PTSD

A key feature of the neurocognitive profile of PTSD is declarative memory impairment. Three independent meta-analysis examining cognitive performance in PTSD have demonstrated medium effect sizes for deficits in verbal declarative memory in PTSD-diagnosed individuals in comparison with controls (Brewin, Kleiner, Vasterling, & Field, 2007; Johnsen & Asbjornsen, 2008; Scott et al., 2015). These effect sizes are largest between PTSD-diagnosed individuals and healthy controls, and smaller but still significant between PTSD-diagnosed and trauma-exposed

individuals. This finding suggests that, over and above any effects of trauma exposure alone, individuals who carry a PTSD diagnosis are likely to have neutral declarative memory impairments. These impairments are also (a) independent of performance on tests of attention (i.e., impaired memory is not a secondary effect of impaired attention), (b) not significantly associated with level of depression or with degree of past alcohol abuse, and (c) independent of trauma type (Brewin et al., 2007; Gilbertson, Gurvits, Lasko, Orr, & Pitman, 2001; Jelinek et al., 2006).

Daytime neutral declarative memory deficits in PTSD-diagnosed individuals are characterized prominently by difficulties with immediate and delayed recall, but not with retention of information (Brewin, 2011; Samuelson, 2011). Because these individuals do not lose information over the interval between immediate and delayed recall at a higher rate than control participants (Scott et al., 2015), it looks as if they do not have daytime consolidation difficulties. However the findings suggest that they might have difficulty encoding information, and might struggle to implement efficient retrieval strategies.

Neuroimaging studies suggest that, in PTSD, decreased hippocampal volume may be responsible for neutral declarative memory deficits (Woon, Sood, & Hedges, 2010). Specifically, several studies have found that the degree of declarative memory impairment is positively associated with degree of decrease in hippocampal volume (Bremner et al., 1995; Tischler et al., 2006; Vythilingam et al., 2005; Woon et al., 2010), and that individuals with PTSD show altered patterns of hippocampal/parahippocampal and PFC activation during associative learning and memory tasks (Geuze, Vermetten, Ruf, de Kloet, & Westenberg, 2008). Other studies have, however, failed to demonstrate the association between memory performance and hippocampal volume in PTSD (Lindauer, Olff, van Meijel, Carlier, & Gersons, 2006; Woodward et al., 2009), suggesting that the relationship between neutral declarative memory deficits and decreased hippocampal volume is not as robust as it was initially considered to be. Some authors speculate

that the pattern of declarative memory deficits in PTSD may not be consistent with an exclusive association with hippocampal volume (Scott et al., 2015). This is because neutral declarative memory deficits are characterized by deficits in immediate and delayed recall, rather than retention, which is most strongly mediated by the hippocampus (Samuelson, 2011). These results suggest that factors other than purely hippocampal volume and functioning may influence declarative memory performance in PTSD-diagnosed individuals.

Although the hypothesis that neutral declarative memory deficits in PTSD can be accounted for by purely neuroanatomical accounts has been challenged, almost no studies have considered the role of chronic sleep disturbance as a contributor to declarative memory deficits in this population. Considering the robust findings regarding the importance of healthy sleep for memory consolidation, it is likely that chronic sleep disturbance may affect sleep-dependent memory consolidation in PTSD. Furthermore, PTSD-diagnosed individuals experience sleep disruption at both SWS and REM sleep stages, and undisturbed sleep during these stages is critical for memory consolidation. Decreased SWS in PTSD may result in a lack of integration of newly acquired declarative information into other networks of knowledge and an overall saturation of networks and brain structures including the hippocampus. This saturation may negatively affect next-day encoding, which may result in the typical pattern of daytime difficulties marked by immediate and delayed recall deficits. Furthermore, disrupted REM sleep may result in disrupted theta and PGO waves and a decrease in individual synaptic strengthening. This decrease in synaptic strengthening may result in overall poorer memory consolidation across the night, rather than across waking. These specific SWS and REM sleep disruptions may underpin, at least to some degree, the deficits in declarative memory frequently documented in PTSD.

Empirical studies examining sleep-dependant neutral declarative memory consolidation in PTSD. Only three recent studies, from different laboratories, have directly

investigated memory processing during sleep in PTSD. First, van Liempt, Vermetten, Lentjes, Arends, and Westenberg (2011) showed that male combat veterans with PTSD (n = 13) experienced more fragmented sleep during the first, SWS-rich, half of the night than did trauma controls (i.e., veterans who had experienced trauma but who did not meet diagnostic criteria for PTSD; n = 15) and healthy controls (i.e., individuals who had never experienced a DSM-IV A1 criterion traumatic event; n = 15). Additionally, van Liempt and colleagues demonstrated that morning recall of a word list learned 3 hours before sleep was poorer in the PTSD group than in the healthy control group, and that the number of awakenings during sleep was an independent predictor of this delayed recall performance. Clearly, the findings from this study are consistent with the theoretical accounts presented above. It appears that early-night SWS-rich sleep is critical for consolidation of declarative information acquired during waking hours, and that this sleep-dependent consolidation process may be disrupted in PTSD-diagnosed individuals as a result of fragmented SWS.

Second, Brownlow, Brown, and Mellman (2014) examined the relationship between sleep and performance within several cognitive domains in 18 men and 26 women (59% women) who had experienced a variety of traumas, including sexual assault, violent crime, accident, or unexpected death of someone close to them. The sample included 14 participants with no PTSD diagnosis, 14 participants with a lifetime PTSD diagnosis, and 16 participants with a current PTSD diagnosis. The authors did not report any between-group differences in polysomnographically-monitored sleep or in verbal memory performance, but showed that the latter was positively correlated with REM sleep quantity (r = 0.43). This finding suggests that individuals who experienced more REM sleep also had better verbal memory performance, but the analyses did not detect any significant difference between those who had trauma exposure only versus those that had a PTSD diagnosis. Furthermore, the study did not include a healthy

control group, which limits its capacity to make distinctions between those that have a trauma experience and those that do not.

Third, a recent study conducted in our laboratory (Lipinska, Timol, Kaminer, & Thomas, 2014) delivered similar results to those presented by van Liempt et al. (2011). We recruited three groups of women: PTSD-diagnosed survivors of sexual assault (n = 16), trauma-exposed controls (n = 15), and healthy controls (n = 14). We administered a declarative memory task and a procedural memory task before and after a full night (8 hours) of sleep. We recorded sleep variables using sleep-adapted EEG. Our results showed that PTSD-diagnosed individuals experienced less sleep efficiency and a lower REM sleep percentage, and experienced more awakenings and a higher wake percentage in the second half of the night, than did participants in the other two groups. Furthermore, participants in the PTSD group, in comparison with those in the other two groups, retained less declarative information, but not procedural ability, over the night. Most importantly, a lower REM percentage predicted poorer retention in PTSD-diagnosed individuals, suggesting that memory consolidation was compromised by REM sleep disturbance.

The studies emerging from our laboratory and from van Liempt and colleagues (2011) suggest, at least indirectly, that consolidation during sleep is central to the declarative memory deficits observed in PTSD. In addition, although the study by Brownlow and colleagues did not show between-group differences it also demonstrated an association between memory performance and sleep variables

Although these three studies demonstrated an association between sleep disruption and memory deficits in PTSD, their results differed in some respects. Primary among these differences is the finding that where van Liempt and colleagues found SWS related changes in sleep-dependent neutral declarative memory consolidation, both Brownlow et al. and Lipinska et al. found associations between REM sleep and declarative memory in PTSD-diagnosed individuals. Considering that both SWS and REM sleep are known to enhance memory

consolidation in healthy individuals via discreet neurobiological mechanisms, more research is needed to clarify the contribution of these different sleep stages to neutral declarative memory impairment in PTSD.

Furthermore, none of these studies included a day condition to control for the passage of time. The results of these studies (and, hence, the state of the empirical literature in this field) do not allow for the inference that the observed memory differences are not simply the consequence of the passage of time – that is, that PTSD-diagnosed individuals simply lose more information than controls over a given interval, rather than because of sleep- specific deficits in consolidation.

Healthy Sleep Enhances Consolidation of Declarative Emotional Memories

A wide body of research has shown that memories carrying high emotional content are remembered better than those with neutral content in both experimental settings and real-life accounts (Anderson, Yamaguchi, Grabski, & Lacka, 2006; Bradley, Greenwald, Petry, & Lang, 1992; Buchanan & Lovallo, 2001; Heuer & Reisberg, 1990). Furthermore, it seems clear that emotion modulates the initial encoding of memories (Phelps, 2004).

Although a full review of emotional memory processing during waking in healthy individuals is beyond the scope of this project (see, e.g., Phelps (2006) and Nader (2015) for a complete review of this area), a brief description of key neurobiological findings is useful to mention here. Primary among these is that a network of disparate brain regions is important for emotional memory processing. Regarding the encoding of such memories, the amygdala is a critical structure. It facilitates the initial acquisition of emotional information by enhancing activation in medial temporal structures, including the hippocampus (McGaugh, 2004). This initial enhancement of emotional memories at encoding may also tag these memories for future consolidation (Hutchison & Rathore, 2015). Further, the reactivity of the amygdala to emotional information is controlled by frontal structures. For instance, the medial prefrontal cortex (mPFC)

exerts top-down control over the amygdala in healthy processing of emotional memory (Phelps, 2006). The amygdala is also important for activation of the autonomic nervous system (ANS) in response to emotional or stressful experiences by influencing structures responsible for the release of neurochemicals such as noradrenaline, adrenaline, and cortisol (McGaugh, 2004).

Regarding the consolidation of emotional memories, recent research has emphasized the importance of sleep, especially REM sleep.

Sleep-related emotional declarative consolidation. Human studies have shown that sleep benefits the consolidation of emotional memories more than it does neutral memories. In this section, I focus on the consolidation of emotional declarative memory, although a considerable amount of work has been devoted to increasing understanding of sleep-dependent processing and consolidation of non-declarative aspects of memory, such as fear conditioning and extinction (for a recent review see, Pace-Schott, Germain, and Milad (2015)), this body of research is beyond the scope of this review.

Initial reports suggested that emotional memories appear to persist, or are even enhanced, over periods containing sleep (Kleinsmith & Kaplan, 1963; Levonian, 1972). Only more recently, however, have researchers begun to investigate the fundamental question of whether it is sleep or simply the passage of time that has selective benefits for consolidation of emotional material. Hu, Styllos-Allen, and Walker (2006) compared the consolidation of emotionally arousing and non-arousing pictures over a 12-hour period of sleep versus a 12-hour period of waking. Consolidation benefits were observed for the emotionally arousing material only following a night of sleep, suggesting that sleep, rather than simply the passage of time, benefited emotional memory consolidation. These results have been replicated in several independent studies (Groch, Zinke, Wilhelm, & Born, 2013; Morgenthaler et al., 2014; Nishida, Pearsall, Buckner, & Walker, 2009; Wagner, Hallschmid, Rasch, & Born, 2006), but some have also failed to show preferential sleep-dependent consolidation of emotional memory over neutral

memory (Baran, Pace-Schott, Ericson, & Spencer, 2012; Cairney, Durrant, Hulleman, & Lewis, 2014).

Regarding which stages of sleep benefit emotional memory consolidation, some studies have found a relationship between SWS and such consolidation (e.g. Cairney et al., 2014). However, most studies consistently report a selective function for REM sleep in emotional memory consolidation. SWS contributions to emotional memory consolidation are related to the neutral location and contextual aspects of memory (such as color or the position of images), rather than the actual content or valence of emotional memories (Groch et al., 2015).

Consolidation during REM sleep. Researchers have theorized that REM sleep offers emotional memory consolidation benefits because of its unique physiology (Walker & van der Helm, 2009). During REM, the same brain regions active in waking emotional processing are also activated in off-line processing, suggesting that an active consolidation process is underway. Areas such as the amygdala, hippocampus, anterior cingulate, and ventral mPFC are all well established as being involved in waking processing of emotional memory. These areas also show enhanced activation during REM sleep (Vandekerckhove & Cluydts, 2010).

Because REM sleep provides a distinctive environment for emotional memory consolidation, several behavioral studies have examined whether REM sleep benefits emotional memory consolidation in healthy individuals. For example, Wagner, Gais, and Born (2001) showed that retention of previously learned emotional texts was better than that of neutral texts following a period of sleep, but not following a period of waking. However, this benefit was present only for late-night sleep, which is rich in REM. Wagner and colleagues (2006) followed up the participants of Wagner et al. (2001) and showed that, even four years later, those in the sleep group retained significantly more emotional, but not neutral, information compared to their waking-group counterparts. This persistence of emotional memory following sleep-dependent consolidation occurred with no re-exposure to the original stimuli.

In a more recent study, Nishida, Pearsall, Buckner, and Walker (2009) also confirmed that REM sleep selectively favors memory for emotional pictures rather than neutral ones. In that study, participants either remained awake or napped during the day after being exposed to emotionally arousing and neutral pictures. Participants in the sleep group retained more visual information, but only for the emotionally arousing material. Further retention scores were positively correlated with the amount of REM sleep, and with the speed of entry into REM (i.e., REM latency). Spectral analysis of the participants' REM physiology revealed that the magnitude of the right-dominant prefrontal theta power during REM was positively correlated with retention scores. Theta activity may serve as an underlying mechanism of sleep-dependent emotional memory consolidation by allowing for disparate brain regions that were involved in encoding to communicate during sleep (Walker & van der Helm, 2009). This fact may be true not only for neutral non-affective declarative memories, but also for emotional memories, resulting in the consolidation of memory in the emotional centers of the brain.

Recent animal research also supports the importance of theta oscillations in emotional memory consolidation. Boyce and colleagues (2016) found that selectively depriving mice of REM sleep by silencing neurons responsible for that stage of sleep (with no effect on total sleep time or on other sleep stages, as is common in REM sleep deprivation paradigms) prevented theta oscillations and emotional memory consolidation.

However, two recent studies have shown no relationship between REM sleep and emotional memory consolidation. Morgenthaler and colleagues (2014) investigated consolidation of neutral and negative information during a REM sleep deprivation study. Half the participants in the study slept normally, while the remaining participants were woken when they entered REM sleep. All participants also participated in a control wake condition. Participants in the sleep conditions retained significantly more information than those in the wake condition, and consolidation of negative information was significantly greater than that of neutral information.

However, the authors found that selectively depriving individuals of REM sleep did not impair their consolidation of neutral or negative information. Similarly, Baran and colleagues (2012) also showed no relationship between REM sleep and accuracy on an incidental emotional memory task.

In summary, the studies reviewed here suggest that, although associations between REM sleep and emotional memory consolidation are not found consistently, findings from a variety of paradigms support a selective role for REM in such consolidation. These consolidation benefits may arise because of the reactivation of emotional memories in limbic structures during REM sleep, which may be coordinated by theta oscillations during this stage of sleep.

Emotional Memory and Sleep in PTSD

PTSD has been defined as a disorder of emotional memory (van der Kolk, 2000). This definition is apt because a central characteristic of the disorder is that the memory of an emotionally-charged traumatic event results in prolonged abnormal behavior and physiological responses to environmental cues that are similar to those present during the original event (Brewin & Holmes, 2003). Of course, there is a massive literature on disruptions in emotional memory processing in PTSD, conducted from many different theoretical perspectives (for a review, see Brewin, 2011). Given the relatively narrow focus of this project, however, here I review only those studies examining memory-related processing of valenced information (positive, neutral, and negative).

Many studies examining emotional memory in PTSD have focused on memory for valenced material. These studies have shown that PTSD-diagnosed individuals tend to remember more negatively valenced words (both trauma-related and unrelated) than positive or neutral words (Golier, Yehuda, Lupien, & Harvey, 2003; McNally, Metzger, Lasko, Clancy, & Pitman, 1998; Tapia, Clarys, Bugaiska, & El-Hage, 2012). For example, Golier and colleagues (2003) studied neutral and emotional memory in Holocaust survivors with PTSD (n = 31), Holocaust

survivors without PTSD (n = 17), and healthy controls (n = 34). Although Holocaust survivors with PTSD had poorer memory for all material than participants in the other groups, the ratio of their memory for trauma-related emotional information to neutral information was higher than that of other participants. McNally et al. (1998) studied negative, positive, and neutral memory performance in PTSD-diagnosed (n = 14), trauma-exposed (n = 12) and healthy control (n = 12) participants, using both direct remembering and direct forgetting tasks. PTSD-diagnosed participants remembered more negative information in both the direct remembering and direct forgetting tasks (that is, in comparison to control participants, PTSD-diagnosed individuals did not forget negative information as they were instructed to do so). Instead, PTSD-diagnosed participants, during the direct remembering task, tended to forget positive and neutral words. These results suggest that PTSD-diagnosed individuals, in comparison to control participants, have a bias for negatively valenced information over neutral and positive information.

Researchers have also explored the neurobiological underpinnings of emotional memory processing in PTSD. Neuroimaging studies have shown that PTSD-diagnosed individuals experience a marked increase of activity in the amygdala during stressful scripts, cues, and trauma reminders (for review, see Heim & Nemeroff, 2009; Sherin & Nemeroff, 2011) – an area critical to emotional processing, particularly that of negative and highly-arousing stimuli. This increase in amygdala activity in response to such highly-arousing negatively valenced stimuli is coupled with decreased activity in the mPFC, and in particular the anterior cingulate cortex, an area associated with top-down inhibitory control of the amygdala (Heim & Nemeroff, 2009). This pattern of activation has been observed for various stimuli, including that of traumatic scripts, combat pictures, trauma-unrelated negative scripts, and fearful faces (Rauch, Shin, & Phelps, 2006).

Together, these findings highlight emotional memory bias toward arousing and negative in valenced stimuli in PTSD, as well as possible neurobiological mechanisms underlying that

bias. In summary, at the behavioral and cognitive levels, PTSD-diagnosed individuals show memory bias for negative as opposed to neutral or positive information. These biased responses are associated with over-activation of the amygdala and decreased top-down regulation of the amygdala by the mPFC. However, the reasons why this cluster of behavioral, cognitive, and neurobiological phenomena persists over time are still unknown.

One possible answer is that the interaction of various large-scale biological functions, such as sleep and memory processes, contributes to disordered functioning in PTSD. Healthy consolidation of emotional memory during sleep is associated with increased limbic activity in the amygdala, hippocampus, ventral mPFC, and anterior cingulate during REM sleep, specifically. Activation in these areas is coordinated by theta activity. Relying on these findings from healthy individuals, recent studies examining nuanced aspects of REM sleep in PTSD-diagnosed individuals have provided some basis for understanding negative emotional bias in the context of sleep.

Germain et al. (2013) showed that PTSD-diagnosed participants, in comparison to trauma-exposed participants without a PTSD diagnosis, had greater activation of limbic and brainstem regions involved in emotional memory consolidation (e.g., the amygdala, hippocampus, and locus coeruleus), not only during waking but specifically during REM sleep. Furthermore, Cowdin, Kobayashi and Mellman (2014) showed that theta activity over right prefrontal areas during REM sleep was diminished in PTSD-diagnosed participants in comparison with those who were trauma-exposed only. Hence, one type of speculation is that disrupted theta rhythm during REM sleep may fail to recruit and coordinate timely and balanced activation of limbic regions for successful emotional memory consolidation. Following this speculative path, in PTSD-diagnosed individuals hyper-activity of limbic and brainstem regions during REM sleep may in turn lead to an over-consolidation of negatively valenced and highly-

arousing information because activity limbic regions, and in particular the amygdala, is associated with consolidation of negatively arousing information during waking.

Empirical studies examining sleep-dependant emotional memory processing in PTSD. Currently, there are no polysomnographic studies examining the effects of sleep abnormalities on emotional memory processing in PTSD-diagnosed individuals. However, various authors studying sleep in healthy samples have, as described above, theorized about the influence of PTSD-related sleep disruption on emotional memory processing, suggesting that the disrupted REM sleep characteristic of the disorder may underpin the emotional memory biases often observed in PTSD-diagnosed individuals (Goldstein & Walker, 2014; Vandekerckhove & Cluydts, 2010; Walker & van der Helm, 2009). More specifically, the hypothesis arising from this area of the literature is that disrupted sleep in PTSD (and, in particular, REM sleep abnormalities that may include a lack of normal theta activity and hyperactive limbic and brainstem regions) may result in a memory bias for negative information (i.e., an over-consolidation of negative, relative to neutral, information).

Healthy Sleep Attenuates Emotional Reactivity

Emotional reactivity, from a neurophysiological point of view, encompasses reactivity of both the sympathetic and parasympathetic branches of the ANS to emotional stimuli such as pictures, movies, or stories. ANS activity has been measured using physiological markers such as heart rate, heart rate variability (variation in time interval between heart beats), and skin conductance level; neuroendocrine markers such as cortisol, adrenocorticotropic hormone, or noradrenaline levels, and self-report measures examining arousal appraisal (the subjective level of arousal a particular stimulus evokes) (Kragel & Labar, 2013; Kreibig, 2010; Poisson, 2015).

Experimental evidence suggests that, during the day and in response to emotionally salient tasks or situations, levels of autonomic reactivity increase. For example, Hot, Leconte, and Sequeira (2005) found that skin conductance level and self-reported emotional experience

(evaluation of the emotional intensity participants felt toward the task) increased during the day in response to neutral and negative pictures. These objective and subjective measures of autonomic reactivity were greater for negative than for neutral pictures. Similarly, heart rate and noradrenaline increased during the day and especially in response to emotionally salient material and dropped during the night (Krauchi & Wirz-Justice, 1994; Morris, Yang, & Scheer, 2012). Heart rate variability, in which certain measures decrease with elevated autonomic arousal, decreased during the day and especially in response to emotionally salient material and increased during the night (Bonnemeier et al., 2003).

A number of studies suggest that sleep acts to recalibrate emotional reactivity, which tends to rise throughout the day, back to a homeostatic baseline (Goldstein & Walker, 2014). Hence, poor sleep quality or acute sleep deprivation tends to exacerbate emotional reactivity. For example, some studies have found that individuals who have poorer sleep quality are less likely to be able to regulate their emotions successfully (e.g., by employing strategies that cognitively reframe an emotional event so as to dampen its impact). These sleep-deprived individuals have heightened reactivity to emotionally challenging situations (Mauss, Troy, & LeBourgeois, 2013; Perlis & Nielsen, 1993). Neuroimaging studies investigating brain regions responsible for regulation of ANS activity and emotional activity support these behavioral findings. Yoo, Gujar, Hu, Jolesz, and Walker (2007) conducted an fMRI study comparing a group of sleep-deprived participants with a group who had slept normally. They showed that sleep-deprived individuals, in contrast to those who had slept normally, had heightened amygdala activity in response to increasingly negatively valenced images coupled with decreased activation of the mPFC. The latter may result in a lack of top-down regulation of the amygdala. Furthermore, hyperactivation of this brain structure in response to those images in sleep-deprived individuals was associated with increased activity in the locus coeruleus, the noradrenergic center of the brain.

REM sleep attenuates emotional reactivity. Recent studies suggest that REM sleep, specifically, is associated with the emotional regulation effects observed after sleep. For instance, Walker and colleagues propose that REM sleep provides the ideal environment for the attenuation of emotional reactivity that is associated with waking experiences (Goldstein & Walker, 2014; Walker & van der Helm, 2009). This is because previously encoded emotional experiences, consisting of the memory content as well as the emotional tone, are reactivated during REM sleep in an environment devoid of noradrenergic activity. Because the original emotional event would have been encoded in the context of elevated noradrenergic activity, reactivation of the event in an environment sans noradrenergic activity acts to decrease the emotional tone associated with the event. According to Walker and van der Helm (2009), over successive nights containing adequate REM sleep, the emotional tone is progressively stripped away until only the memory of the emotional experience remains.

Several studies have provided indirect support for this theory (Cunningham et al., 2014; Gujar, McDonald, Nishida, & Walker, 2011; Pace-Schott et al., 2011; Rosales-Lagarde et al., 2012; van der Helm et al., 2011). For example, Gujar et al. (2011) and Pace-Schott et al. (2011) both showed that emotional reactivity, as measured by self-report emotional rating and facial electromyography, and by skin conductance response and heart rate deceleration, respectively, decreased over a nap period in contrast to a waking period. Gujar et al. (2011) showed that only participants who entered REM sleep during the nap showed attenuation of negative ratings toward angry and fearful faces. Similarly, Pace-Schott et al. (2011) showed that higher skin conductance responses in reaction to negative pictures were associated with participants not achieving any REM sleep during the nap period.

Van der Helm et al. (2011) investigated the association between REM sleep and emotional reactivity using fMRI. They showed that after a period of sleep, in comparison to waking, participants had decreased amygdala activity and decreased subjective emotional ratings

to a set of previously seen emotional pictures. This decrease in amygdala activity was associated with reduced REM-gamma activity. REM-gamma activity is a validated marker of central adrenergic activity, with more gamma activity during this stage of sleep indicative of increased noradrenergic activity (Cape & Jones, 1998).

However, some studies have found that REM sleep either maintains emotional reactivity at pre-sleep levels, or even enhances emotional reactivity (Baran et al., 2012; Gilson et al., 2015; Lara-Carrasco, Nielsen, Solomonova, Levrier, & Popova, 2009; Wagner, Fischer, & Born, 2002). For example, Baran et al. (2012) showed that REM sleep was associated with preserved self-reported emotional reactivity to negative pictures over a period of sleep in contrast to a period of waking. Wagner et al. (2002) showed increased self-rated emotional negativity to emotional pictures over a period rich in REM sleep in contrast to a period rich in SWS.

In an attempt to explain these discrepant findings, Cunningham et al. (2014) suggested that studies showing associations between REM sleep and enhancement of emotional reactivity tended to use self-report, rather than objective, measures. They state that participants may respond to the pictures in ways they think they should be feeling, rather than according to what they actually experience. Studies that use heart rate, skin conductance, or brain imaging measures generally show decreased emotional reactivity associated with REM sleep, with the exception of Gilson et al. (2015).

In summary, these findings suggest that healthy REM sleep is associated with the attenuation of emotional reactivity to previously experienced emotional stimuli. Currently, however, there is no direct evidence showing that REM-related attenuation of emotional reactivity is underpinned by reactivation of previously experienced emotional information in an environment devoid of noradrenergic activity.

Emotional Reactivity and Sleep in PTSD

A wealth of evidence suggests that PTSD is characterized by elevated autonomic reactivity to negative emotional stimuli (i.e., increased emotional reactivity; Rauch et al., 2006). Most studies examining increased autonomic reactivity in PTSD have involved trauma-related material (scripts, images, and movie-clips), trauma-unrelated negative imagery, and fear conditioning paradigms. Although a review of fear conditioning mechanisms is beyond the scope of this project, findings consistently show that PTSD-diagnosed individuals have increased autonomic reactivity to trauma-related, trauma-unrelated negative, or fear-eliciting stimuli (Amstadter, Nugent, & Koenen, 2009; Blechert, Michael, Vriends, Margraf, & Wilhelm, 2007; Liberzon, Abelson, Flagel, Raz, & Young, 1999; McTeague et al., 2010; Sherin & Nemeroff, 2011).

For example, Schmahl et al. (2004) showed that PTSD-diagnosed individuals, in comparison to participants diagnosed with borderline personality disorder and healthy controls, had elevated systolic blood pressure responses to trauma-related, but not abandonment-related, scripts. McTeague et al. (2010) compared PTSD-diagnosed, trauma-exposed and healthy control participants on heart rate, skin conductance and emotional expressiveness variables. These autonomic variables were measured in response to both trauma-related scripts and trauma-unrelated negative scenes. They found that PTSD-diagnosed participants, in comparison to the control groups, had elevated heart rates, higher skin conductance, and greater emotional expressiveness most prominently for trauma-related scripts, but also for trauma-unrelated negative images. Liberzon, Abelson, Glagel, Raz and Young (1999) corroborated these findings, reporting that combat veterans with PTSD, in comparison to combat veterans without PTSD and healthy controls, had elevated skin conductance, heart rate, plasma adrenaline, and plasma noradrenaline in response to combat sounds in contrast to white noise.

However, it is unknown why PTSD-diagnosed individuals experience such unremitting and persistent autonomic responses to trauma-related, trauma-unrelated negative, and fear-eliciting stimuli, whereas trauma-exposed individuals without the diagnosis experience a gradual normalization of their autonomic responsiveness in the recovery period after trauma (Koresh et al., 2016). One possibility is that sleep disruption may maintain elevated autonomic reactivity because, unlike healthy sleep, sleep in PTSD-diagnosed individuals may not act to recalibrate autonomic reactivity back to baseline.

Disrupted sleep in PTSD-diagnosed individuals may influence emotional reactivity following two distinct processes. First, PTSD-diagnosed individuals show a pattern of brain activation in relation to negative stimuli that is remarkably consistent with sleep deprivation. Both PTSD-diagnosed and sleep-deprived individuals show hyper-activity of the amygdala, decreased connectivity between the amygdala and the mPFC, and increased activity in the locus coeruleus. Although it is unlikely that sleep deprivation in PTSD-diagnosed individuals is the only factor underlying the described pattern of brain activation, it is possible that it may maintain or prevent the recovery of limbic-prefrontal regions to a balanced pattern of activation.

Second, REM sleep alterations in PTSD may interrupt healthy attenuation of emotional reactivity to trauma-related, trauma-unrelated negative, and fear-eliciting stimuli. Drawing from earlier literature in this review, both human and animal studies of PTSD have found decreases in REM percentage (Glaubman et al., 1990; Philbert et al., 2011). Additionally, REM density and REM fragmentation are increased in PTSD, and are predictors of the severity of PTSD symptoms and of PTSD diagnosis, respectively (Mellman et al., 2002; Mellman, David, et al., 1995). Furthermore, REM sleep in PTSD-diagnosed individuals, in contrast to those that are trauma-exposed only, is associated with hyperactivation of limbic regions, beyond the normally elevated activity seen in these regions during REM sleep in healthy individuals (Germain et al.,

2013). Several authors even consider REM dysfunction as the hallmark of disrupted sleep in PTSD (Ross et al., 1994; Spoormaker & Montgomery, 2008).

These REM disruptions may be driven, at least in part, by elevated noradrenergic activity at night in PTSD-diagnosed individuals (Mellman, Kumar, et al., 1995). Because REM sleep is terminated by increases in aminergic activity (including that of noradrenaline), higher levels of noradrenaline during this stage of sleep may result in consistent interruptions of REM sleep, a pattern that is commonly reported in PTSD-diagnosed individuals (e.g., Mellman et al., 2002). These interruptions in REM sleep in PTSD may disrupt the shedding of emotional tone associated with emotional memories that are reactivated in REM sleep. Consequently, PTSD-diagnosed individuals may experience no recalibration of emotional reactivity to emotional stimuli upon waking.

Another possibility explaining elevated daytime emotional reactivity in PTSD is that noradrenergic activity is not completely absent in REM sleep in PTSD-diagnosed individuals. This scenario may result not only in fragmented REM sleep, but also in the reactivation of emotional information in an environment that contains noradrenaline. Such reactivations may in turn result in the consolidation of the emotional tone as well as the emotional information Consequently, when PTSD-diagnosed individuals are re-exposed to the same emotional information during waking, the emotional tone associated with the information may be reactivated.

Empirical studies examining sleep-dependant emotional reactivity in PTSD. There are no published polysomnographic studies examining the effects of sleep deprivation and REM fragmentation on autonomic reactivity to emotional stimuli in PTSD-diagnosed individuals. However, various authors studying sleep in healthy populations have theorized about the influence on autonomic reactivity of these sleep-related abnormalities in PTSD (Goldstein & Walker, 2014; Vandekerckhove & Cluydts, 2010; Walker & van der Helm, 2009). In essence

these authors also identify that elevated noradrenergic activity at night in PTSD-diagnosed individuals may act to disrupt REM sleep and the essential emotional regulatory function that this stage plays. However the precise mechanism is currently unknown.

In summary, two possible mechanisms may explain the maintenance of elevated waking autonomic reactivity to emotional stimuli in PTSD-diagnosed individuals. First, chronic general sleep deprivation may contribute to hyperactivity of limbic structures (most notably, the amygdala) and under-activity of prefrontal structures. Second, elevated noradrenergic activity at night may disrupt continuous REM sleep in PTSD-diagnosed individuals. A consequence of these REM disruptions, irrespective of the precise mechanism, may be a deficiency in the reduction of the emotional tone for emotional stimuli in PTSD-diagnosed individuals. These individuals may therefore experience preservation or even consolidation of emotional tone (i.e., increased autonomic reactivity) during waking re-exposure to trauma-related, trauma-unrelated negative, or fear-eliciting stimuli.

Rationale and Significance Relating PTSD, Disordered Sleep, and Neutral Declarative Memory, Emotional Memory and Emotional Regulation Deficits

The literature on PTSD and sleep suggests the hypothesis that sleep abnormality may have a causal effect on other symptoms of the disorder, rather than being merely a symptom itself. For example, disruptions in sleep shortly after the trauma predict the development of PTSD 6 months later (Harvey & Bryant, 1998; Koren, Arnon, Lavie, & Klein, 2002). That is, disordered sleep *precedes* (and may exacerbate) the development of other symptoms. Related studies have shown that if sleep abnormalities are treated either pharmacologically or psychotherapeutically, then other PTSD symptoms also resolve (Germain et al., 2012; Green, 2014).

Despite evidence highlighting the importance of sleep disruption in the pathophysiology of PTSD, and although both SWS and REM abnormalities are widely reported, current literature

is unclear about the exact nature of sleep disruption in this disorder. Across-study methodological differences may explain these divergent and inconsistent findings. An alternative explanation is that there is a single mechanism underlying sleep difficulties in PTSD-diagnosed individuals, but that this mechanism results in a range of sleep difficulties that are either not captured coherently in single studies, or that vary by individual presentation. One proposed mechanism that may explain sleep disruption in PTSD-diagnosed individuals is the amount of noradrenergic activity these individuals experience at night. There is some evidence to suggest that individuals with the disorder experience elevated nighttime levels of noradrenaline, which disrupts their sleep (Mellman, Kumar, Kulick-Bell, Kumar, & Nolan, 1995). In rats, elevated noradrenergic activity at night results in disrupted sleep continuity that affects both SWS and REM sleep stages (Aston-Jones & Bloom, 1981), which may account for the diversity in findings related to sleep disruption in human studies of PTSD. However, few studies have comprehensively assessed the relationship between disrupted sleep and nighttime noradrenaline levels in PTSD.

A closely related thread in the literature suggests that healthy sleep is important for the consolidation of newly acquired neutral declarative and emotional memories, and for successful attenuation of emotional reactivity. The relevance of these findings for an understanding of PTSD is that, alongside disordered sleep, abnormalities in neutral declarative memory, emotional memory, and emotional reactivity have been widely documented in the disorder.

Few studies of PTSD-diagnosed individuals have, however, examined potential relationships between disordered sleep and (a) neutral declarative memory, (b) emotional memory, and (c) emotional reactivity. With regard to (a), three studies have suggested that disordered sleep in PTSD-diagnosed individuals is associated with neutral declarative memory deficits. However, whereas two of the studies suggest that REM sleep abnormalities are related to neutral declarative memory deficits (Brownlow, Brown, & Mellman, 2014; Lipinska, Timol,

Kaminer, & Thomas, 2014), the third suggests that SWS fragmentation is related to the observed memory deficits (van Liempt, Vermetten, Lentjes, Arends, & Westenberg, 2011). None of these studies included a day condition to control for the passage of time. Furthermore, none of the three could comment on how nighttime consolidation deficits in PTSD may relate to waking neutral declarative memory deficits, which are characterized primarily by immediate and delayed recall deficits.

With regard to (b) and (c), no studies have directly investigated whether sleep disruption in general, and REM abnormalities more specifically (such as lower REM percentage and REM fragmentation), are associated with negative emotional memory bias and increased emotional reactivity in PTSD.

The current investigation of these four core questions (sleep disruption in PTSD and a-c) is significant and innovative in three primary ways. First, it will examine, using a firm neurobiological grounding, why sleep disruption, neutral declarative memory impairment, negative emotional memory bias, and increased emotional reactivity may co-exist in PTSD. If such relationships between symptoms are demonstrated, one implication is that the co-occurrence of these symptoms is neither incidental nor accidental. Second, because the research seeks to demonstrate that sleep disruption is an active component of PTSD psychopathology, rather than a passive symptom, it might have treatment implications. It might, for instance, suggest that treating sleep disruption will alleviate other symptoms of the disorder, thus offering a unique addition to the arsenal of PTSD therapies (a potentially ground-breaking addition, given that many PTSD-diagnosed individuals do not respond to pharmacological or psychotherapeutic intervention). Third, the research will bolster the neuroscientific view of sleep as a critical biological process linked integrally to psychological well-being.

Hypotheses

In light of the rationale outlined above, I have investigated four core questions. The first of these is related to the nature and mechanism of sleep disruption in PTSD-diagnosed individuals. The rest are related to whether disordered sleep in PTSD-diagnosed individuals is associated with (a) neutral declarative memory deficits, (b) bias for negative emotional memories, and (c) increased emotional reactivity. Naturally, the bases for investigation of (a) to (c) rest on the demonstration of disordered sleep in PTSD. Therefore, the first overarching hypotheses that are intrinsic to (a) to (c) are focused on sleep in PTSD.

Disordered sleep in PTSD. Considering the contrasting results reported by studies investigating sleep in PTSD-diagnosed individuals, I aim to clarify the nature of sleep disruption in that population in two important ways. First, I aim to establish whether sleep disruption in PTSD-diagnosed individuals is consistent with the results of the meta-analysis by Kobayashi et al. (2007); i.e., that it is characterized, relative to controls, by more NREM1 and SWS and REM sleep abnormalities. Furthermore, based on increasing evidence highlighting the significance of REM sleep abnormalities in PTSD-diagnosed individuals (e.g. Germain et al., 2013; Mellman, Bustamante, Fins, Pigeon, & Nolan, 2002), I will examine more nuanced aspects of REM sleep, such as REM sleep fragmentation. Second, I aim to determine whether increased nighttime levels of noradrenaline (relative to healthy control participants) explain sleep disruption in PTSD-diagnosed individuals. Hence, I will test these hypotheses:

1. PTSD-diagnosed participants, in comparison with trauma-exposed (TE) and healthy control (HC) participants, will experience more subjectively and objectively measured sleep disruption.
    a. Objective sleep disruption in PTSD-diagnosed participants, in comparison with TE and HC participants, will be characterized by non-specific insomnia-related sleep disruption (increased sleep latency, decreased sleep efficiency, increased

awakenings at night, increased time spent awake after sleep onset) and/or sleep-stage specific disruptions (increased NREM1, decreased SWS percentage, decreased REM sleep percentage, increased REM latency, fragmentation of REM sleep).

2. PTSD-diagnosed participants, in comparison with TE and HC participants, will have higher levels of noradrenergic activity (as indexed by noradrenergic metabolites derived from urine) at night than during the day.
3. In all participants, elevated nighttime noradrenergic activity will be associated with increased sleep disruption.
    a. More specifically, PTSD-diagnosed participants with elevated nighttime noradrenergic activity will have increased sleep disruption.

Neutral declarative memory processing during sleep in PTSD. On daytime measures of neutral declarative memory, PTSD-diagnosed individuals show performance deficits on tests of immediate and delayed recall, but not on tests of retention (the percentage of information that is retained or lost between the immediate and delayed recall trials). Here, I aim to demonstrate that PTSD-diagnosed individuals, in comparison with control participants, have neutral declarative memory deficits in retention across the night – that is, that their nighttime consolidation of information is impaired. I also aim to show that the sleep disruption in PTSD-diagnosed individuals (as observed in testing the first set of hypotheses listed above) contributes to deficits in neutral declarative memory. Hence, I will test these hypotheses:

1. PTSD-diagnosed participants, in comparison with TE and HC participants, will have neutral declarative memory deficits in immediate and delayed recall during the day, and neutral declarative memory deficits in retention (a measure of memory consolidation) across the night.

2. In all participants, sleep disruption will be associated with deficits in neutral declarative memory retention after a sleep-filled delay.
    a. More specifically, PTSD-diagnosed participants with sleep disruption will have decreased neutral declarative memory retention after a sleep-filled delay.

Emotional memory processing during sleep in PTSD. PTSD-diagnosed individuals, in comparison with control participants, have bias for negative highly-arousing information. Here I aim to show that the sleep disruption in PTSD-diagnosed individuals (as observed in testing the first set of hypotheses listed above), especially that related to REM sleep parameters, contributes to negative memory bias for emotional information. Hence, I will test these hypotheses:

1. PTSD-diagnosed participants, in comparison with TE and HC participants, will have enhanced memory consolidation for negative highly-arousing information (relative to positive highly-arousing or neutral information) across the night and in comparison with the day.
2. In all participants, sleep disruption (especially that related to REM sleep alterations) will be associated with biased memory consolidation toward negative and highly-arousing information.
    a. More specifically, PTSD-diagnosed participants with sleep disruption will have biased memory consolidation toward negative and highly-arousing information.

Emotional reactivity regulation during sleep in PTSD. PTSD-diagnosed individuals, in comparison with control participants, have increased emotional reactivity characterized by increased autonomic reactivity to negative and highly-arousing stimuli. Here I aim to show that the sleep disruption in PTSD-diagnosed individuals (as observed in testing the first set of hypotheses listed above), especially that related to REM sleep parameters, contributes to this increased emotional reactivity. Hence, I will test these hypotheses:

1. PTSD-diagnosed participants, in comparison with TE and HC participants, will have increased emotional reactivity for negative highly-arousing stimuli (relative to positive highly-arousing or neutral stimuli) across the night and in comparison with the day. In this investigation, emotional reactivity will be indexed by parameters associated with autonomic reactivity (such as heart rate and skin conductance).
2. In all participants, sleep disruption (especially that related to REM sleep alterations) will be associated with elevated emotional reactivity, especially in response to negative and highly-arousing stimuli.
    a. More specifically, PTSD-diagnosed participants with sleep disruption will have elevated emotional reactivity, especially in response to negative and highly-arousing stimuli.

CHAPTER THREE: GENERAL METHODS

In this section, I will begin by describing the methods common to the entire project, which consist of addressing four main avenues of inquiry – *describing sleep disruption in PTSD, neutral declarative memory processing during sleep in PTSD, emotional memory processing during sleep in PTSD,* and *emotional reactivity regulation during sleep in PTSD*. The specific questions of interest within these four broad avenues of inquiry were investigated in the same participants, during the same study sessions. Figure 1 shows the relationship between the four investigations. Once I have discussed aspects common to all four investigations, I will describe each one separately and in detail.

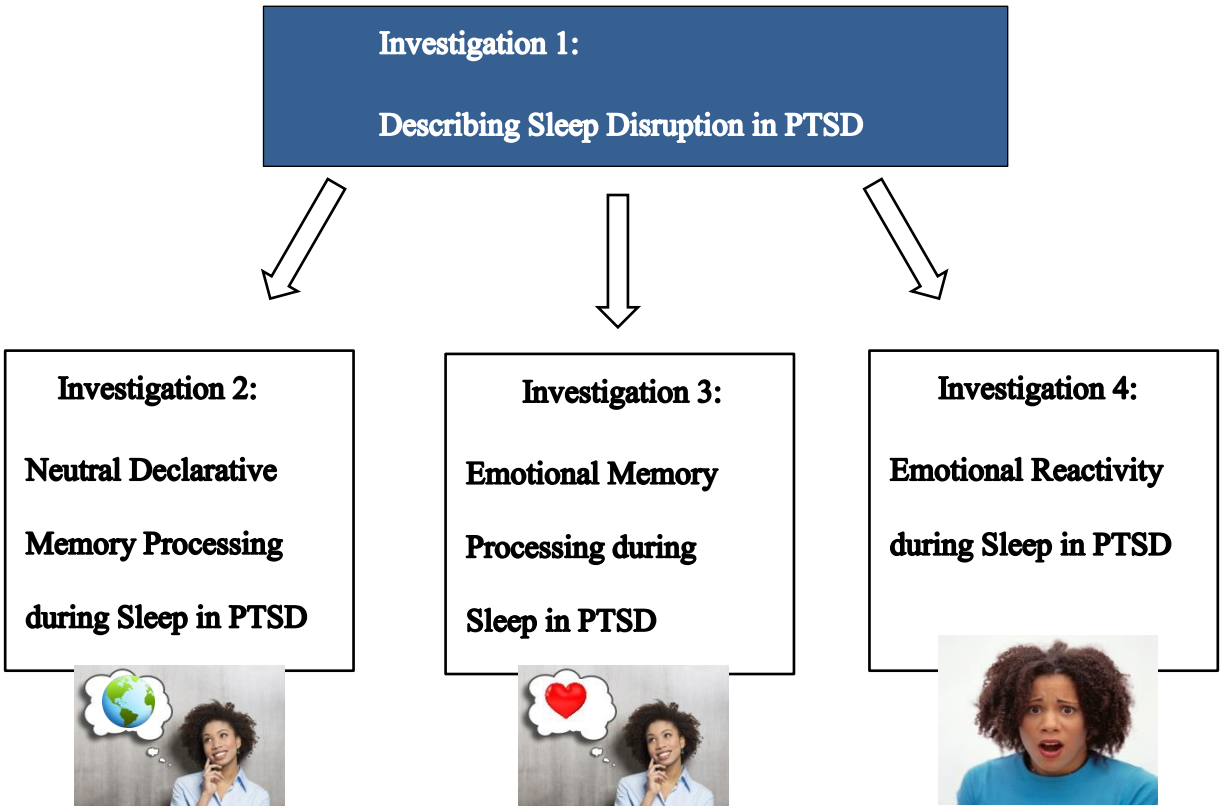

Figure 1. The relationship between the four investigations

Study Design

The design of each investigation is described separately. However, as a whole, the study was comprised of mixed repeated-measures and between-group, cross-sectional design. That is, I recruited three groups of participants (for between-group comparisons), and those participants were exposed to two conditions (for within-subjects comparisons).

Participants

Participants were recruited from branches of the Rape Crisis Cape Town Trust located in Observatory, Athlone, and Khayelitsha, and through advertisements placed in local newspapers distributed to those areas. With regard to individuals recruited in the former way, I worked closely with counselors at the Rape Crisis centers to identify potential participants. With regard to individuals who responded telephonically to advertisements placed in local newspapers, I administered a number of short questions to ascertain basic demographic information (e.g., age) as well as previous history of trauma (e.g., type and timing of trauma).

I conducted a power analysis to determine the sample size required to detect effects of the size commonly reported in PTSD sleep and cognition studies. In my previous work examining sleep and memory in PTSD-diagnosed individuals (Lipinska, Timol, Kaminer, & Thomas, 2014), effect sizes ranged from $f = 0.33$ to $f = 0.73$, with an average effect size of $f = 0.53$. The power analysis revealed that to achieve statistical power of 0.8 with an effect size of $f = 0.53$, with α set at 0.05, I needed to recruit 39 participants. The power analysis also revealed that effect sizes of $f = 0.1$ (small) and $f = 0.25$ (medium) would require 567 and 93 participants respectively. I opted to recruit participants in such a way as to be able to detect medium-to-large effects, using conservative estimates from my previous study.

I recruited 107 individuals for screening. Based on the eligibility criteria outlined below, 66 met the criteria for inclusion and were invited to the next stage of the study. However, six

individuals withdrew from the study after screening, due to work or other commitments, leaving a final sample of 60 participants.

After screening, each of those 60 participants was included in one of three groups: PTSD (n = 21), trauma-exposed non-PTSD (TE; n = 19), and healthy control (HC; n = 20). All participants recruited to the study were females fluent in English, and all participants in the trauma groups (PTSD and TE) were survivors of sexual assault. Groups were matched in terms of age, level of education, IQ, income level, employment status, language, and smoking status. Smokers were included in the sample. Although studies show that smoking influences sleep (Zhang, Samet, Caffo, & Punjabi, 2006), the strict eligibility criteria described below were already restrictive, with a large number of potential participants excluded from the study. To ensure the recruitment of an adequate sample, smokers were permitted to participate provided no statistically significant differences in smoking status existed between the PTSD, TE, and HC groups. Furthermore, the actual differences between smokers and non-smokers are relatively small: For example, smokers take approximately 5 minutes longer to fall asleep, experience 14 minutes less sleep, and have approximately 6% less SWS than non-smokers (Zhang et al., 2006).

Figure 2 outlines the recruitment flow related to the study, while Table 1 specifies the demographic information.

I chose to only recruit female survivors of sexual assault because most PTSD studies recruit male war veterans, and several authors have highlighted that studies recruiting female participants with trauma aetiologies other than war are important for understanding the whole spectrum of the disorder (Hall Brown, Akeeb, & Mellman, 2015; Santiago et al., 2013). Furthermore, I included the TE group to differentiate between the experience of trauma and a diagnosis of PTSD. Only a small percentage of individuals who experience a traumatic event go on to develop PTSD (Kaminer, Grimsrud, Myer, Stein, & Williams, 2008; Kessler, Sonnega,

Bromet, Hughes, & Nelson, 1995). From this perspective, it is important to differentiate between those who develop psychopathology in the aftermath of trauma and those who do not.

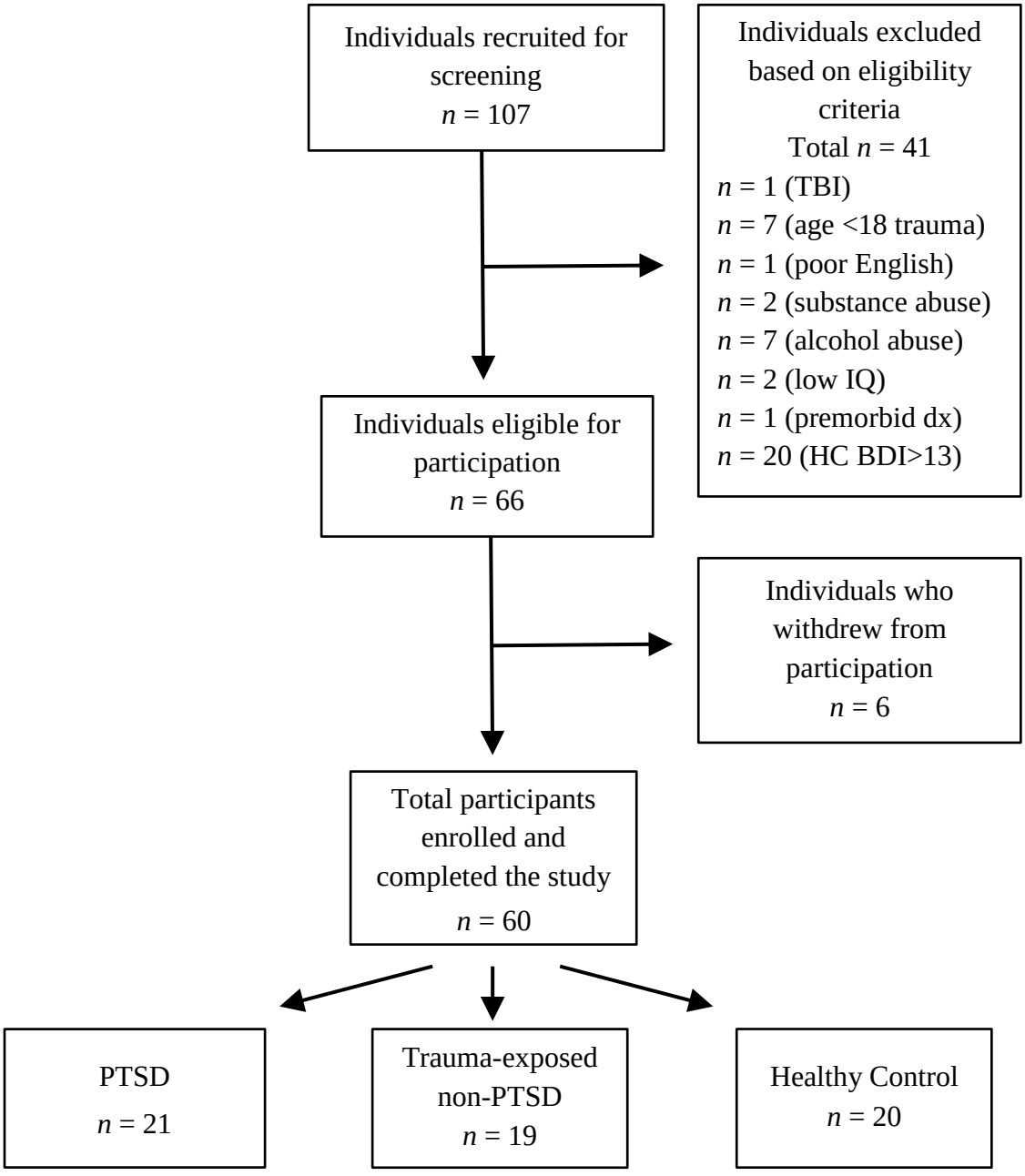

Figure 2. Recruitment of participants into the four investigations. TBI = traumatic brain injury; age <18 trauma = sexual assault at age 17 or younger; premorbid dx = premorbid psychiatric diagnosis; Low IQ = Performance IQ more than 1.5 standard deviations below the sample mean; HC BDI>13 = Healthy control participants with Beck Depression Inventory - Second Edition score greater than 13

Table 1. Sociodemographic and IQ Data for the Current Sample (N = 60)

	Group				
	PTSD	TE	HC		
Variable	(*n* = 21)	(*n* = 19)	(*n* = 20)	F / χ^2	p
Age	25.54 (4.35)	24.42 (4.53)	25.30 (4.62)	0.33	0.72
Years of Education	11.67 (1.59)	12.53 (2.09)	12.90 (2.00)	2.28	0.11
WASI PIQ	77.14 (14.98)	84.26 (11.02)	83.80 (14.21)	1.76	0.18
Income				12.42	0.10
R0-R999	1	1	1		
R1000-R2499	3	6	5		
R2500-R5499	12	7	5		
R5500-R9999	0	4	5		
R10 000+	5	1	4		
Employment				6.68	0.15
Unemployed	7	8	10		
Employed	11	6	3		
Student	3	5	7		
Language				5.14	0.56
Xhosa	15	16	16		
Afrikaans	3	0	2		
English	2	1	2		
Other	1	2	0		
Smoking				5.01	0.09
Yes	7	1	5		
No	14	18	15		
HIV				3.80	0.19
Positive	1	5	1		
Negative	18	16	19		

Note. For Age, Years of Education, and PIQ, means are presented with standard deviations in parentheses. Income is presented in South African Rands. At the time of study, the ZAR:US$ exchange rate was 11.45. Degrees of freedom are (2, 57) for analyses of each of those variables. For Income, Employment, Language, and Smoking, Fisher's exact test statistic is presented as data are categorical in nature. WASI PIQ = Wechsler Abbreviated Scale of Intelligence Performance IQ score.

Inclusion and exclusion criteria. The following eligibility criteria were strictly enforced:

1. Potential participants diagnosed with any DSM-IV (A.P.A., 2000) Axis I disorders (except PTSD) were excluded, as the sleep patterns and memory deficits characteristic of these psychiatric disorders may serve as confounds (Harvey, Jones, & Schmidt, 2003). However, individuals in the PTSD and TE groups who presented with other anxiety and mood disorders secondary to the trauma were not excluded.
2. Potential participants with a 1-year history of alcohol or other substance abuse were excluded. Alcohol or other substance abuse is associated with both disordered sleep and memory dysfunction, and previous sleep studies have demonstrated the confounding effects of these variables (Stewart, Pihl, Conrod, & Dongier, 1998).
3. Potential participants below the age of 18 years and above the age of 40 years were excluded. Normal ageing is associated with hippocampal atrophy, mild memory decline, and altered sleep cycles (Lupien et al., 1994; McEwen, 1999), and the sleep cycles of children and adolescents differ from those of adults (Grigg-Damberger, 2012).
4. Potential participants who, at the time of recruitment, were taking sedative medication to regulate their sleeping patterns, or who were prescribed psychoactive medication (including antidepressants), were excluded. Sleeping pills alter natural sleep cycles, and psychoactive medications have demonstrable effects on memory processing and on brain structure and function (see, e.g., Vermetten, Vythilingam, Southwick, Charney, & Bremner, 2003).
5. Potential participants who had experienced trauma more than 5 years or fewer than 6 months prior to screening were excluded. Proximity to the trauma has implications for both memory and sleeping patterns. Also, irrespective of the time since trauma, any participants who had experienced trauma as children or teenagers were excluded because

childhood trauma can affect the developmental trajectory of memory processes and can have long-lasting implications for neuroendocrinological functioning (De Bellis, Hooper, & Sapia, 2005).

6. Potential participants who carried neurological conditions (e.g., epilepsy, traumatic brain injury) with the potential to influence the outcomes of the study were excluded. During screening, seven participants revealed that they were HIV-positive but did not present with any HIV- or AIDS-related disorders and were regarded as asymptomatic (they had no weight loss, recurrent fever, cognitive changes, or opportunistic infections). Research shows that individuals diagnosed with HIV who have preserved immune function and who are not abusing drugs or alcohol are far less likely to experience HIV-associated neurocognitive disorders (Elbirt et al., 2015). From this point of view, asymptomatic HIV diagnosed individuals were included in the sample.
7. Potential participants who were not fluent in English were excluded from the study. A number of measures employed in the study are only available in English and no local translations are available.

Materials and Apparatus

Diagnostic and screening instruments. The *MINI International Neuropsychiatric Interview* (MINI version 5.0.0; Sheehan et al., 1998) is a structured diagnostic interview that assesses the major DSM-IV Axis I psychiatric disorders. The MINI's developers report that the instrument has good psychometric properties, and that it can be administered within approximately 15 minutes. Furthermore, South African studies have used the MINI in a variety of community research settings (e.g., Onah, Field, van Heyningen, & Honikman, 2016; Seedat, Fritelli, Oosthuizen, Emsley, & Stein, 2007). In the current research, this instrument was used to confirm diagnoses of PTSD, and to exclude the presence of other DSM-IV Axis I psychiatric conditions across all groups, with the exception of anxiety and mood disorders secondary to the

trauma in the PTSD and TE groups. Potential participants in the PTSD and TE groups who had experienced psychopathology prior to the traumatic event were excluded. I also used this instrument to exclude participants who met criteria for alcohol and substance abuse and dependence. The MINI was also the primary instrument used to determine the selection of the healthy control group: These participants were required to carry no MINI-assessed psychiatric diagnoses, and were screened carefully to ensure that they had not experienced anything that qualified as a DSM-IV-TR PTSD criterion A traumatic event.

The *Clinician Administered PTSD Scale* (CAPS; Blake et al., 1995) is a structured interview designed to assess for the presence of core and associated PTSD symptoms. The CAPS assesses both intensity and frequency of symptoms by asking standard questions and utilizing an explicit, behaviorally-anchored rating scale. The instrument's developers indicate that it is a good indicator of PTSD severity, and that it has excellent reliability and validity for determining PTSD diagnoses (Blake et al., 1995). Furthermore, it has been used in several studies conducted in South Africa (e.g., Martenyi, Brown, Zhang, Prakash, & Koke, 2002; Suliman et al., 2015). In the current study, this instrument was used to validate the PTSD diagnosis provided initially by the MINI.

There are nine different ways of scoring the CAPS, all with good to excellent reliability (Weathers, Keane, & Davidson, 2001). In this study, the *Frequency ≥ I / Intensity ≥2 / Total Severity ≥ 45 (F1/12/TSEV45)* method was used. This method combines the *Frequency ≥ I / Intensity ≥ 2 (F1/I2)* and the *Total Severity ≥ 45 (TSEV45)* rules. According to the first rule (F1/I2), a symptom is present if the frequency with which it occurs is scored as 1 or higher and the intensity is scored as 2 or higher. For a diagnosis of PTSD to be made, the individual had to meet DSM-IV criteria in terms of the correct distribution of symptoms across clusters. This rule is considered lenient (Weathers et al., 2001). The second rule (TSEV45) takes a total score of at least 45 as the basis for a valid diagnosis of PTSD. This rule is considered moderate. Used

together, these rules stipulate that a CAPS score of at least 45 must be reached for a diagnosis of PTSD to be made, and that there must be the appropriate distribution of symptoms across clusters.

This combined rule is considered moderate, and is recommended for application in situations where a diagnosis of PTSD is to be confirmed or a PTSD group needs to be homogenous (Weathers et al., 2001). In the present research, both of these situations were applicable: The CAPS was used to confirm the MINI diagnosis, and, given the fairly small sample size, homogenous groups were necessary to ensure the best possible results.

The *Beck Depression Inventory – Second Edition* (BDI-II; Beck, Steer, & Brown, 1996) is a standardized 21-item self-report questionnaire that assesses current presence and severity of depression in adults. The BDI-II is used both in clinical settings and as a research tool, including in South Africa (e.g., Berard, Boermeester, & Viljoen, 1998; Stellenberg & Abrahams, 2015), and its developers report that it has adequate reliability and validity. This instrument was used to help provide information about the level of depression reported by participants in the PTSD and TE groups. Potential participants in the HC group with a BDI score of ≥14 were excluded.

The *Wechsler Abbreviated Scale of Intelligence* (WASI; The Psychological Corporation, 1999) is a short, four-subtest version of the Wechsler Adult Intelligence Scale (WAIS). Using the Vocabulary, Similarities, Block Design, and Matrix Reasoning subtests, this instrument provides a reliable and valid estimate of WAIS Verbal, Performance, and Full Scale IQ scores. The WASI takes approximately 30 minutes to complete and can be used with subjects aged 6-89 years. It is used extensively in research that requires an overall IQ measure, including that conducted in South Africa (e.g. Hoare et al., 2012). Because participants were not first-language English speakers and no appropriate and standardized translation is available, the Performance scale of this test was used as an estimate of general intellectual functioning to ensure there were no major between-group differences in terms of general cognitive ability. Performance IQ (PIQ)

is a reliable estimate of Full Scale IQ; for the WASI, the correlation is reported to be 0.87 (The Psychological Corporation, 1999).

Appendix A shows the demographic and screening forms that were used to record participant responses regarding age, time of trauma, sedative and psychoactive drug use, and history of neurological conditions.

Procedure

Here I describe the experimental procedures common to all aspects of four investigations. Figure 3 provides an overview of the general research procedure.

Overall, the procedure included an initial screening, followed by three separate testing sessions at the sleep laboratory. The screening took place in a private, quiet room in the UCT Department of Psychology. Where necessary, transport was provided for participants. I began each screening session by explaining the aims and content of the research. Each participant read and sign a detailed informed consent document (Appendix B), after which the screening measures listed above were administered. When screening potential PTSD and TE participants I also took a careful clinical history alongside the screening measures, to ensure that other psychopathologies (such as panic disorder) were secondary to the traumatic experience and did not precede the trauma.

At the conclusion of these screening and diagnostic procedures, I debriefed the participant about the study procedures up to that point. If the participant was deemed suitable for continued enrolment, I schedule an appointment for the first of three study sessions and assigned the participant to one of the three groups. These study sessions included a *Day* condition, an adaptation night, and a *Night* condition. Participants were counterbalanced so that they either attended the *Day* condition first, followed by the adaptation night and *Night* condition, or the adaptation night and *Night* condition followed by the *Day* condition. The adaptation night and

Night condition were always consecutive; however the adaptation night/*Night* condition and *Day* condition were separated by 2-7 days, depending on the participant's availability.

Only one night of sleep was recorded for statistical analysis. However, participants attended an adaptation night prior to the *Night* condition so that they could become habituated to the laboratory setting. In other words, the adaptation night served to ensure that their sleep architecture in the laboratory would resemble their natural sleep architecture as closely as possible. Many previous studies have shown evidence of the first-night effect, where polysomnographic recordings show more awakenings and less REM sleep (Le Bon & Arpi, 2003). The adaptation night consisted of a full 8-hour period of sleep in the laboratory, and included the placement of electrodes.

During all study sessions participants were asked to refrain from daytime naps, excessive exercise, and alcohol. For the *Night* condition, participants were asked to only ingest drinks containing caffeine (coffee, Coke, energy drinks) first thing in the morning and not during the rest of the day. For the *Day* condition, participants were asked to refrain from caffeinated drinks altogether. Smoking participants were allowed to smoke conservatively (at or below their normal intake), because studies show that acute withdrawal is worse for sleep and cognitive functioning than continued smoking (Jaehne et al., 2015; Zhang et al., 2006).

Once all sessions were completed, the participants were fully debriefed about the study procedures. Each participant was shown her sleeping patterns, with explanations about the various sleep stages. Where appropriate, I briefed the participant about best practice regarding sleep hygiene. Each participant was also remunerated ZAR150 (at the time of the study, approximately US$ 11) for each of the three study sessions of the project.

Ethical Considerations

Participants were given an informed consent document to fill out before being formally enrolled in the study (Appendix B). This document ensured that participants were fully informed

about the study procedures and its risks and benefits, and provided them with the assurance that they could opt out at any stage of the study without penalty. Participants were assured that all their personal details would remain strictly confidential. They were also assured that the tests would not harm them in any way and that they would be compensated for their time.

Because participants in the trauma groups were particularly vulnerable, and this vulnerability was particularly salient during the screening/interview session when they were faced with relatively specific questions about previous exposure to traumatic events, participants were verbally assured throughout the screening that they could withdraw from the study at any point without penalty, and that they did not have to give more details than what they were comfortable with. Furthermore, participants who were struggling with PTSD or depressive symptoms were referred to appropriate clinics and clinicians in their areas. At the conclusion of the study procedures, participants in the PTSD and TE groups were provided with a list of trauma counseling centers and counselors.

All study procedures were approved by the Research Ethics Committees of the University of Cape Town's Department of Psychology and Faculty of Health Sciences (HREC 428/2013).

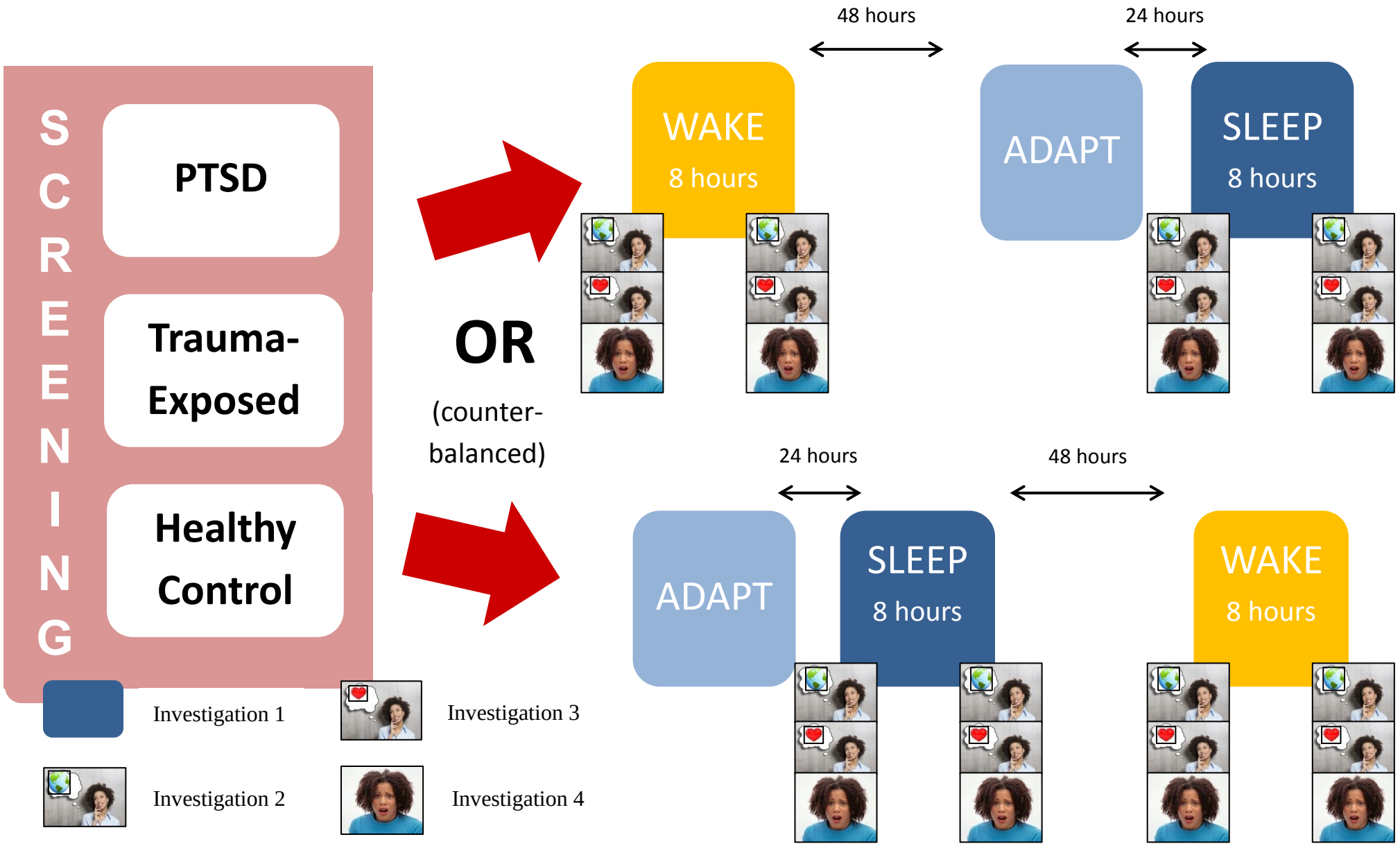

Figure 3. Procedure for the four investigations. Investigation 1: Describing sleep disruption in PTSD; Investigation 2: Neutral declarative memory processing during sleep in PTSD; Investigation 3: Emotional memory processing during sleep in PTSD; Investigation 4: emotional reactivity regulation during sleep in PTSD.

CHAPTER FOUR: INVESTIGATION 1 – DESCRIBING SLEEP DISRUPTION IN PTSD

Numerous studies, emerging from independent laboratories and using participants of various ages and different trauma histories, show that PTSD is marked by persistent subjective sleep disruption (e.g., Gehrman, Harb, Cook, Barilla, & Ross, 2015; Giosan et al., 2015; Waldrop, Back, Sensenig, & Brady, 2008). However, a separate line of literature, reporting on objective polysomnographic (PSG) studies of sleep in PTSD-diagnosed individuals in comparison with control participants, shows mixed results. Some of these studies report disruption consistent with insomnia symptoms (prolonged sleep latency, reduced sleep efficiency, increased awakenings at night; e.g., Capaldi, Guerrero, & Killgore, 2011), whereas others report evidence of sleep-stage specific disruption (increased NREM1 sleep, decreased SWS or REM sleep; e.g., Mellman, Kobayashi, Lavela, Wilson, & Hall Brown, 2014; Yetkin, Aydin, & Ozgen, 2010). Still other PSG studies report that PTSD is marked by more subtle disruptions, such as fragmentation of REM sleep (e.g., Breslau et al., 2004). Finally, some PSG studies find no evidence of sleep disruption in PTSD-diagnosed individuals in comparison with control participants (e.g., Engdahl, Eberly, Hurwitz, Mahowald, & Blake, 2000).

Meta-analytic findings examining sleep architecture suggest that sleep in PTSD is characterized by more NREM1 light sleep, less SWS, and increased REM density (Kobayashi, Boarts, & Delahanty, 2007). Kobayashi et al. (2007) did not, however, examine more subtle aspects of sleep disruption in PTSD-diagnosed individuals, such as REM fragmentation.

In trying to make sense of these disparate findings, researchers have attempted to identify, and describe the workings of, a common mechanism that may drive sleep disruption in PTSD. Several authors have suggested that the disrupted sleep commonly associated with the disorder may be related to increased autonomic activity at night in PTSD-diagnosed individuals.

Increased autonomic activity in studies of sleep in PTSD has been indexed by noradrenergic activity, heart rate variability, and self-reported symptoms of hyperarousal (Kobayashi, Lavela, & Mellman, 2014; Mellman, Kumar, Kulick-Bell, Kumar, & Nolan, 1995; van Wyk, Thomas, Solms, & Lipinska, 2016).

In this investigation, I aimed to show that sleep in PTSD-diagnosed individuals is characterized by both subjective and objective sleep disruption. By running a highly controlled study, I aimed to clarify the nature of objective sleep disruption in PTSD. That is, I aim to clarify whether sleep disruption in PTSD is characterized by (a) more general symptoms associated with insomnia, or (b) sleep-stage specific disruptions. Furthermore, I set out to investigate whether sleep in PTSD is also characterized by more subtle disruptions of PSG sleep measures, such as REM fragmentation. I also investigated whether subjective and objective sleep disruption in PTSD-diagnosed individuals is predicted by elevated autonomic activity at night, indexed by noradrenergic activity. These aims are summarised by the following hypotheses:

1. PTSD-diagnosed participants, in comparison with trauma-exposed (TE) and healthy control (HC) participants, will experience more subjectively and objectively measured sleep disruption.
    a. Objective sleep disruption in PTSD-diagnosed participants, in comparison with TE and HC participants, will be characterized by non-specific insomnia-related sleep disruption (increased sleep latency, decreased sleep efficiency, increased awakenings at night, increased time spent awake after sleep onset) and/or sleep-stage specific disruptions (increased NREM1, decreased SWS percentage, decreased REM sleep percentage, increased REM latency, fragmentation of REM sleep).
2. PTSD-diagnosed participants, in comparison with TE and HC participants, will have higher levels of noradrenergic activity at night in comparison with daytime measures.

3. In all participants, elevated nighttime noradrenergic activity will be associated with increased sleep disruption.
    a. More specifically, PTSD-diagnosed participants with elevated nighttime noradrenergic activity will have increased sleep disruption.

Overall, then, the intention here was to go beyond mere description of disrupted sleep in PTSD-diagnosed individuals; instead, I aimed to provide evidence for a mechanism that may govern sleep disruption in this clinical population.

Investigation 1, therefore, formed the platform from which I would explore other aspects of cognitive and emotional functioning as they relate to sleep in PTSD-diagnosed individuals.

Methods

Study Design

This investigation comprised of a cross-sectional quasi-experimental design. Group membership was the independent variable, and measures of subjective sleep (self-report), objective sleep (PSG), and noradrenergic activity (daytime versus nigh-time) were the outcome variables. The second aim was to investigate whether nighttime noradrenergic activity could predict measures of objective and subjective sleep. Specifically, I aimed to test the prediction that PTSD-diagnosed individuals that have elevated noradrenergic activity at night have disrupted sleep in comparison with control participants. Measures of nighttime noradrenergic activity were the predictors, while both subjective and objective measures of sleep were the outcome variables.

Experimental measures

Subjective sleep measures. The *Pittsburgh Sleep Quality Index* (PSQI; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) is a 19-item self-report questionnaire that was used to characterize subjective sleep quality. It has been used in clinical and research settings, including in South Africa (Henry, Wolf, Ross, & Thomas, 2015), and has a statistically

significant diagnostic sensitivity of 89.6% for distinguishing between individuals with healthy and poor sleep (Buysse et al., 1989). The PSQI takes approximately 10 minutes to complete. I scored the instrument following procedures recommended by the authors, and thus calculated a GlobalScore.

I also adapted the standard PSQI, which assesses sleep quality over the month prior to laboratory attendance, to assess subjective sleep quality in the laboratory so that I could compare participants' subjective sleep quality over the past month to that of their sleep quality in the laboratory. I used this approach rather than conventional sleep diaries, because the PSQI and my adapted version calculate a sleep quality score. I calculated this score using the same equations and criteria stipulated for the PSQI Global Score. This adapted PSQI (Laboratory PSQI) is presented in Appendix C.

Furthermore, I asked two additional questions related to subjective sleep quality in the laboratory: '*Did the equipment bother you?*' with options on a 4-point scale (0 = not at all; 1 = a little; 2 = quite a lot; 3 = a lot) and *'How did you sleep in the lab in comparison with your home?'* with options on a 4-point scale (0 = better; 1= same; 2 = little worse; 3 = worse). I also asked participants to qualitatively reflect on their laboratory sleep quality in comparison with their normal sleep at home and noted their responses verbatim.

Sleep laboratory equipment. PSG recordings of sleep were completed at the UCT Department of Psychology's sleep laboratory, which is equipped with two 16-channel Nihon Kohden NeuroFax EEG9000 electroencephalographs (EEG) adapted for sleep research. This equipment maps out sleep architecture and consists of EEG electrodes that measure brain activity, electrooculograph (EOG) electrodes that monitor eye movements, electromyograph (EMG) electrodes that measure muscle tone, and electrocardiograph (ECG) electrodes that measure heartbeat. These different measures are essential in identifying REM sleep, as it is not always reliably identified through brain activity measures alone (Keenan, 2009).

Our laboratory equipment meets the requirements of all the digital system regulations (such as filters on each channel), the rules for display and display manipulation (such as the ability to view the sleep data in variable time frames, from 5 seconds to 2 minutes), as well as the digital analysis specifications (such as the ability to score the data either electronically or manually).

I used a bipolar longitudinal montage, including the bipolar derivations F3-C3, C3-P3, P3-O1 and F4-C4, C4-P4, P4-O2 in combination with a referential montage using F3-A2, C3-A2, O1-A2 and F4-A1, C4-A1, O2-A1 derivations. I used a combination approach to ensure the integrity of all records. Referential montages provide excellent EEG resolution, but are susceptible to signal loss if one of the referential electrodes (A1 or A2) fails. Bipolar derivations, in contrast, do not provide as good a resolution, but are less dependent on specific electrodes. All electrodes were placed according to the international 10-20 system.

Standardized filters for recording sleep were employed for the EEG and EOG (0.5-35Hz), EMG (10-70Hz) and ECG (1-70Hz) leads to ensure integrity of the signal. The ground electrode was placed on the middle of the forehead.

Urinary normetadrenaline and metadrenaline metabolite collection. Participants were asked to collect their urine at a number of collection periods in the study to measure normetadrenaline metabolites as a measure of central nervous system noradrenergic activity. In line with another study comparing nighttime and daytime noradrenergic activity in PTSD-diagnosed individuals (Mellman et al., 1995), I asked participants to provide urine during three collection periods: midnight to 8am, 8am to 4pm and 4pm to midnight. The first collection period occurred within the *Night* condition, whereas the second and third periods occurred during the *Day* condition. During each collection period, participants voided into a receptacle and transferred their urine to the appropriately marked container holding 10ml 6M HCl preservative. During these periods, urine was kept in a small cooler box convenient to the

participant, or refrigerated in the laboratory. Within 24 hours each bottle was transferred to the local National Health Laboratory Service at Red Cross Children's Hospital where volumes for the three collections were measured, creatinine levels were recorded and aliquots obtained. The samples were then frozen at -80º for assay at a later time.

The samples were then analyzed using gas chromatography (GC) and mass spectrometry (MS). An Agilent Technology 7890A gas chromatographer and Agilent Technology 5975C mass spectrometer were used for analysis. The samples were analysed according to standard GC-MS procedures described elsewhere (Burtis, Ashwood, & Bruns, 2012). Standard quantitative urine controls were used with each batch analysis to ensure quality control. Furthermore the GC-MS was calibrated according to standardised methods for noradrenaline and adrenaline metabolite measurement. Raw values were compared to reference ranges appropriate to the participant's age.

Procedure

Night condition. Participants arrived at the UCT Sleep Sciences laboratory approximately 2 hours before their bed-time on the adaptation night and approximately 3 hours before their bed-time on the experimental night. Participants were brought from their homes to the university using a local cab service. Upon arrival on the adaptation night, each participant was briefed about the procedures for the evening and the morning. Participants were shown their rooms and provided with details about their environment, such as the use of the bathroom as well as emergency procedures should they require any assistance during the night.

Thereafter, I prepared each participant for a night's sleep while attached to the polysomnograph. More specifically, I attached the EEG electrodes to the head using EC2 paste, and the EOG, EMG, and ECG electrodes to the face and chest using stickers designed as electrodes. Once the sleep equipment was set up, I tested that all the channels were working correctly by asking the participant to perform simple actions such as blinking and biting. I

recorded the impedance to ensure that it was below 5 ohms for all channels. Participants were also reassured that they could sleep in their normal body positions. Participants were then allowed an 8-hour period of sleep, commencing within half an hour of their regular bed-time. After 8 hours, they were woken and all the PSG equipment was removed.

During the experimental night, measures related to *Investigations 2-4* were administered before bed-time (these are described in detail in the appropriate sections below). Thereafter, the procedure was identical to that of the adaptation night. However, participants were additionally briefed before bed-time about using the receptacle and marked container to collect their urine after midnight and for their first void in the morning (first collection period during the study: midnight – 8am).

In the morning, after dressing and preparing for the day, each participant completed the morning testing phase after the experimental night (once again discussed in detail within the appropriate sections below).

Day condition. No EEG measures were taken during the *Day Condition.* During this condition, I asked participants to provide urine samples during 2 collection periods between 8am and 4pm, and the second collection period was between 4pm and midnight..

At 8am, participants completed some procedures related to *Investigations 2-4*. Once they had completed these procedures, they were free to carry on with their daily activities for 8 hours until the afternoon session related to *Investigations 2-4*. During this 8-hour time interval, they were instructed to collect their urine in the first container (the one marked 8am-4pm). They were also instructed that at 4pm they should begin using the second container (i.e., that marked 4pm – midnight). During the afternoon session, I collected the first container from participants and stored it in a refrigerator. Once participants completed the second session, they went home with the cooler box, temporary receptacle, and 4pm-midnight container. They were instructed to void each time into the container until they went to bed or until midnight, whichever came first. They

were also asked to store the container in the cooler box. In the morning, I travelled to the participant's home and collected the container before transporting it to the National Health Laboratory Service for processing.

Statistical Analysis

Before statistical analyses were conducted on sleep variables, I, together with other members of the UCT Sleep Sciences research team, scored the data according to the criteria based on Rechtschaffen and Kales (1968), but recently updated in the latest version of the American Academy of Sleep Medicine's scoring manual (Berry et al., 2016). UCT Sleep Sciences members are trained in sleep scoring to international standards in accordance with the AASM. All record names and identification numbers were recoded by a colleague not involved in the scoring process. Sleep records were therefore scored blind to the group allocation of each participant. Inter-rater reliability was established at 85-95%. In addition to the standard scoring of sleep stages and arousals, arousals specifically arising during REM sleep were manually recorded. These arousals were recorded in two separate categories. First, all REM arousals that met the standard criteria were recorded; second, REM arousals that met the standard criteria, but resulted in NREM1 or waking, were recorded separately.

Testing hypothesis 1. Inferential statistical analyses were completed using SPSS version 23, with alpha set at .05 for all decisions regarding statistical significance. I first examined the data for deviations from normality and variance distribution. If I found any such deviations I have noted them prior to the each results description. If I found no deviations, then I proceeded with the analysis. I conducted my statistical analysis by first examining between-group differences for subjective and objective sleep variables. Regarding subjective measures of sleep, I conducted two sets of one-way ANOVAs to evaluate between-group differences in previous-month subjective sleep quality and laboratory sleep quality, respectively. These analyses had two

main aims. The first aim was to determine whether PTSD-diagnosed individuals, in comparison with TE and HC participants, report poorer subjective sleep quality in their daily lives. The second aim was to determine whether the same pattern of sleep quality, within and between groups, persisted in the laboratory. The comparison of these two analyses would reveal whether participants experience sleep in the laboratory in a similar way to their everyday experience. I also used one-way ANOVA to examine whether there were any between-group differences in how participants responded to the two additional subjective sleep quality questions ('*Did the equipment bother you?*' and *'How did you sleep in the lab in comparison with your home?'*).

To evaluate objective PSG sleep measures I carried out a series of one-way ANOVAs on the measures of sleep latency, sleep efficiency, the number of awakenings (defined as a period longer than 1.5 minutes after sleep onset), the number of spontaneous arousals (defined as a period of abrupt EEG shift during the night, usually an increase in EEG frequency, lasting at least 3 or more seconds), the number of minutes spent awake after sleep onset, NREM1 percentage, NREM 2 percentage, SWS percentage, REM percentage, REM latency, REM arousals, and REM arousals leading to NREM1 or waking. I also created a composite variable combining NREM1 percentage and SWS percentage, based on the findings by Kobayashi et al. (2007) that NREM1 and SWS disruptions are the most prominent objective sleep stage deficits in PTSD-diagnosed individuals. To create this composite variable, I transformed each participants NREM1 percentage and SWS percentage into a *z*-score, using the mean and standard deviation for each variable. Because sleep disruption is marked by *increased* NREM1 percentage and *decreased* SWS percentage, I multiplied all *z*-transformed NREM1 values by -1 so that *z*-transformed NREM1 and SWS scores could be combined. I then averaged the *z*-score calculated for NREM1 percentage and SWS percentage to form the NREM1/SWS composite for each participant.

Although it is common for PSG sleep variables to violate the assumption of normality (e.g. Chervin et al., 2006; Parker, Bliwise, Bailey, & Rye, 2005), according to Field (2009) ANOVA is robust to this violation provided there are relatively equal numbers of participants in each group and there are at least 20 degrees of freedom. Both these conditions are met in the current study, and for this reason the ANOVA statistic was retained in this analysis and elsewhere in this research where such violations would occur. Furthermore, in my Master's thesis I ran both nonparametric and ANOVA statistical analyses, and they delivered identical patterns of results (Lipinska, 2011).

Significant omnibus ANOVA results were followed up with orthogonal planned comparisons to test where significant group differences lay (Figure 4).

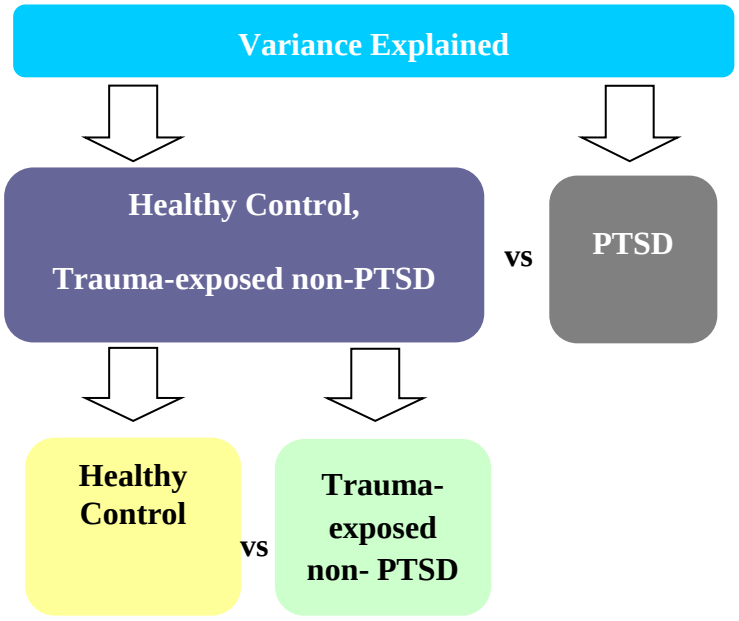

Figure 4. Schema showing the set of orthogonal planned comparisons conducted on data from the sleep outcome variables

Testing hypothesis 2. Here, I compared PTSD, TE, and HC participants with respect to daytime and nighttime measures of noradrenergic activity. Hence, I ran a 3 x 3 mixed design ANOVA, with noradrenergic collection time (midnight - 8am, 8am -4pm, 4pm – midnight) as

the repeated measure and group (PTSD, TE, and HC) as the between-subjects factor. Before I ran the analysis, I examined the data for assumptions of normality, homogeneity of variance and sphericity. If I found any such deviations I have noted them prior to the each results description. If I found no deviations, then I proceeded with the analysis.

Testing hypothesis 3. I ran a series of Spearman's correlational analyses to determine whether nighttime normetadrenaline and metadrenaline metabolites were associated with subjective and objective sleep variables. I was particularly interested in seeing whether any sleep variables on which there were significant between-group differences were correlated significantly with normetadrenaline and metadrenaline measures. Where such a correlation existed, I ran a general linear model to determine whether normetadrenaline and metadrenaline variables interacted with group membership to predict the value of the sleep variable in question.

Results

Psychiatric Characteristics of the Sample. Data from the MINI, BDI, CAPS, and clinical interview were used to characterize the psychiatric conditions, symptom presentation, counselling attendance record, and symptom severity in the PTSD and TE groups. Participants in the HC group were, by definition, free of any psychiatric disorders and free of experiences that would meet the characteristics of a DSM-IV-TR Criterion A traumatic event. Table 2 describes the psychiatric characteristics of the sample.

A few aspects of Table 2 are worth mentioning. The first is that the experimental manipulation to ensure that PTSD and TE participants differed in symptom severity, was successful. That is, PTSD-diagnosed participants had significantly greater PTSD-related symptom severity than TE participants. Second, other clinical characteristics between the PTSD and TE groups were not significantly different. These included length of time between trauma exposure and study participation, current counselling attendance, number of counselling sessions attended, and number of psychiatric diagnoses secondary to trauma. These results suggest that

these clinical characteristics do not need to be included in subsequent analyses as covariates. The only exception to this pattern in clinical characteristics between the PTSD and TE participants is related to the severity of depression.

In terms of depression severity as measured by the BDI, a one-way ANOVA detected statistically significant between-group differences. A set of post-hoc planned orthogonal contrasts first compared the average score of the PTSD group to the average score across the TE and HC groups, and then compared the average scores of TE and HC groups.

The first contrast detected a statistically significant between-group difference, with the order of means suggesting that, on average, participants in the PTSD group reported more depressive symptoms than those in the other two groups. This finding is consistent with previous research showing that more severe trauma symptoms are associated with greater depression (Weathers, Keane, & Davidson, 2001). The second contrast also detected a statistically significant between-group difference, with the order of means suggesting that, on average, participants in the TE group reported more depressive symptoms than those in the HC group. Again, this result was expected. In fact, consistent with the study's selection criteria, HC participants indicated no presence of depression.

A careful patient history and administration of the MINI revealed that most participants in the PTSD and TE groups had other DSM-IV-TR mood- and anxiety-related psychiatric diagnoses secondary to the trauma experience. Appendix D provides more details. Furthermore, participants in the trauma groups had experienced only one event of sexual assault, which was considered the index trauma.

Table 2.Psychiatric Characteristics of the Current Sample (N =60)

	Group				
	PTSD	TE	HC		
Variable	(*n* = 21)	(*n* = 19)	(*n* = 20)	*F* / t / χ^2	p
BDI-II Score	30.14 (6.26)	17.72 (7.98)	6.20 (3.41)	78.86	<.001***
Contrast 1				10.55	<.001***
Contrast 2				5.81	<.001***
CAPS Total Score	67.67 (14.12)	28.95 (11.69)		9.39	<.001***
Time Since Trauma	1.30 (1.02)	1.21 (1.07)		0.28	.78
Counselling Sessions	3.77 (2.32)	4.20 (3.49)		-0.38	.71
Number of MINI dx	2.10 (1.22)	1.37 (1.67)		1.58	.12
Current Counselling				3.48	.09
Yes	9	3			
No	12	16			

Note. Means are presented with standard deviations in parentheses. BDI-II = Beck Depression Inventory-Second Edition CAPS = Clinician-Administered PTSD Scale; Time Since Trauma = time, in years, between trauma exposure and study participation; Counselling Sessions = total number of counselling sessions attended by participants since trauma; Number of MINI dx = the number of Mini International Neuropsychiatric Inventory diagnoses. Degrees of freedom are: (2, 57) for BDI-II Score; (38) for CAPS Total Score, Time Since Trauma and Number of MINI dx; (26) for Counselling Sessions; (1) for Current Counselling. Contrast 1 compares the PTSD group to the combined TE and HC groups; Contrast 2 compares the TE and HC groups. *** $p < .001$

Testing Hypothesis 1: Between-group differences on subjective and objective sleep measures

Before testing whether PTSD-diagnosed individuals had significantly more sleep disruption than TE and HC participants, I checked to see whether there were any significant between-group differences in bed-time. Such differences may reflect circadian variance between participants, which may independently influence sleep quality. A one-way ANOVA detected no significant between-group difference in self-reported bed-time, F (2, 57) = 0.538, p = .587. Circadian variation, therefore, did not need to be accounted for in subsequent analyses.

Subjective sleep quality in PTSD. The PSQI and the Laboratory PSQI (Appendix C) characterized participants' subjective sleep quality. Whereas the PSQI assessed participants'

reports of their sleep quality over the month immediately prior to responding, the Laboratory PSQI assessed their sleep quality during the laboratory night. I ran two sets of one-way ANOVAs to determine whether (a) PTSD-diagnosed individuals, in comparison with TE and HC participants, report poor everyday subjective sleep quality, and (b) whether this pattern of self-reported sleep disruption was replicated in the sleep laboratory environment.

Before I began the analyses I tested the assumptions of normality and homogeneity of variance. PSQI data were not normally distributed. Specifically, although the data from the PTSD and TE groups were normally distributed, $D(20) = 0.96$, $p = .61$ and $D(17) = 0.92$, $p = .17$, respectively, data from the HC group were not, $D(19) = 0.79$, $p = .001$. This latter distribution was skewed to the right because most participants reported very low scores. No other assumptions related to PSQI and Laboratory PSQI were violated. Because the violation of the assumptions underlying ANOVA were mild in this case, and because ANOVA is robust to violations of normality especially under certain conditions (outlined under *Statistical Analyses, Testing hypothesis 1*), I retained the conventional ANOVA analysis.

Table 3 presents the results of the analyses examining between-group differences for PSQI and Laboratory PSQI.

The results presented in Table 3 show that, on the PSQI, PTSD-diagnosed individuals reported poorer everyday sleep quality in the last month in comparison with the combined TE and HC groups. Furthermore, according to the cut-off score associated with the PSQI (a score greater than 5 indicating sleep disruption), PTSD-diagnosed individuals had, on average, clinically significant subjective sleep disruption, with only one participant in the group demonstrating a score less than 5. There was, however, no significant difference in everyday subjective sleep quality between the TE and HC groups. TE participants had approximately equal numbers of participants falling below or above the clinical cut off score (PSQI >= 5: 10 participants; PSQI < 5: 7 participants). The majority of HC participants experienced no sleep

disruption (PSQI < 5: 15 participants) with a small minority experiencing minimal sleep disruption (PSQI = 5 or 6: 4 participants). From a clinical point of view, TE participants had some disrupted subjective sleep quality, while HC participants experienced little subjective sleep quality disruption.

The analyses detected no significant between-group differences in laboratory-based sleep quality. This result suggests that the usual pattern of subjective sleep disruption reported by PTSD-diagnosed individuals was not replicated in the laboratory.

Follow-up paired-sample t-tests, with Bonferroni adjustment, revealed that whereas TE and HC participants had approximately equivalent sleep quality on the PSQI and Laboratory PSQI, TE: $t(16) = 0.60$, $p = .56$; HC: $t(18) = 0.23$, $p = .82$, PTSD-diagnosed participants had lower Laboratory PSQI score, $t(19) = 4.06$, $p < .01$; $M_{\text{Laboratory PSQI}} = 5.29$; $M_{\text{PSQI}} = 9.65$). These results suggest that PTSD-diagnosed participants reported improved subjective sleep quality in the laboratory in comparison with their everyday home sleep quality. Appendix E lists each participant's qualitative response to the difference or similarity between their sleep quality in the laboratory versus their sleep quality at home. The most common response, in particular for PTSD-diagnosed individuals, was the feeling that the sleep laboratory environment was quieter, safer, more comfortable, and freer from distractions than the home environment.

Table 3. Subjective Sleep Quality: Descriptive statistics and between-group comparisons (N = 60)

	Group					
	PTSD	TE	HC			
Variable	(*n* = 21)	(*n* = 19)	(*n* = 20)	F/ t	p	ESE
PSQI[a]	9.65 (4.18)	5.88 (3.00)	4.16 (2.65)	13.54	< .001***	.34
Contrast 1				4.92	< .001***	1.38
Contrast 2				1.53	.13	0.61
Laboratory PSQI	5.29 (3.07)	5.26 (3.83)	4.05 (1.96)	1.09	.34	.04

Note. Means are presented with standard deviations in parentheses. For PSQI *n* = 20 for PTSD, *n* = 17 for Trauma-Exposed, and *n* = 19 for Healthy Controls due to participant error on the PSQI. Contrast 1 compares the PTSD group to the combined TE and HC groups; Contrast 2 compares the TE group to the HC group. Degrees of freedom were (2, 53) for PSQI and (2, 57) for Laboratory PSQI. ESE = effect size estimate (in this case, η^2 for *F* statistic and Cohen's *d* for *t* statistic). ****p* < .001

To further characterize participants' subjective sleep quality, with emphasis on the difference between home and laboratory sleep, I also examined between-group differences in participants' responses to two questions. Analysis of the first question ('*Did the equipment bother you?'*), revealed no significant between-group differences, F(2, 57) = 0.20, *p* = .82. This result suggests that, on average, participants across the three groups rated the contribution of the equipment to their sleep quality similarly. Furthermore, the modal response indicated that participants felt that the equipment did not bother them at all (*n* = 52: equipment did not bother them at all; *n* = 8: equipment bothered them a little). Results related to the second question (*'How did you sleep in the lab in comparison with your home?'*), also showed no significant between-group differences, *F*(2, 54) = 2.09, *p* = .13. On average, participants across the three groups compared home and laboratory sleep quality similarly. Furthermore, the modal rating indicated that approximately equal numbers of participants felt that they slept either better or the same in the laboratory in comparison with their home environment (*n* = 26: slept better in the laboratory; *n* = 25: slept the same in the laboratory as at home; *n* = 6: slept a little worse in the laboratory).

In summary, these results provide confirmation for Hypothesis 1: In this sample, PTSD-diagnosed individuals reported poorer subjective sleep quality than TE and HC participants. However, this pattern of everyday poor subjective sleep was not replicated in the sleep laboratory for PTSD-diagnosed individuals in comparison with TE and HC participants.

Objective sleep quality in PTSD. Before analyzing the PSG sleep outcome variables, I explored the assumptions of normality and homogeneity of variance. The Shapiro-Wilk test showed that normality was violated by all variables except for NREM1 percentage (PTSD: $D(20) = 0.96$, $p = .57$; TE: $D(19) = 0.96$, $p = .50$; HC: $D(20) = 0.93$, $p = .14$). Levene's statistic revealed that all variables met the assumption of homogeneity of variance except for the number of awakenings ($F(2, 57) = 4.73$, $p = .01$), and the number of spontaneous arousals ($F(2, 57) = 5.38$, $p < .01$). I attempted various ways to normalise the data, such as log and square-root transformations, but because these violations occurred systematically in the data, most commonly in the PTSD and the TE groups, transformations tended to affect the distributions of data from the HC group adversely. There was no transformation that satisfied the assumption of normality for all variables across all three groups. Because ANOVA is robust to violations of its assumptions, and for the reasons outlined under *Statistical Analyses, Testing hypothesis 1*, I retained the ANOVA analysis.

Table 4 shows the results of the series of analyses examining between-group differences in objective sleep quality.

Table 4. Objective Sleep Quality: Descriptive Statistics and Results from Between-Group Comparisons

	Group					
	PTSD	TE	HC			
Variable	(*n* = 21)	(*n* = 19)	(*n* = 20)	F/t	p	ESE
Sleep Latency	27.93 (34.44)	15.18 (11.87)	26.75 (33.41)	1.16	.32	.04
Sleep Efficiency	84.79 (14.57)	90.87 (5.69)	87.55 (7.65)	1.77	.18	.06
Awakenings	3.57 (3.17)	2.05 (1.62)	3.45 (2.48)	2.17	.12	.07
Arousals	126.76 (63.61)	107.16 (33.54)	111.55 (31.39)	1.02	.37	.03
WASO	45.40 (58.55)	30.55 (23.26)	34.63 (23.01)	0.77	.47	.03
NREM1%	16.85 (7.08)	13.91 (4.01)	12.30 (5.32)	3.40	.04*	.11
Contrast 1[a]				2.44	.02*	0.67
Contrast 2[a]				0.88	.38	0.34
NREM2%	56.24 (8.52)	57.20 (5.83)	53.74 (6.33)	1.27	.29	.04
SWS%	8.90 (8.62)	9.27 (8.05)	14.66 (7.30)	3.25	.04*	.10
Contrast 1[b]				-2.54	.01*	0.70
Contrast 2[b]				-0.15	.88	-0.04
REM%	17.91 (5.97)	19.63 (4.22)	19.31 (4.30)	0.71	.50	.02
REM Latency	90.10 (31.13)	97.37 (58.56)	104.60 (42.61)	0.51	.60	.02
REM Arousals	20.20 (8.56)	20.68 (11.07)	21.35 (9.60)	0.07	.93	< .01
REM ➔NREM1/W	10.75 (4.33)	10.53 (6.78)	8.55 (4.45)	1.05	.36	.04
NREM1% + SWS%	-0.32 (0.84)	-0.08 (0.67)	0.41 (0.78)	4.81	.01*	.14
Contrast 1[a]				-2.36	.02*	-0.63
Contrast 2[a]				-2.10	.04*	-0.67

Note. Means are presented with standard deviations in parentheses. Awakenings = the number of awakenings after sleep onset; Arousals = the number of arousals after sleep onset; WASO = the number of minutes spent awake after sleep onset; NREM1% = NREM1 percentage; NREM2% = NREM2 percentage; SWS% = SWS percentage; REM% = REM percentage; REM ➔ NREM1/W = REM arousals leading to NREM1 or wake; NREM1% + SWS% = composite of NREM1 percentage and SWS percentage. Contrast 1[a] compares the PTSD group to the combined TE and HC groups; Contrast 2[a] compares the TE group to the HC group. Contrast 1[b] compares the HC group to the combined TE and PTSD groups; Contrast 2[b] compares the TE group to the PTSD group. Degrees of freedom were (2, 57) for all variables except REM Latency, REM Arousals and REM ➔ NREM1/W where there were (2, 56) degrees of freedom because 1 participant in the PTSD group did not achieve REM sleep. ESE = effect size estimate (in this case, η^2 for *F* statistic and Cohen's *d* for *t* statistic). *$p < .05$

These results indicate that the analyses detected few significant between-group differences in objective sleep quality. NREM1 percentage, SWS percentage and NREM1/SWS composite reached omnibus ANOVA significance. I followed up significant omnibus ANOVA results with planned orthogonal comparisons. Follow-up planned comparisons revealed that, on average, participants in the PTSD group experienced significantly more NREM1 percentage sleep than those in TE and HC groups combined. There was no significant difference in NREM1 percentage between TE and HC groups. Regarding SWS percentage, follow-up planned comparisons showed that, on average, the PTSD and TE groups combined had less SWS percentage than the HC group. However, the PTSD and TE groups did not differ significantly on this variable. Regarding the NREM1/SWS composite, planned comparisons revealed that, on average, participants in the PTSD group experienced a combination of more NREM1 sleep and less SWS percentage than those in the TE and HC groups combined. Similarly, TE participants achieved higher values of that composite variable than HC participants.

These results indicate that the most significant objectively measured sleep differences between PTSD, TE, and HC participants are related to a combination of NREM1 percentage and SWS percentage. PTSD-diagnosed individuals appear to experience a combination of increased NREM1 percentage and decreased SWS percentage relative to TE and HC participants. Similarly, TE participants experience a combination of increased NREM1 percentage and decreased SWS percentage relative to HC participants. These results are associated with effect sizes of moderate magnitude.

In summary, these results provide some confirmation for Hypothesis 1: In this sample, PTSD-diagnosed individuals, compared to TE and HC individuals, experienced some objectively measured sleep disruption. This sleep disruption was sleep-stage specific, rather than related to more general aspects of sleep architecture such as sleep latency or sleep efficiency. However, the results indicate no REM-related between-group differences.

Testing Hypothesis 2: Between-group differences in noradrenergic activity

Here I wanted to determine whether PTSD-diagnosed individuals, in comparison with TE and HC individuals, had increased noradrenergic activity at night, in comparison with daytime activity. Three participants (two in the PTSD group and one in the TE group) did not follow the correct protocol for urine collection. Consequently, their data were excluded from the analyses described in this section. To test this hypothesis, I conducted a 3 (noradrenergic collection time) x 3 (group membership) mixed-design ANOVA, with noradrenergic collection time as the repeated measure and group membership as the between-subjects factor. I began my analysis by exploring the assumption of normality. Both normetadrenaline measurements taken between midnight and 8am (*Night* condition), and 4pm and midnight (*Day condition, measurement 2*) violated the assumption of normality. I applied a square-root transformation to each of these distribution, which successfully corrected non-normality. Table 5 presents the results of the Shapiro-Wilk test performed on the square-root transformed normetadrenaline variables.

The assumptions of sphericity and homogeneity of variance were upheld throughout.

Table 5. Noradrenergic Variables: Results of the Shapiro-Wilk test of normality (N = 57)

Square-Root	Group					
Transformed	PTSD		TE		HC	
Normetadrenaline	(*n* = 19)		(*n* = 18)		(*n* = 20)	
Values	D	p	D	p	D	p
Midnight to 8am	0.97	.78	0.90	.06	0.94	.25
8am to 4pm	0.98	.89	0.96	.68	0.98	.94
4pm to Midnight	0.97	.69	0.93	.18	0.95	.40

Note: Degrees of freedom for the PTSD, TE and HC groups are 19, 18 and 20 respectively

Table 6. Normetadrenaline: Descriptive statistics and Repeated Measures and Between-Group Comparisons (N = 57)

	Group					
	PTSD	TE	HC			
Variable	(*n* = 19)	(*n* = 18)	(*n* = 20)	F	p	ESE
Normet. midnight to 8am	17.15 (4.90)	18.74 (5.46)	16.67 (4.13)			
Normet. 8am to 4pm	15.97 (3.34)	16.05 (3.37)	15.64 (3.99)			
Normet. 4pm to midnight	16.17 (7.23)	17.79 (4.58)	17.26 (3.51)			
Normet. Time				2.10	.13	.04
Group				0.78	.47	.03
Normet. Time x Group				0.39	.81	.01

Note. Means (ug/L) are presented with standard deviations in parentheses. Normet. = square root transformed normetadrenaline values; Normet. Time = normetadrenaline collection time. Degrees of freedom were: Normet. Time (2, 54); Group (2, 54); Normet. Time x Group (4; 108). ESE = effect size estimate (in this case, η^2).

Table 6 presents the results of the ANOVA. As the Table shows, the analysis detected no significant main effects of noradrenergic collection time, no significant main effects of group, and no significant interaction effect. These results suggest that PTSD-diagnosed participants, in comparison to TE and HC participants, do not have nighttime specific elevations in noradrenergic activity. Hence, these analyses disconfirm Hypothesis 2.

Testing Hypothesis 3: Predicting sleep disruption in PTSD using nighttime normetadrenaline levels

Because PTSD-diagnosed participants, in comparison with TE and HC participants, did not have elevated nighttime noradrenergic levels, I did not expect nighttime noradrenergic activity to predict sleep disruption in PTSD-diagnosed individuals. However, I conducted a correlational analysis to examine whether nighttime noradrenergic activity was associated with any subjective or objective sleep variables, irrespective of group. I used the untransformed

nighttime noradrenergic values in this analysis for three reasons. First, most of the sleep variables that were to be correlated with nighttime noradrenergic values violated the assumption of normality. This means that a non-parametric correlation is more appropriate irrespective of the non-normality of normetadrenaline variables. Second, Field (2009) states that using the original data, if a non-parametric option can easily be applied, is preferable to transforming the data. Third, a non-parametric correlation statistic (Spearman's *rho*) is readily available.

Table 7 presents the resulting correlation matrix. As can be seen, the analyses detected no significant associations between nighttime noradrenergic activity and either subjective or objective sleep outcome variables, thus disconfirming Hypothesis 3. Hence, I did not run a general linear model exploring the contribution of noradrenergic activity to sleep disruption.

Table 7. Correlation Matrix: Associations (Spearman's rho) between night-time normetadrenaline and sleep variables (N = 60)

Variable	Normet. 12am-8am Correlation	Normet. 12am-8am p
PSQI	-0.10	.48
Laboratory PSQI	-0.11	.67
Sleep Latency	0.03	.84
Sleep Efficiency	0.18	.17
WASO	-0.23	.08
Number of awakenings	-0.9	.51
Number of spontaneous arousals	-0.08	.57
NREM1 percentage	-0.05	.68
NREM2 percentage	0.20	.13
SWS percentage	-0.07	.58
REM percentage	-0.02	.89
REM latency	-0.04	.78
REM arousals	0.07	.62
REM → NREM1/W	0.09	.51
NREM1/SWS composite	-0.06	.65

Note. Normet. 12am-8am = Normetadrenaline measurement taken between midnight and 8am; PSQI = Pittsburgh Sleep Quality Index; WASO = the number of minutes spent awake after sleep onset; REM → NREM1/W = REM arousals leading to NREM1 or wake.

Secondary Analyses: Relationship between subjective and objective measures of sleep

Analyses of between-group differences related to subjective measures of sleep revealed that PTSD-diagnosed participants experienced significant everyday sleep disruption in comparison to TE and HC participants. However, this pattern of subjective sleep disruption was not replicated in the laboratory, with PTSD-diagnosed participants reporting only very mild difficulties with sleep in that environment. Furthermore, PTSD-diagnosed participants experienced, relative to TE and HC participants, some but not substantial objective sleep disruption in the laboratory. Taken together, these results suggest that sleep measured in the laboratory (whether that measure is objective or subjective) is different than that measured in the

home. Furthermore, the results suggest that PTSD-diagnosed individuals, specifically, experienced improved sleep quality in the laboratory relative to their home environment.

To follow up on this observed pattern of results, I correlated (a) everyday subjective sleep quality with objective measures of sleep, and (b) laboratory subjective sleep quality with objective measures of sleep. I ran these correlations for the entire sample, and for each group separately. Table 8 presents the correlation matrices.

These results show that although there was some association between everyday subjective sleep quality and objective sleep measures (for example, PSQI was correlated with (i) REM percentage for all participants, and (ii) REM latency for HC participants), the most prominent associations were between laboratory subjective sleep quality and various objective measures of sleep in the laboratory. Regarding correlations within the entire sample, analyses suggested that poorer laboratory subjective sleep quality was associated with lower sleep efficiency, increased awakenings, increased NREM 1 percentage and a combination of less SWS percentage and more NREM 1 percentage (medium-strength correlations). These results demonstrate that subjective reports of sleep in the laboratory were congruent with objective measures of sleep in the laboratory. Furthermore, the Laboratory PSQI measure contained items asking about overall sleep quality and awakenings, which may be likened to objective measures of sleep efficiency and the number of objective awakenings – the specific PSG measures that were part of significant correlations. This set of results further highlights the congruence between self-reported laboratory sleep quality and objective measures of sleep in the laboratory.

Regarding within-group correlations between subjective and objective sleep measures, PTSD-diagnosed participants had the largest number of significant associations. Within that group, poorer laboratory subjective sleep quality was associated with less sleep efficiency, more time spent awake after sleep onset, and more frequent awakenings (medium-to-large correlations). Within the TE group, the analysis detected no significant correlations between

subjective and objective sleep measures. Within the HC group, individuals with poorer laboratory subjective sleep quality took longer to fall asleep and had decreased sleep efficiency (large correlations).

Together, these results suggest that when one desires a subjective representation of objective sleep, a specific laboratory measure of subjective sleep quality is more appropriate than an everyday measure. The results also strengthen the findings that demonstrated that PTSD-diagnosed individuals experienced relatively improved sleep quality in the laboratory, whereas participants in the other groups did not. Not only did PTSD-diagnosed individuals report that their sleep was improved in the laboratory in comparison with their everyday sleep (described earlier), but objective sleep measures were congruent with their subjective sleep quality in the laboratory. Because objective measures of sleep in PTSD-diagnosed individuals showed some, but relatively little, sleep disruption, and there is congruency between subjective and objective measures of sleep in this clinical group, it is likely that PTSD-diagnosed individuals did experience some improvement in their sleep quality in the laboratory.

Table 8. Correlation Matrix: Associations (Spearman's rho) between subjective and objective sleep measures (N = 60)

	Entire sample (*N* = 60)				Group											
					PTSD (*n* = 60)				TE (*n* = 60)				HC (*n* = 60)			
	PSQI		Lab. PSQI		PSQI		Lab. PSQI		PSQI		Lab. PSQI		PSQI		Lab. PSQI	
Objective Sleep Variable	rho	p	rho	p	rho	p	rho	p	rho	p	rho	p	rho	p	rho	p
Sleep Latency	-0.02	.88	0.22	.08	-0.58	.81	0.22	.34	0.05	.86	0.12	.62	-0.15	.55	0.54	**.01***
Sleep Efficiency	-0.08	.54	-0.43	**< .01****	0.04	.88	-0.53	**.01***	-0.26	.31	-0.44	.06	0.16	.53	-0.53	**.02***
WASO	0.11	.41	0.35	**< .01****	0.04	.88	0.49	**.03***	0.25	.33	0.39	.10	-0.18	.45	0.03	.90
No. awakenings	0.05	.72	0.25	.06	0.17	.48	0.45	**.04***	-0.09	.74	0.19	.45	-0.32	.18	0.17	.48
No. spontaneous arousals	0.01	.94	-0.05	.70	-0.13	.59	-0.17	.47	-0.34	.19	-0.01	.99	0.04	.88	0.12	.61
NREM1 percentage	0.21	.12	0.32	**.01***	0.18	.44	0.35	.12	-0.09	.73	0.17	.49	-0.26	.28	0.44	.06
NREM2 percentage	-0.03	.83	0.10	.45	-0.29	.22	0.16	.49	0.12	.66	-0.01	.99	0.07	.78	-0.18	.94
SWS percentage	0.06	.65	-0.17	.20	0.44	.06	-0.15	.51	-0.06	.83	-0.04	.87	0.31	.19	-0.19	.41
REM percentage	-0.32	**.02***	-0.24	.07	-0.42	.07	-0.40	.07	0.04	.89	-0.09	.73	-0.32	.18	-0.19	.42
REM latency	0.04	.79	0.11	.41	0.13	.59	0.18	.45	-0.18	.50	0.10	.68	0.61	**< .01****	0.16	.51
REM arousals	-0.24	.08	-0.19	.14	-0.21	.38	-0.28	.23	-0.44	.08	-0.23	.34	-0.20	.42	-0.01	.99
REM → NREM1/W	-0.05	.72	-0.08	.54	0.10	.69	-0.20	.40	-0.39	.12	-0.12	.62	-0.35	.15	0.01	.97
NREM1/SWS composite	-0.09	.53	-0.28	**.03***	0.15	.53	-0.35	.13	0.04	.88	-0.06	.81	0.33	.17	-0.37	.11

Note. PSQI = Pittsburgh Sleep Quality Index; Lab. PSQI = Laboratory PSQI; WASO = the number of minutes spent awake after sleep onset; REM → NREM1/W = REM arousals leading to NREM1 or wake. For PSQI *n* = 20 for PTSD, *n* = 17 for TE, and *n* = 19 for HC due to participant error on the PSQI. *$p < .05$.**$p < .01$.

Summary of results. The results of this investigation suggest, first, that PTSD-diagnosed individuals report poorer everyday subjective sleep quality than TE and HC individuals. This pattern of poorer subjective sleep in PTSD was not replicated in the sleep laboratory, however. Furthermore, the analyses detected no between-group differences in subjective sleep quality in the laboratory, and revealed that almost half of the sample rated their sleep as better in the laboratory than in their homes. An analysis of objective measures of sleep revealed few between-group differences. Perhaps the most prominent of the differences that were detected was that PTSD-diagnosed individuals participants, in comparison with participants in the other two groups, experienced a combination of more NREM1 light sleep and less SWS percentage. None of these between-group differences could be accounted for by increased nighttime noradrenergic activity in PTSD-diagnosed individuals, however.

A secondary analysis revealed that there was congruency between objective sleep measures and laboratory subjective sleep quality, but that everyday subjective sleep quality was not prominently correlated with objective sleep measures. This pattern of associations was especially strong for PTSD-diagnosed participants, and highlighted that, considering their mild objective sleep disruptions, this group of individuals likely experienced improved sleep quality in the laboratory.

CHAPTER FIVE: INVESTIGATION 2 – NEUTRAL DECLARATIVE MEMORY PROCESSING DURING SLEEP IN PTSD

Many studies have documented that PTSD-diagnosed individuals experience deficits in neutral declarative memory (Brewin, Kleiner, Vasterling, & Field, 2007; Johnsen & Asbjornsen, 2008; Scott et al., 2015). Alongside these deficits in cognition, several studies have demonstrated that particular neuroanatomical characteristics of PTSD may, at least in part, explain these memory deficits. These neuroanatomical characteristics include decreased hippocampal volume and a pattern of hippocampal activation that is different from control participants (Geuze, Vermetten, Ruf, de Kloet, & Westenberg, 2008; Woon, Sood, & Hedges, 2010). However, the literature is equivocal as to whether there is a consistent association between deficits in neutral declarative memory and decreased hippocampal volume in PTSD. Some studies find no association between neutral declarative memory performance and hippocampal volume; that is to say, those PTSD-diagnosed individuals who have smaller hippocampi do not necessarily perform poorly on memory tasks (Woodward et al., 2009).

Another reason why poor declarative memory within the disorder may not be wholly accounted for by decreased hippocampal volume is that PTSD-diagnosed individuals exhibit a pattern of neutral declarative memory impairment that is not completely consistent with hippocampal dysfunction. Memory impairments in PTSD are characterised by deficits in immediate and delayed recall, but not by retention difficulties (Johnsen & Asbjornsen, 2008). That is, PTSD-diagnosed individuals do not lose more information over time than what might be expected ordinarily. Because information retention over time is considered to be heavily reliant on

hippocampal function, this pattern of deficit is not completely consistent with hippocampal dysfunction (Samuelson, 2011).

Hence, purely anatomical explanations for the neutral declarative memory deficits that are characteristic of PTSD do not seem sufficient. Few studies have, however, considered alternative mechanisms, and even fewer have considered whether, or to what extent, poor sleep may account for these deficits. Considering the importance of healthy sleep for intact memory consolidation, and therefore memory retention, it is plausible to investigate whether the widely-reported sleep difficulties in PTSD impact on nighttime memory consolidation in this clinical population. In *Investigation 1*, I showed that PTSD-diagnosed individuals had poorer subjective sleep quality and more NREM 1 percentage (light sleep) than HC participants. I also showed that PTSD-diagnosed participants had a combination of more NREM 1 percentage and less SWS percentage than both HC and TE participants, and that TE participants showed the same pattern of results in comparison to HC participants. Because SWS is robustly implicated in intact memory consolidation (Diekelmann & Born, 2010; Marshall, Helgadottir, Molle, & Born, 2006), here I investigated whether the observed sleep disruption in PTSD-diagnosed individuals altered nighttime memory consolidation. Broadly these aims are summarised by the following hypotheses:

1. PTSD-diagnosed participants, in comparison with TE and HC participants, will have neutral declarative memory deficits in immediate and delayed recall during the day, and neutral declarative memory deficits in retention (a measure of memory consolidation) across the night.
2. In all participants, sleep disruption will be associated with deficits in neutral declarative memory retention after a sleep-filled delay.
    a. More specifically, PTSD-diagnosed participants with sleep disruption will have decreased neutral declarative memory retention after a sleep-filled delay.

Methods

Study Design

This investigation also comprised of a cross-sectional quasi-experimental design. First, I aimed to show that although daytime measures of neutral declarative memory in PTSD-diagnosed individuals are characterized by deficits in immediate and delayed recall, nighttime measures are characterised by deficits in memory consolidation (as indexed by retention measures, i.e., the comparison of scores on immediate and delayed recall trials). Group status (PTSD, TE and HC membership) was the independent or predictor variable. Scores on immediate and delayed recall trials, as well as retention measures of neutral declarative memory across the *Night* or *Day* conditions, were the dependent or outcome variables.

Second, I aimed to demonstrate that the observed memory deficits are correlated with and predicted by sleep-related measures. Here, sleep variables (specifically those sleep variables that showed between-group differences in *Investigation 1* and those that were associated with memory consolidation in previous research) were the predictor variables. A measure of the amount of neutral declarative information retained across a sleep-filled delay (referred to as *Night* condition memory retention) was the outcome variable. I was specifically interested in *Night* condition memory retention because it represents the information that undergoes consolidation during the defined period (i.e. across a period of sleep).

Experimental Measures

Neutral declarative memory. I measured neutral declarative memory using three different measures. A number of studies investigating sleep-dependent memory consolidation in healthy individuals have shown contrasting results, perhaps because of cross-study differences in measures (Conte & Ficca, 2013). By using three different tasks, I aimed to avoid results that are test-specific, and instead deliver results that are construct-specific (i.e., that examine neutral declarative memory performance).

The *Logical Memory* (LM) subtest of the Wechsler Memory Scale-Third Edition (WMS-III; The Psychological Corporation, 1998) was used as the first measure of neutral declarative memory. The WMS-III can be administered to participants aged 16-89 years. Regarding psychometric properties, it has excellent test-retest reliability, reported at .79 - .88 for LM. Furthermore, its authors report sound content and construct validity. The WMS-III subtests have been used for research purposes in the South African context (e.g., Emsley, Spangenberg, Roberts, Taljaard, & Chalton, 1993; Schoeman, Carey, & Seedat, 2009).

The LM subtest consists of two stories, each of a similar length and content. One individual story was used per condition, although in the standard WMS-III administration both stories are presented serially. The stories were counterbalanced across participants, so that one participant experienced the first story during the *Day* condition and the second story during the *Night* condition, while the next participant experienced the stories in the reverse order.

However, the procedure for administration of each story followed the conventional format outlined in the test manual. That is, after each story was read to the participant, I asked her to give an account of all the story elements that she remembered. During the delayed recall trial, participants were asked to recall everything they could remember of the stories. The stories were not presented again for the delayed recall trial.

The *Word List* (WL) subtest of the Wechsler Memory Scale-Third Edition (WMS-III; The Psychological Corporation, 1998) was used as a second measure of neutral declarative memory. This subtest has excellent test-retest reliability, reported at .79 -.80. In the standard administration, 12 words are read aloud to participants on each of 4 learning trials. Following each trial, the participant is asked to recall as many words as possible from the list. The sum of these recall occasions forms the immediate recall score. After presentation of a distractor list (balanced for word type and length with the primary list), a short-delay recall trial is administered. After a delay of 25-

35 minutes, a long-delay recall trial is administered. On each of those delayed recall trials, the participant is asked to recall, uncued, as many words from the list as possible.

In this study, I used the distractor list as a parallel form. In other words, the primary list was used in conventional form during the *Day* condition, while the distractor list replaced it during the *Night* condition in a counterbalanced way, so that one participant experienced the primary list during the *Day* condition and the distractor list during the *Night* condition, while the next participant experienced the word lists in the reverse order.

Each list was administered four times during the learning phase, consistent with standardised administration of the test. After the delay (8 hours of sleeping or of waking activity), participants were asked to recall the words without further presentation of the stimuli, also according to standardised administration.

The *Story Memory* (SM) subtest of the Wide Range Assessment of Memory and Learning (WRAML-II; Sheslow & Adams, 2003) was used as a third measure of neutral declarative memory. The WRAML-II can be administered to participants aged 5-90 years old. Regarding psychometric properties, it has good test-retest reliability, reported at .75 for the SM subtest. Furthermore, its authors report sound content and construct validity. The WRAML-II subtests have been used for research purposes in other low- and middle-income countries (e.g., Ezeamama et al., 2012).

This subtest is comprised of two stories, which during the standard administration are presented consecutively. In contrast to this standard administration, but similarly to the way the LM subtest was administered here, one story was presented during the *Day* condition while the other story was presented during the *Night* condition. This was done in a counterbalanced way, so that one participant experienced the first story during the *Day* condition and the second story during the *Night* condition, while the next participant experienced the stories in the reverse order.

I administered each story according to the standardised procedure described in the manual. That is, after I read each story to the participant, I asked her to give an account of all the story

elements that she remembered. During the delayed recall trial, participants had to recall, uncued, everything they could remember of the story.

Procedure

Figure 5 presents the procedure specific to this investigation. (The procedure of the whole study is presented in Figure 3.)

Night condition. Prior to sleep on the experimental night (*Night* condition), I tested neutral declarative memory. I first administered the LM subtest, then the WL subtest, and finally the SM subtest. After each trial of each subtest I recorded the free-recall responses of each participant. For each subtest, the sum of these responses constituted the immediate recall score. Participants were explicitly asked to remember the material for further testing upon waking. After all evening procedures were complete, participants slept for 8 hours.

In the morning, I administered the delayed recall version of each of the LM, WL, and SM subtests, in that order. For each subtest, the number of words/story elements recalled constituted the delayed recall score.

Day condition. Participants were administered the parallel forms of the LM, WL, and SM subtests, in that order. Administration of the immediate and delayed recall phases was identical to that described above for the *Night* condition, except that the immediate and delayed recall phases were separated by 8 hours of waking instead of 8 hours of sleep. During the 8-hour waking interval participants could carry on with their daily activities but were reminded not to nap, drink caffeinated or sugary drinks, or exercise excessively.

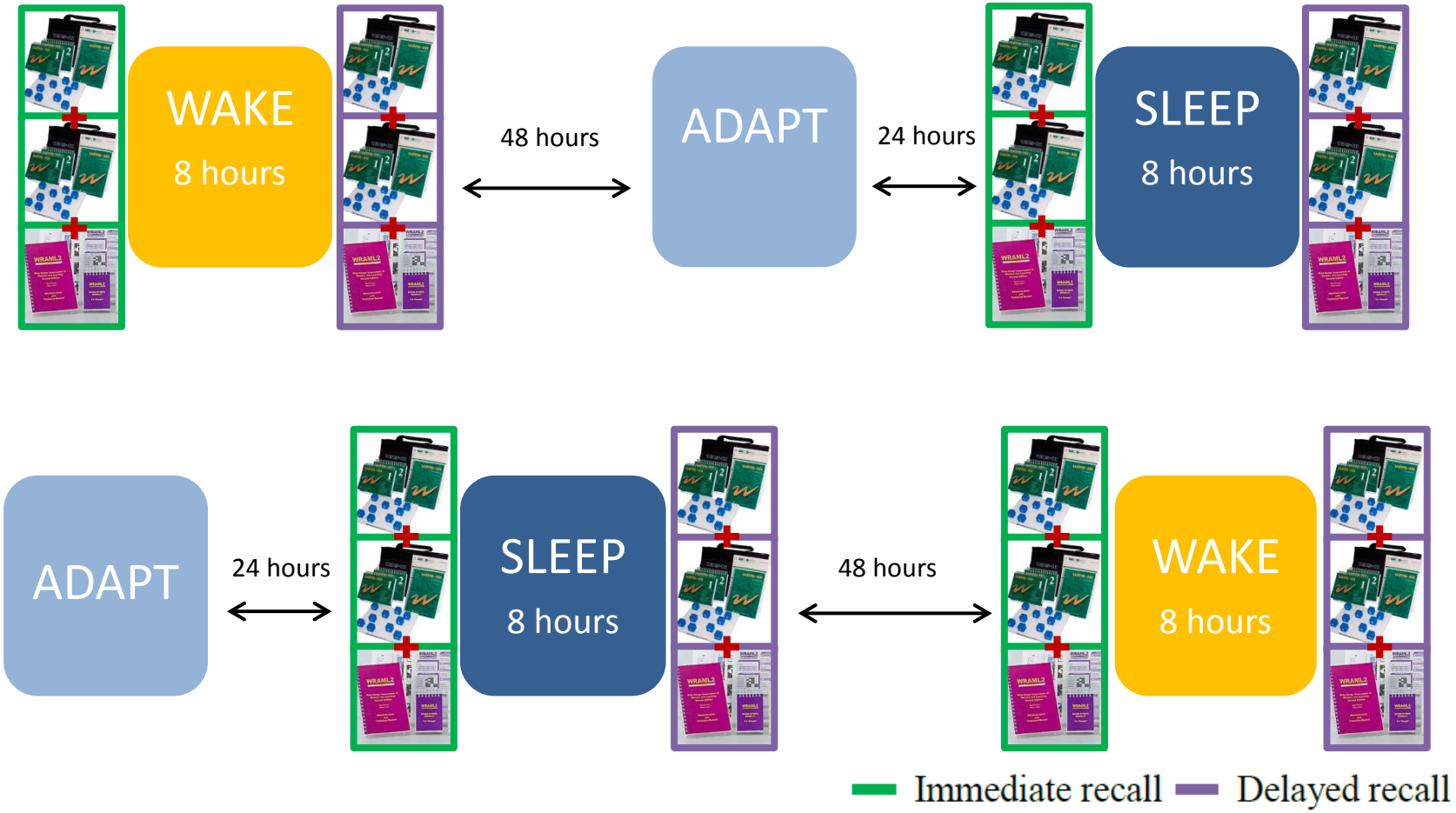

Figure 5. Study procedure for Investigation 2. Participants either completed (a) or (b) in a counterbalanced design

Statistical Analysis

The three subtests yielded measures of immediate and delayed recall, as described above. To create a retention score for each subtest, I divided the delayed recall score by the immediate recall score and expressed this value as a percentage (i.e., the retention score reflected the percentage of initially-learned information recalled after a delay).

Because I used three different measures that tested the same construct (neutral declarative memory), I combined the results of the three measures into three composite scores: one for immediate recall, one for delayed recall, and one for retention. So, for instance, to create the immediate recall composite score, for each of the LM, WL, and SM subtests I transformed each participant's raw score into a *z*-score, and then averaged the *z*-scores to form one composite score for immediate recall. Composites for delayed recall and retention were created similarly.

Testing hypothesis 1. Because I wanted to specifically contrast immediate recall, delayed recall, and retention composite outcome measures for each of the *Night* and *Day* conditions, I used a multivariate statistic. I analysed the *Night* and *Day* conditions respectively using MANOVA. Group membership (PTSD, TE, or HC) was the between-subjects factor, while immediate recall, delayed recall, and retention composites formed the multivariate outcome variables for each of the *Day* and *Night* conditions. Before I began these analyses I first examined the composite variables for deviations from normality and variance distribution. I also tested for MANOVA's assumption of equality of covariance matrices. If I found any violations of the underlying assumptions governing MANOVA I have noted them prior to the each results description. If I found no deviations, then I proceeded with the analysis.

Testing hypothesis 2. Here, I wanted to determine whether sleep disruption in PTSD-diagnosed individuals was associated with deficits in the amount of neutral declarative information that was retained across a period of sleep (*Night* condition memory retention). I used this specific measure because it represents the information that is consolidated during the defined

period. First, I correlated sleep variables on which there were between-group differences in *Investigation 1,* or that were empirically associated with memory consolidation, with the *Night* condition memory retention composite. I then ran a series of general linear models to explore whether those sleep variables that correlated with the *Night* condition memory retention composite predicted *Night* condition memory retention. I was particularly interested in determining whether these sleep variables interacted with group membership to predict the amount of neutral declarative information that was retained across a period of sleep.

Results

Table 9 shows the means and standard deviations for scores on the immediate and delayed recall trials, and for the retention score, of all three memory tests (LM, WL, SM), for both the *Night* and *Day* condition, within each of the three groups.

Table 9.Neutral Declarative Memory: Descriptive statistics for LM, WL, SM tasks

	Condition					
	Night			Day		
	PTSD	TE	HC	PTSD	TE	HC
Variable	(*n* = 21)	(*n* = 19)	(*n* = 20)	(*n* = 21)	(*n* = 19)	(*n* = 20)
LM						
Immediate Recall	23.90 (11.80)	25.79 (8.18)	25.00 (9.61)	18.67 (6.95)	26.05 (11.11)	27.45 (9.58)
Delayed Recall	10.19 (5.48)	12.26 (4.52)	13.50 (3.95)	8.29 (3.84)	11.84 (6.12)	12.85 (5.20)
Retention	70.06 (19.74)	78.93 (14.78)	86.18 (11.79)	66.21 (18.75)	76.96 (24.58)	77.13 (20.09)
WL						
Immediate Recall	30.05 (6.58)	32.16 (5.23)	33.75 (3.46)	28.95 (5.17)	32.68 (5.14)	31.25 (4.52)
Delayed Recall	5.91 (2.28)	6.42 (2.61)	8.00 (2.13)	4.71 (1.76)	5.68 (2.79)	5.95 (2.06)
Retention	63.33 (18.49)	65.00 (21.21)	75.36 (18.55)	53.91 (22.56)	54.70 (23.96)	62.03 (19.94)
SM						
Immediate Recall	12.81 (7.67)	17.79 (9.24)	17.25 (7.00)	13.71 (7.98)	17.47 (6.92)	17.35 (7.05)
Delayed Recall	9.71 (7.77)	14.32 (8.07)	14.80 (6.72)	9.81 (7.54)	13.84 (6.64)	12.60 (7.07)
Retention	68.32 (32.52)	78.82 (11.69)	83.05 (20.17)	67.76 (33.84)	75.35 (24.83)	70.97 (22.54)

Note. Means are presented with standard deviations in parentheses. LM = Logical Memory task of the Wechsler Memory Scale-Third Edition; WL = Word List task of the Wechsler Memory Scale-Third Edition; SM = Story Memory task of the Wide Range Assessment of Memory and Learning.

Examining the circadian confound with respect to immediate and delayed recall. Before I began examining between-group differences in neutral declarative memory performance, I first checked whether there were significant circadian differences in immediate and delayed recall scores across the *Night* and *Day* condition. Such circadian differences (i.e., differences based solely on the time of day the neutral declarative memory measurement was taken) represent a potential confound to future analyses in this investigation.

I ran a 2 (condition) x 3 (group membership) mixed design ANOVA related to the immediate and delayed recall composites. There were no differences in immediate recall across the *Night* and *Day* condition for all participants, or when taking group membership into account, $F(1, 57) = <0.01$, $p = .95$ and $F(1, 57) = 0.90$, $p = .41$ respectively. There were also no differences in delayed recall across the *Night* and *Day* condition for all participants, or when taking group membership into account, $F(1, 57) = <0.01$, $p = .98$ and $F(1, 57) = 0.73$, $p = .49$ respectively. This set of results suggests that circadian differences are unlikely to confound further analyses.

Testing hypothesis 1: Between-group differences in neutral declarative memory performance. I tested the MANOVA assumption of equality of covariance matrices using Box's test. For the *Day* condition, the assumption of equality of covariance matrices was met, but for the *Night* condition it was not. I therefore applied a square root transformation to the three composite measures related to the *Night* condition. This transformation was successful. There were no other violations of the parametric assumptions of normality or homogeneity of variance.

Table 10 shows the results of the MANOVAs for the *Night* and *Day* condition. Figures 6 and Figure 7 show the results of the follow-up univariate ANOVAs and contrasts for the *Night* and *Day* condition. Regarding the *Night* condition, the MANOVA detected significant between-group differences across the set of dependent variables. Follow-up univariate ANOVA revealed there were significant between-group differences with respect to delayed recall and retention, but

not immediate recall. Planned post-hoc contrast analyses detected, for both delayed recall and retention, significant differences between the PTSD and HC groups. Specifically, data for the delayed recall composite suggested that PTSD-diagnosed individuals remembered significantly less information after a period of sleep than did HC participants. Similarly, data for the retention composite suggested that PTSD-diagnosed individuals, relative to HC participants, retained significantly less information over the sleep period taking into account how much they had originally learnt. Contrast analyses detected no significant differences between the PTSD and TE groups, or between the TE and HC groups, for either the delayed recall or retention composite variables.

Regarding the *Day* condition, the MANOVA also detected significant between-group differences across the set of dependent variables. Follow-up univariate ANOVA revealed t there were significant between-group differences with respect to immediate and delayed recall, but not retention. Planned post-hoc contrast analyses detected, for both immediate recall and delayed recall, significant differences between the PTSD and HC groups. Specifically, data for the immediate recall composite suggested that PTSD-diagnosed individuals remembered significantly less information directly after the learning trials than did HC participants. Similarly, data for the delayed recall composite suggested that PTSD-diagnosed individuals remembered significantly less information after a period of wakefulness than did HC participants. Contrast analyses also detected significant differences between the PTSD and TE participants for both the immediate and delayed recall composite variables, indicating that PTSD-diagnosed participants recalled less information than TE participants on each trial. There were no significant differences between the TE and HC groups with respect to immediate or delayed recall.

Taken together, these results suggest that PTSD-diagnosed individuals, in comparison with healthy controls, experience different kinds of neutral declarative memory deficits across the night and day. Although it is unclear why PTSD-diagnosed individuals did not exhibit

deficits in immediate recall related to the *Night* condition (especially since prior analyses did not indicate circadian differences with respect to immediate recall), their pattern of memory deficits across a night of sleep was characterised by impaired performance on measures of delayed recall and retention. However across a period of waking PTSD-diagnosed individuals demonstrate impaired performance on measures of immediate and delayed recall.

Table 10. Neutral Declarative Memory across the Night and Day Conditions (N = 60)

	Condition											
	Night						Day					
Variable	PTSD (*n* = 21)	TE (*n* = 19)	HC (*n* = 20)	F/MD	p	ESE	PTSD (*n* = 21)	TE (*n* = 19)	HC (*n* = 20)	F/MD	p	ESE
Multivariate analysis[a]				3.85	.01*	.18				3.07	.04*	.14
IR Composite	1.32 (0.34)	1.42 (0.32)	1.46 (0.23)	1.12	.34	.04	1.59 (0.70)	2.25 (0.94)	2.20 (0.75)	4.32	.02*	.13
Contrast 1				-0.14	.16	-0.48				-0.61	.02*	-0.84
Contrast 2				-1.39	.17	-0.30				-2.54	.02*	-0.80
Contrast 3				-0.3	.73	-0.14				-0.05	.84	0.06
DR Composite	1.30 (0.29)	1.40 (0.28)	1.52 (0.22)	3.39	.04*	.11	1.63 (0.60)	2.18 (0.88)	2.22 (0.68)	4.30	.02*	.13
Contrast 1				-0.22	.01*	-0.85				-0.59	.01*	-0.92
Contrast 2				-1.55	.13	-0.28				-2.34	.03*	-0.74
Contrast 3				-0.12	.17	-0.48				-0.04	.85	-0.05
Retention Composite	1.34 (0.23)	1.40 (0.17)	1.53 (0.22)	3.96	.03*	.13	1.81 (0.71)	2.10 (0.67)	2.13 (0.64)	1.52	.23	.05
Contrast 1				-0.18	< 0.01**	-0.84				-0.32	.11	-0.47
Contrast 2				-1.55	.13	-0.24				-1.25	.22	-0.42
Contrast 3				-0.12	0.07	-0.66				-0.05	.81	-0.05

Note. Means are presented with standard deviations in parentheses. MD = mean difference; ESE = effect size estimate (for ANOVA, η^2; for follow-up contrast analyses, Cohen's *d*); IR = Immediate recall; DR = Delayed recall. Contrast 1: PTSD vs HC; Contrast 2: PTSD vs TE; Contrast 3: TE vs HC. Degrees of freedom were: MANOVA analysis (3, 56); ANOVA analysis (2, 57).

[a]MANOVA Roy's Largest Root, appropriate for small samples, is presented. *$p < .05$. **$p < .01$.

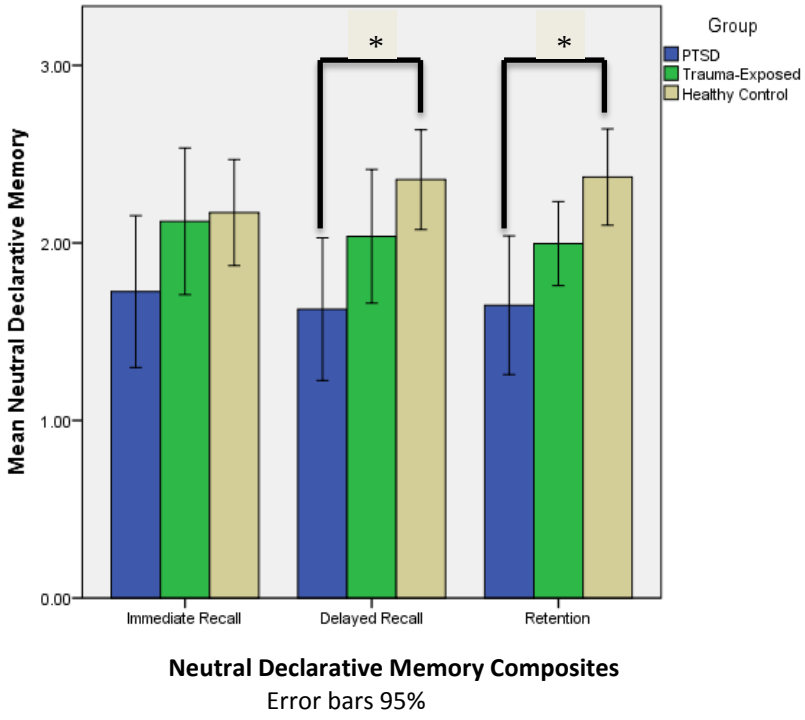

Figure 6. Night condition: Between-group differences in neutral declarative memory performance. Error bars represent the 95% confidence interval. *p < .05.

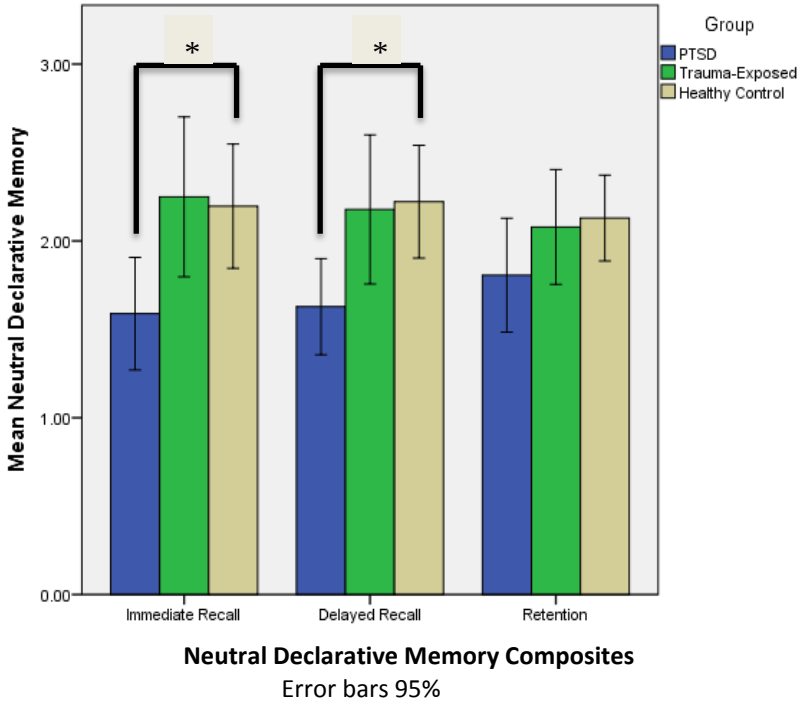

Figure 7. Day condition: Between-group difference in neutral declarative memory performance. Error bars represent the 95% confidence interval. *p < .05.

Testing hypothesis 2: Do sleep variables predict information retention across a period of sleep in PTSD? To examine the relationship between retention of neutral declarative information across a period of sleep and sleep variables, I first correlated participants' *Night* condition retention scores (using the retention composite variable) with subjective and objective measures of sleep. Subjective measures of sleep included the PSQI and Laboratory PSQI. Objective measures of sleep included the variables in *Investigation 1* that demonstrated significant between-group differences, and variables empirically associated with memory consolidation. Hence, the objective sleep variables included in the analyses were NREM 1 percentage, SWS percentage, NREM 1/SWS composite, REM percentage, REM latency, REM arousals, and REM arousals that lead to NREM 1 or waking. Furthermore, I also correlated participants' BDI-II scores with the *Night* condition retention composite, because participants in the PTSD and TE groups were not matched on depression severity.

Table 11 shows the results of the correlations examining associations between the *Night* condition retention composite, sleep variables, and depression severity. The analyses detected no significant correlations between the *Night* condition memory retention composite and subjective measures of sleep. In contrast, several objective measures of sleep correlated well with the *Night* condition memory retention composite. Specifically, analyses detected:

(1) A moderate negative correlation between retention and NREM 1 percentage. This result suggests that a higher NREM 1 percentage was associated with poorer retention of neutral declarative information across the sleep-filled delay.

(2) Small negative correlations between retention and REM arousals, and between retention and REM arousals that lead to NREM 1 or waking. These results suggest that increases in both kinds of REM arousals was associated with poorer retention of neutral declarative information across the sleep-filled delay.

(3) A small positive correlation between retention and NREM 1/SWS composite. This result suggests that a combination of decreased NREM 1 percentage and increased SWS percentage was associated with poorer retention of neutral declarative information across the sleep-filled delay.

(4) A moderate negative correlation between retention and BDI-II scores. This result suggests increasing severity of depression was associated with poorer retention of neutral declarative information across the sleep-filled delay.

In summary, these results indicate that both disrupted sleep (objectively measured) and depression severity are associated with impairments in retention of neutral declarative information across a period of sleep.

Table 11. Correlations between Night condition memory retention composite, Subjective and Objective Sleep Variables, and Depression Severity (N = 60)

Variable	PSQI	Laboratory PSQI	NREM 1%	SWS%	REM%	REM Latency	REM Arousals	REM ➔ NREM 1/W	NREM 1 + SWS	BDI-II
Retention Composite										
rho	-0.16	0.11	-0.31**	0.16	-0.16	0.08	-0.22*	-0.24*	0.29*	-0.40**

Note. Retention Composite = composite of nighttime three neutral declarative memory measures of retention related to the Night condition; *rho* = Spearman's *rho*; PSQI = Pittsburgh Sleep Quality Index; REM ➔ NREM 1/W = REM arousals leading to NREM 1 or wake; NREM 1 + SWS = composite of NREM 1 percentage and SWS percentage; BDI-II = Beck Depression Inventory–Second Edition. *$p < .05$. **$p < .01$

As a second step in testing the hypothesis under consideration, I used general linear modelling to predict retention of neutral declarative information across the sleep-filled delay using objective sleep variables and depression severity. Regarding those sleep variables, I only included in the model those variables for which the analyses above had detected significant correlations with retention (i.e., I included only NREM 1 percentage, REM arousals, REM arousals leading to NREM 1 or waking, NREM 1/SWS composite and BDI-II). I also included group membership as a predictor, to determine whether there were any interactions between group membership and sleep variables in predicting retention. That is, I wanted to determine whether PTSD-diagnosed individuals, in comparison with TE and HC individuals, had disrupted sleep that predicted decreased retention.

To construct the models, I entered depression severity (BDI-II score) first, followed by group membership, one sleep variable (NREM 1 percentage; REM arousals leading to NREM 1 or waking; or NREM 1/SWS composite), and all two-way interactions associated with these variables. I only entered six variables or associated interactions at a time, to ensure that there was no inflation of Type I error as a result of a large number of terms in comparison with the sample size. After I had entered all the terms, I examined the model for significant contributors to the variance, as well as the overall variance explained. I removed non-contributing variables, starting with two-way interactions. I worked iteratively towards a significant model that parsimoniously explained the largest variance in retention.

The model-building process revealed that neither NREM 1 percentage nor NREM 1/SWS composite were significant predictors of variance in retention scores, either independently or in interaction with other variables. As an example, Table 12 shows the best-fit model with NREM 1/SWS composite, indicating no significant contribution of that variable.

Although the amount of REM arousals variable was a significant predictor of variance in retention scores, $F(3, 56) = 4.94$, $p = 0.03$, the associated effect size, $\eta_p^2 = 0.08$, was small. REM arousals also did not interact significantly with other variables, including group membership.

The best-fitting model was one showing that REM arousals leading to NREM 1 or waking predicted retention scores (Table 13). As the Table shows, the analysis detected a significant interaction between group membership and REM arousals leading to NREM 1 or waking. Examining the means revealed that PTSD-diagnosed individuals had more REM arousals leading to NREM 1 or waking ($M = 10.75$), followed by TE participants ($M = 10.53$), and then HC participants ($M = 8.55$). Furthermore, a correlation analysis revealed that REM fragmentation was strongly negatively correlated with neutral declarative memory retention after a sleep-filled interval in PTSD-diagnosed individuals ($r = -.50$, $p = .03$), an effect which was not demonstrated in TE ($r = -.13$, $p = .60$) and HC ($r = .17$, $p = .47$) participants. Hence, the suggestion here is that PTSD-diagnosed individuals who have relatively increased REM arousals leading to NREM 1 or waking have poorer retention of neutral declarative information across a sleep-filled delay. This result was associated with a medium to large effect size, $\eta_p^2 = .22$.

The modelling process also suggested that depression severity did not contribute significantly to variance in retention scores, either independently or in interaction with other predictors.

Table 12.General Linear Model: Predicting retention of neutral declarative information over a sleep-filled delay using variables related to sleep depth (N = 60)

	Type III SS	df	MS	F	p	ESE
Corrected model	5.67	3	1.89	4.21	< .01**	.18
Group	3.74	2	1.87	4.16	.02*	.13
NREM 1 + SWS	0.32	1	0.32	0.71	.40	.01

Note. SS = sums of squares; MS = mean square; ESE, effect size estimate (in this case, η_p^2). NREM 1 + SWS = composite of NREM 1 percentage and SWS percentage. For the overall model, $R^2 = 0.18$, adjusted $R^2 = 0.14$. *$p < .05$. **$p < .01$

Table 13.General Linear Model: Predicting retention of neutral declarative information over a sleep-filled delay using REM-related variables (n = 60)

	Type III SS	df	MS	F	p	ESE
Corrected model	12.57	5	2.51	7.32	< .001***	.41
Group	1.72	2	0.86	2.50	.09	.09
REM → NREM 1/W	2.87	1	2.87	8.34	< .01**	.14
Group x REM → NREM 1/W	4.99	2	2.49	7.26	< .01**	.22

Note. For the overall model, $R^2 = 0.41$, adjusted $R^2 = 0.35$. REM → NREM 1/W = REM arousals leading to NREM 1 or wake; Group x REM → NREM 1/W = interaction between group membership and REM → NREM 1/W; ESE, effect size estimate (in this case, η_p^2). $^{**}p < .01$. $^{***}p < .001$.

In summary, the number of REM arousals that led to NREM 1 or waking predicted retention of neutral declarative information across a sleep-filled delay. PTSD-diagnosed individuals who had more of these REM arousals had lower retention scores. This result was not replicated for REM arousals that were non-specific, or for SWS-associated sleep variables.

Summary of Investigation 2 results. The results of *Investigation 2* suggest that PTSD-diagnosed individuals, in comparison with HC participants, recalled and retained less neutral declarative information after a sleep-filled delay. This result is not consistent with those reported by most other studies in the field. Those previously published studies suggest that PTSD-diagnosed individuals do not generally experience deficits in retention of neutral declarative information, although they have not measured retention across a sleep-filled delay. Consistent with previous studies, and in contrast to measures related to the *Night* condition, neutral declarative memory associated with the *Day* condition in PTSD-diagnosed individuals was characterised by deficits on measures of immediate and delayed recall. Furthermore, general linear modelling showed that objective measures of sleep (specifically, increased REM arousals leading to NREM 1 or waking) predict the amount of neutral declarative information that was retained over the sleep-filled delay. This result suggests that fragmented REM sleep affects processes of memory consolidation negatively. Although this result applied to all participants,

the analysis also revealed that PTSD-diagnosed individuals who experienced increased REM fragmentation had poorer retention of neutral declarative information across the sleep-filled delay. In contrast to findings from previously published studies, SWS-related variables did not affect memory retention across the same delay.

CHAPTER SIX: INVESTIGATION 3 – EMOTIONAL MEMORY PROCESSING DURING SLEEP IN PTSD

Emotional memory in PTSD-diagnosed individuals, in comparison with control individuals, is characterised by a tendency to remember highly-arousing negative information more than highly-arousing positive or low-arousing neutral information (e.g., Golier, Yehuda, Lupien, & Harvey, 2003). Furthermore, PTSD-diagnosed individuals also have a bias toward highly-arousing negative information: For example, when told to forget negative information, they tend to remember it quite accurately, while forgetting positive and neutral information about which they have been given the same instruction (McNally, Metzger, Lasko, Clancy, & Pitman, 1998).

Several studies have shown that healthy sleep is important for emotional memory consolidation; that is, sleep selectively promotes the consolidation of highly-arousing information (regardless of whether the valence is negative highly-arousing or positive) over low-arousing neutral information (Groch, Wilhelm, Diekelmann, & Born, 2013; Hu, Stylos-Allan, & Walker, 2006; Nishida, Pearsall, Buckner, & Walker, 2009). Sleep therefore leaves individuals with balanced emotional memory for both highly-arousing negative and highly-arousing positive information (Walker, 2009).

This consolidation effect appears to be supported by REM sleep, specifically (Boyce, Glasgow, Williams, & Adamantidis, 2016; Wagner, Gais, & Born, 2001). Recent studies of PTSD-diagnosed individuals show that, during REM sleep, their limbic structures are over-activated relative to those of control participants (Germain et al., 2013). One proposition based on such empirical findings is that abnormal hyperactive limbic regions during REM sleep in these individuals may lead to an over-consolidation of highly-arousing and negatively valenced

information because activity in limbic regions (in particular, in the amygdala) is associated with consolidation of highly-arousing negative information during waking.

In this investigation, I aimed to demonstrate that PTSD-diagnosed individuals, in comparison with TE and HC participants, have enhanced accuracy and bias for highly-arousing negative information over highly-arousing positive and low-arousing neutral information on an emotional memory recognition task. Specifically, I aimed to show that this effect is prominent across sleep rather than waking. Furthermore, I aimed to establish that this nighttime effect is predicted by sleep variables, especially those related to REM sleep. Stated otherwise, I aimed to show that REM sleep disruption in PTSD-diagnosed individuals contribute to enhanced recognition accuracy and recognition bias for highly-arousing negative information. These aims are summarised by the following hypotheses:

1. PTSD-diagnosed participants, in comparison with TE and HC participants, will have enhanced memory consolidation for negative highly-arousing information (relative to positive highly-arousing or neutral information) across the night and in comparison with the day.
2. In all participants, sleep disruption (especially that related to REM sleep alterations) will be associated with biased memory consolidation toward negative and highly-arousing information.
    a. More specifically, PTSD-diagnosed participants with sleep disruption will have biased memory consolidation toward negative and highly-arousing information.

Methods

Study Design

First, I aimed to show that increased memory and bias towards highly-arousing negative information experienced by PTSD-diagnosed individuals, in comparison with control participants, is prominent after a sleep-filled, rather than wake-filled delay. Condition (*Night* versus *Day*) and Picture Type (highly-arousing negative versus highly-arousing positive versus low-arousing neutral stimuli) formed the repeated measures, while group membership (PTSD versus TE versus HC) formed the between-subjects factor. The outcome variables were recognition accuracy and recognition bias. Unlike *Investigation 2* where the outcome memory variables were based on free recall, here the outcome variables was based on a recognition memory task. Second, I aimed to show that recognition accuracy and recognition bias for highly-arousing negative information in PSTD-diagnosed individuals, in comparison with control participants, was predicted by the degree of sleep disruption (a) related to those variables for which *Investigation 1* detected between-group differences, or (b) REM-related variables that are empirically associated with emotional memory consolidation.

Experimental Measures

I used a subset of pictures from **t**he *International Affective Picture System* (IAPS; Lang, Bradley, & Cuthbert, 2008). The IAPS is a set of color photographs that provides a set of normative stimuli for experimental investigations of emotion and emotional memory. Normative ratings of emotion (valence: negative, neutral and positive; and arousal: arousing and low-arousing) are associated with each photograph. Regarding its use in South Africa, the IAPS contains several pictures that are outdated and that might not be applicable to the South African context. For example, some pictures are of sports (e.g., skiing), scenes (e.g., ice skating), objects (e.g., croquet needles), or people (e.g., Hispanic people) that may not be readily familiar to South Africans from low-SES backgrounds. However research in our laboratory suggests that the

standardised IAPS valence ratings are highly correlated with those of low SES South Africans, $r(28) = .913$ (Nestadt & Kantoor, 2015) suggesting that the IAPS stimuli do evoke emotions that are largely consistent with those proposed by the standardised IAPS manual.

The experiment consisted of three trials and was designed to match other similar investigations (e.g. Nishida et al., 2009). *Trial 1* included the presentation of a set of pictures that participants were asked to remember. *Trial 2* consisted of the presentation of the same pictures from *Trial 1*, interspersed with new pictures. The subsequent trial was a *Recognition Trial* where participants had to distinguish between pictures presented for the first time in the *Trial 1* and new pictures presented in *Trial 2*. I selected two subsets of 90 IAPS pictures for *Trial 1* of the *Night* and *Day* conditions respectively. For *Trial 2*, I added an additional two sets of 45 pictures for the *Night* and *Day* conditions respectively (hence, for this trial there were a total 135 pictures in each condition). Stimuli across both conditions and both trials were balanced for valence and arousal as well as picture characteristics (faces, scenes, non-living objects, human figures, and luminescence). Appendix F lists all the IAPS pictures and provides a summary of their properties with regard to valence and arousal.

All negatively and positively valenced pictures were chosen so that they fell into the *arousing* category, while the neutral pictures were *non-arousing*. This is in contrast with many research protocols that control for either valence or arousal (i.e. keep either valence or arousal constant; e.g. Hu et al., 2006; but see, Nishida et al., 2009). However, research studies suggest that PTSD-diagnosed individuals show emotional memory bias for negative *and* highly-arousing stimuli. To ensure the strongest possible contrast and ecological validity with real-life situations (where stimuli of neutral valence tend to be associated with low arousal, and stimuli of negative valence tend to be associated with higher arousal (Sharot, Delgado, & Phelps, 2004)), I decided to include neutral low-arousing pictures as a control set for highly-arousing negative pictures. Highly-arousing positive pictures were included so as to present participants with a balanced

spectrum of emotional valence. Stated differently, this study incorporates highly-arousing negative, highly-arousing positive and low-arousing neutral pictures. From this point forward I refer to highly-arousing negative and positive pictures as Negative and Positive pictures respectively and low-arousing neutral pictures as Neutral. Appendix G shows the statistically significant differences in arousal and valence between the categories of pictures, demonstrating that the picture categories could be meaningfully differentiated from each other.

The pictures were presented using E-prime software (Schneider, Eschman, & Zuccolotto, 2002) on a standard 19-inch computer monitor at full size. For *Trials 1* and *2*, each picture presentation began with a fixation cross (2000 ms). The target picture was then presented (6000 ms), and was followed by a blank screen (5000 ms). In total, then, the inter-stimulus interval was 7000 ms (see Figure 8). These presentation durations are commonly reported in other experiments using the IAPS (Balconi, Brambilla, & Falbo, 2009; Palomba, Angrilli, & Mini, 1997).

The pictures were presented in a pseudorandom order so that no more than three pictures of the same Picture Type category were presented consecutively. During *Trial 1*, 10 alertness-control stimuli were randomly intermixed to ensure that participants did not get habituated to the repetitive presentation of pictures. During *Trial 2*, 15 such alertness-control stimuli were presented. Each alertness-control stimulus consisted of a number (one of '0' through to '9') appearing on the screen. Participants then had to press the corresponding number on the keyboard during the blank screen period. During picture and alertness-control stimulus presentation, measures of autonomic reactivity unrelated to this investigation were recorded (these methods are described in *Investigation 4*).

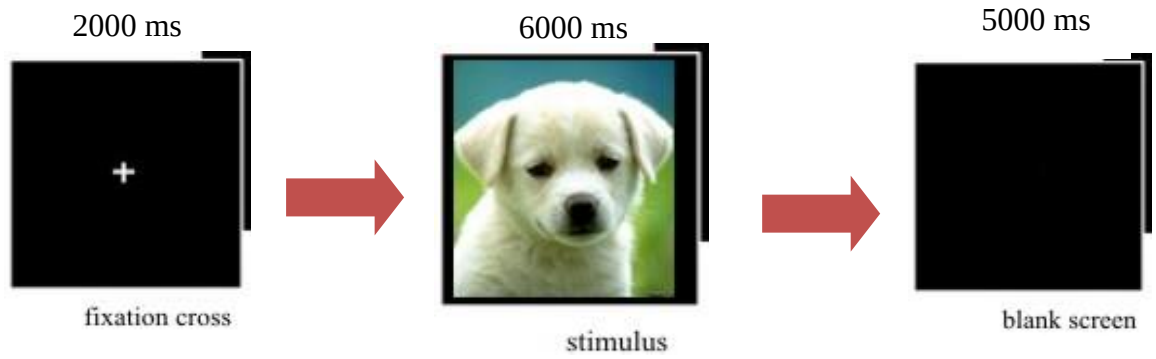

Figure 8. IAPS stimulus presentation order in the current experiment.

During the *Recognition Trial*, participants were presented with all 135 pictures, presented using the same pseudorandom technique utilised in Trials 1 and 2. Each picture was preceded by a 2000 ms fixation cross, and each was presented for 2000 ms. Participants then had to provide a forced-choice recognition response to each picture (yes, indicating the picture had been presented in *Trial 1*, or no, indicating it had not), before the next fixation cross and picture appeared. They pressed the '1' key on the keyboard to indicate a 'yes' response. They pressed the '2' key to indicate a 'no' response.

Procedure

Figure 9 presents the procedure specific to this Investigation (the procedure of the entire study is presented in Figure 3).

Night condition. Prior to sleep, participants completed *Trial 1* of the IAPS emotional memory task. They were instructed to view all 90 pictures and to respond to the alertness-control stimuli. As part of the instructions, they were told that the picture set would consist of Negative, Positive, and Neutral pictures, and that they should try to remember each one. At the start of the task, participants were shown three practice pictures and one alertness-control stimulus, presented in the same way as during the trial itself. Thereafter, participants began *Trial 1*. They were seated 50cm away from the screen in a sound- and light-proofed room. During trial presentations, participants were alone and the lights were turned off, to ensure that their full

attention was directed at the pictures. I, or a research assistant, watched participants via infrared CCTV camera in the adjoining control room to ensure that they watched all the pictures in the trial. If participants looked away from the screen, they were given a brief reminder via intercom to continue looking at the pictures.

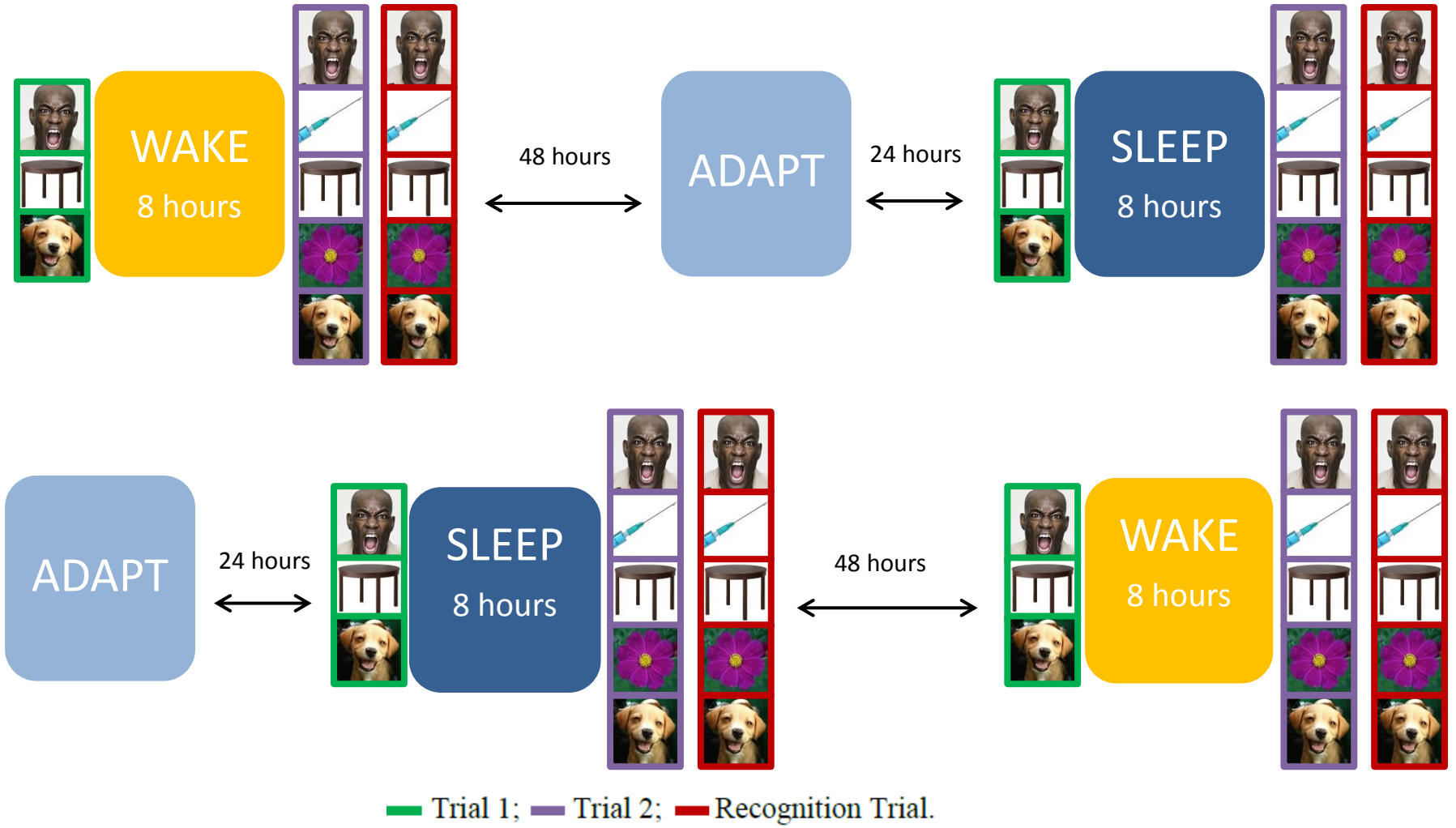

Figure 9. Study procedure for Investigations 3. Participants either completed sequence (a) or sequence (b), in a counterbalanced design.

After all the evening tasks related to Investigations 2-4 were completed, participants slept for 8 hours. In the morning, after waking up, preparing for the day and completing tasks related to *Investigation 2*, participants started *Trial 2* of the IAPS emotional memory task. I told them they would see the same 90 pictures as in *Trial 1*, but interspersed with those pictures would be 45 new pictures, as well as the alertness-control stimuli. *Trial 2* proceeded identically to *Trial 1*, with participants viewing the pictures silently and only responding to the alertness-control stimuli. Thereafter, they were given a 20-minute break before starting the *Recognition Trial*.

Before beginning the *Recognition Trial*, I explained to participants that they needed to identify whether each picture had been presented during *Trial 1* the previous evening or not. I used the three practice pictures from *Trial 1* and a novel practice picture to teach them how to respond. After the practise stimuli, participants completed the *Recognition Trial*.

Day condition. I used the same procedure as for the *Night* condition, except that an alternative and formally parallel set of pictures was used. Participants spent the 8-hour interval awake rather than asleep, and were free to continue with their usual daily activities, but were reminded not to nap, drink caffeinated or sugary drinks, or exercise excessively.

Statistical Analysis

Before I examined between-group differences in emotional memory, I tested whether there were any differences in participant alertness (as measured by accuracy (the number of correct responses) and reaction time on the alertness-control trials) during the *Night* and *Day* conditions. I did so to determine whether there were significant circadian differences that might have impacted on the outcomes of interest. For each of the alertness-control accuracy and reaction time variables, I compared performance during the first session of the *Night* condition (evening session) with that during the first session of the *Day* condition (morning session), by using a mixed-design ANOVA, with condition as the repeated measure and group membership as the between-subjects factor. Using an identical analysis, I compared performance during the

second session of the *Night* condition (morning session) with that during the second session of the *Day* condition (afternoon session).

To investigate the accuracy of participants' responses on the *Recognition Trial* of the IAPS emotional memory task, I used signal detection theory (SDT) (Macmillan, 2002). Within the SDT framework, this task yields four kinds of responses: a correct identification of a picture presented initially on *Trial 1* (*hit*); an incorrect identification of a *Trial 1* picture as having been presented initially on *Trial 2* (*miss*); a correct identification of a picture as having been presented initially on *Trial 2*, but not *Trial 1* (*correct rejection*); and an incorrect identification of a *Trial 2* picture as having been presented initially on *Trial 1* (*false alarm*). Using the sums of these four kinds of responses across the *Recognition Trial* stimuli, I calculated a *d'* accuracy measure and a *c* bias measure. Accuracy is defined as the difference between the *z*-transformed (normalized) probabilities of hit and false alarm rates, according to the following formula:

$$d' = z(\text{hit rate}) - z(\text{false alarm rate})$$

Bias is defined as the addition of the *z*-transformed (normalized) probabilities of hit and false alarm rates adjusted by a factor of -0.5, according to the following formula:

$$c = (-0.5)*(z(\text{hit rate}) + z(\text{false alarm rate}))$$

Hence, negative values of *c* correspond to liberal biases, where participants tend to indicate erroneously that pictures belong to *Trial 1*. Positive values of *c* correspond to conservative biases, where participants erroneously indicate that pictures do not belong to *Trial 1*.

Testing hypothesis 1. Here, I aimed to determine whether PTSD-diagnosed individuals, in comparison with TE and HC individuals, have more accurate recognition memory and greater bias for Negative pictures than for Positive or Neutral pictures, and whether this difference is particularly salient over a sleep-filled delay (the *Night* condition) relative to a wake-filled delay (the *Day* condition). I used a mixed-design 2 (Condition: *Night* versus *Day*) x 3 (Picture Type:

Negative versus Positive versus Neutral) x 3 (Group: PTSD versus TE versus HC) ANOVA to investigate this aim. Before I began the analysis I first examined the data for deviations from normality, sphericity and homogeneity of variance. If I found any such deviations I have noted them prior to the each results description. If I found no deviations, then I proceeded with the analysis.

Testing hypothesis 2. Here, I aimed to determine whether sleep disruption in PTSD-diagnosed individuals was associated with increased recognition accuracy and bias toward for Negative pictures after sleep. Firstly, I correlated (a) sleep variables on which there were significant between-group differences in *Investigation 1*, or REM-related variables that were empirically associated with emotional memory consolidation, with (b) accuracy and bias related to Negative pictures. Sleep variables that correlated with measures of recognition accuracy and recognition bias at the significance level of $p < .10$ were used in subsequent analyses. I then ran a series of general linear models to explore whether these sleep variables predicted accuracy and bias for Negative pictures. I was particularly interested in determining whether REM-related sleep variables interacted with group membership to predict recognition accuracy and bias toward Negative pictures.

Results

Two participants in the PTSD group did not complete the IAPS emotional memory task. One accidentally switched off the computer during the *Night* condition recognition trial, and a power failure interrupted the *Night* condition recognition recording for the other. Hence, all data from these participants were excluded from the analysis, and so the final sample for which IAPS emotional memory task data were analyzed was: PTSD, $n = 19$; TE, $n = 19$; HC, $n = 20$.

Alertness Associated with the Night and Day Conditions

I assessed between-condition differences regarding accuracy and reaction time on the alertness-control trials. The analyses detected no significant differences, in either accuracy or reaction time, between the first session of the *Night* condition (evening session) and the first session of the *Day* condition (morning session), $F(1, 57) = 1.07$, $p = .35$, and $F(1, 57) = 0.01$, $p = .92$, respectively, or between the second session of the *Night* condition (morning session) and the second session of the *Day* condition (afternoon session), $F(1, 56) = 0.80$, $p = .37$, and $F(1, 56) = 3.61$, $p = .06$, respectively. These results indicate that circadian differences in alertness were unlikely to influence performance on the IAPS emotional memory task.

Testing Hypothesis 1: Between-group differences in recognition accuracy and recognition bias

Accuracy. I conducted a mixed-design 2 x 3 x 3 ANOVA to examine between-group differences in recognition accuracy for Negative, Positive and Neutral pictures (3 level factor of Picture Type) for both the *Night* and *Day* condition (2 level factor of condition).

Table 14 presents the results of the ANOVA related to recognition accuracy. Here I focus exclusively on significant results, although the entire spectrum of results is described in Table 14. The analysis detected a significant main effect of Picture Type. Post-hoc planned contrasts revealed that, regardless of group assignment, (a) participants had greater recognition accuracy for Negative pictures than for Neutral pictures, and that (b) Positive pictures and Neutral pictures were recognized equally well.

Furthermore the analysis detected a significant interaction between Picture Type and Condition, suggesting that the accuracy with which pictures of differing arousal and valence were identified differed depending on the condition within which the identification was made (see Figure 10). Post-hoc planned contrasts revealed that while recognition accuracy was similar across conditions for Negative and Positive pictures, there was a significant between-condition

difference for Neutral pictures. Specifically, participants, regardless of group assignment, recognized Neutral pictures more accurately across the *Night* condition than across the *Day* condition (i.e., when a sleep-filled delay, rather than a wake-filled delay, separated the learning trials from the recognition trial). Participants' recognition accuracy for Neutral pictures was the lowest of the three picture types across the *Day* condition, while across the *Night* condition their recognition accuracy was similar for all picture types. These results suggest that sleep improves recognition accuracy for Neutral pictures, in contrast to waking which is characterised by poor recognition accuracy for Neutral pictures in comparison with the other Picture Type categories.

Table 14 Recognition Accuracy: The influence of picture type and group membership across the night and day conditions (N = 58)

	Group					
Variable/Effect	PTSD (*n* = 19)	TE (*n* = 19)	HC (*n* = 20)	F	p	ESE
Night Condition						
Negative	2.09 (1.12)	2.33 (0.63)	2.47 (0.82)			
Positive	1.74 (0.96)	1.94 (0.74)	1.95 (0.77)			
Neutral	1.94 (0.91)	2.09 (0.85)	2.16 (0.88)			
Day Condition						
Negative	2.35 (0.90)	2.43 (1.01)	2.26 (0.79)			
Positive	1.81 (1.01)	1.82 (0.95)	1.85 (0.84)			
Neutral	1.76 (1.11)	1.74 (0.94)	1.51 (0.74)			
Main Effects						
Picture Type				36.33	< .001***	.40
Contrast 1[a]				47.62	< .001***	0.46
Contrast 2[b]				0.09	.77	<0.01
Condition				1.54	.22	.03
Group				0.13	.88	.01
Interaction Effects						
Picture Type x Condition				7.75	< .01**	.12
Contrast 1[c]				11.95	< .01**	0.19
Contrast 2[d]				9.68	< .01**	0.15
Picture Type x Group				0.37	.83	.01
Condition x Group				1.03	.37	.04
Picture Type x Condition x Group				0.54	.71	.02

Note. Means are presented with standard deviations in parentheses. [a]This contrast compared Negative pictures vs Neutral pictures. [b]This contrast compared Positive pictures vs Neutral pictures. [c]This contrast compared Negative pictures vs Neutral pictures across the Night and Day conditions. [d]This contrast compared Positive pictures vs Neutral pictures across the Night and Day conditions. Degrees of freedom were: Picture Type (2, 110); Condition (1, 55); Group (2, 55); Picture Type x Condition (2, 110); Picture Type x Group (4, 110); Condition x Group (2, 55); Picture Type x Condition x Group (4, 110). ESE = effect size estimate (in this case, η^2 for omnibus tests and Cohen's *d* for contrast analyses).

**$p < .01$. ***$p < .001$.

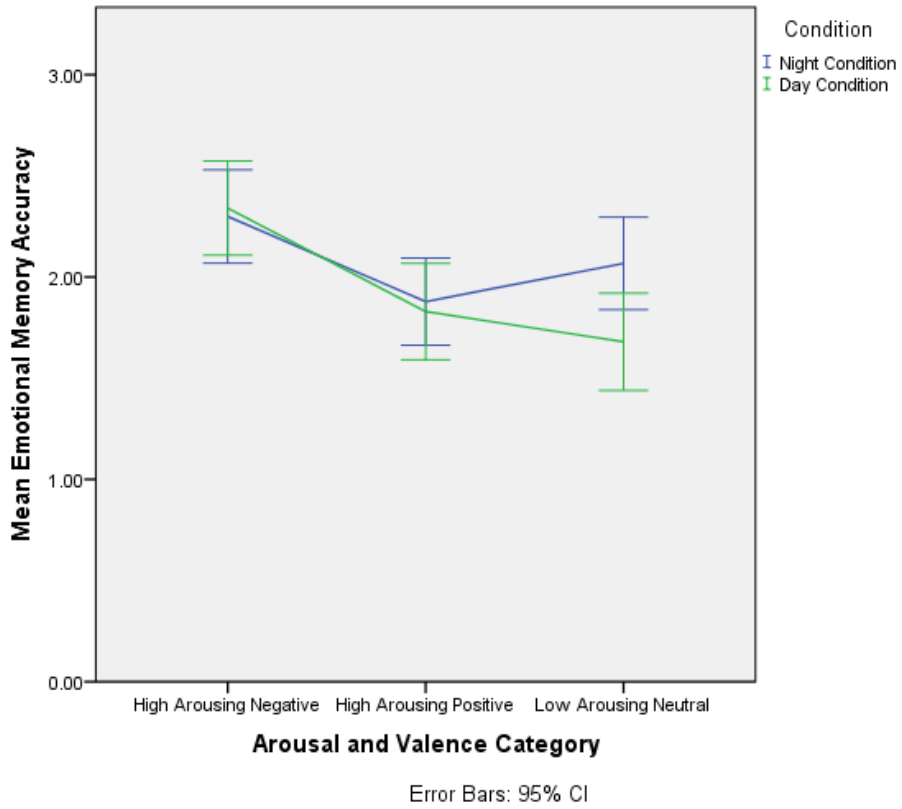

Figure 10 Recognition accuracy: Comparing Picture Type across the Night and Day conditions. Error bars represent 95% confidence intervals.

Bias. A similar mixed-design ANOVA as described above tested the hypothesis that PTSD-diagnosed participants in comparison with TE and HC individuals would demonstrate bias toward recognizing stimuli characterized by high arousal and negative valence. Furthermore I aimed to determine whether this pattern of bias was more salient across a sleep-filled delay rather than a wake-filled delay. Table 15 presents the results of that analysis. Again, I focus exclusively on statistically significant effects.

As Table 15 shows, the analysis detected a significant main effect of Picture Type. A set of post-hoc planned contrasts suggested that, regardless of group, all participants had a significant liberal memory bias for Negative pictures, a significant conservative memory bias for Neutral pictures, and were relatively unbiased with regard to Positive pictures. In other words, on the recognition task participants were relatively over-inclusive of Negative pictures and

relatively under-inclusive of Neutral pictures, but showed little bias either way when presented with Positive pictures.

The analysis also detected a significant Picture Type x Condition interaction (see Figure 11). To help interpret this interaction, I again conducted a set of post-hoc planned pairwise comparisons. These analyses suggested that the source of the significant effect was this: Whereas across the *Day* condition there were no significant differences in the bias scores for Negative and Neutral pictures, across the *Night* condition there were significant differences between the scores. Specifically, across the *Night* condition participants showed a strong liberal bias toward Negative pictures (they tended to over-include them on the recognition task) and a strong conservative bias toward Neutral pictures (they tended to under-include them). The contrast comparing bias scores for Positive and Neutral pictures detected no significant differences within either the *Night* or *Day* conditions.

Table 15 Emotional Memory Bias: The influence of picture type and group membership across the night and day conditions (N = 58)

	Group					
	PTSD	TE	HC			
Variable/Effect	(*n* = 19)	(*n* = 19)	(*n* = 20)	F	p	ESE
Night Condition						
Negative	-0.21 (0.43)	-0.20 (0.43)	-0.14 (0.35)			
Positive	0.04 (0.42)	0.14 (0.53)	0.16 (0.27)			
Neutral	0.23 (0.34)	0.25 (0.38)	0.23 (0.34)			
Day Condition						
Negative	-0.04 (0.39)	-0.16 (0.39)	0.04 (0.31)			
Positive	0.03 (0.44)	-0.16 (0.50)	0.09 (0.37)			
Neutral	0.02 (0.40)	0.03 (0.43)	0.25 (0.34)			
Main Effects						
Picture Type				33.68	< .001***	.38
Contrast 1[a]				63.52	< .001***	0.54
Contrast 2[b]				10.56	< .01**	0.16
Condition				0.66	.42	.03
Group				1.14	.33	.01
Interaction Effects						
Picture Type x Condition				12.45	< .001***	.19
Contrast 1[c]				22.40	< .001***	0.29
Contrast 2[d]				0.04	.85	< 0.01
Picture Type x Group				0.19	.94	< .01
Condition x Group				1.17	.32	.04
Picture Type x Condition x Group				1.36	.25	.05

Note. Means are presented with standard deviations in parentheses. [a] This contrast compared Negative pictures vs Neutral pictures. [b] This contrast compared Positive pictures vs Neutral pictures. [c] This contrast compared Negative pictures vs Neutral pictures across the Night and Day conditions. [d] This contrast compared Positive pictures vs Neutral pictures across the Night and Day conditions. Degrees of freedom were: Picture Type (2, 110); Condition (1, 55); Group (2, 55); Picture Type x Condition (2, 110); Picture Type x Group (4, 110); Condition x Group (2, 55); Picture Type x Condition x Group (4, 110). ESE = effect size estimate (in this case, η^2 for omnibus tests and Cohen's *d* for contrast analyses).

** $p < .01$, *** $p < .001$

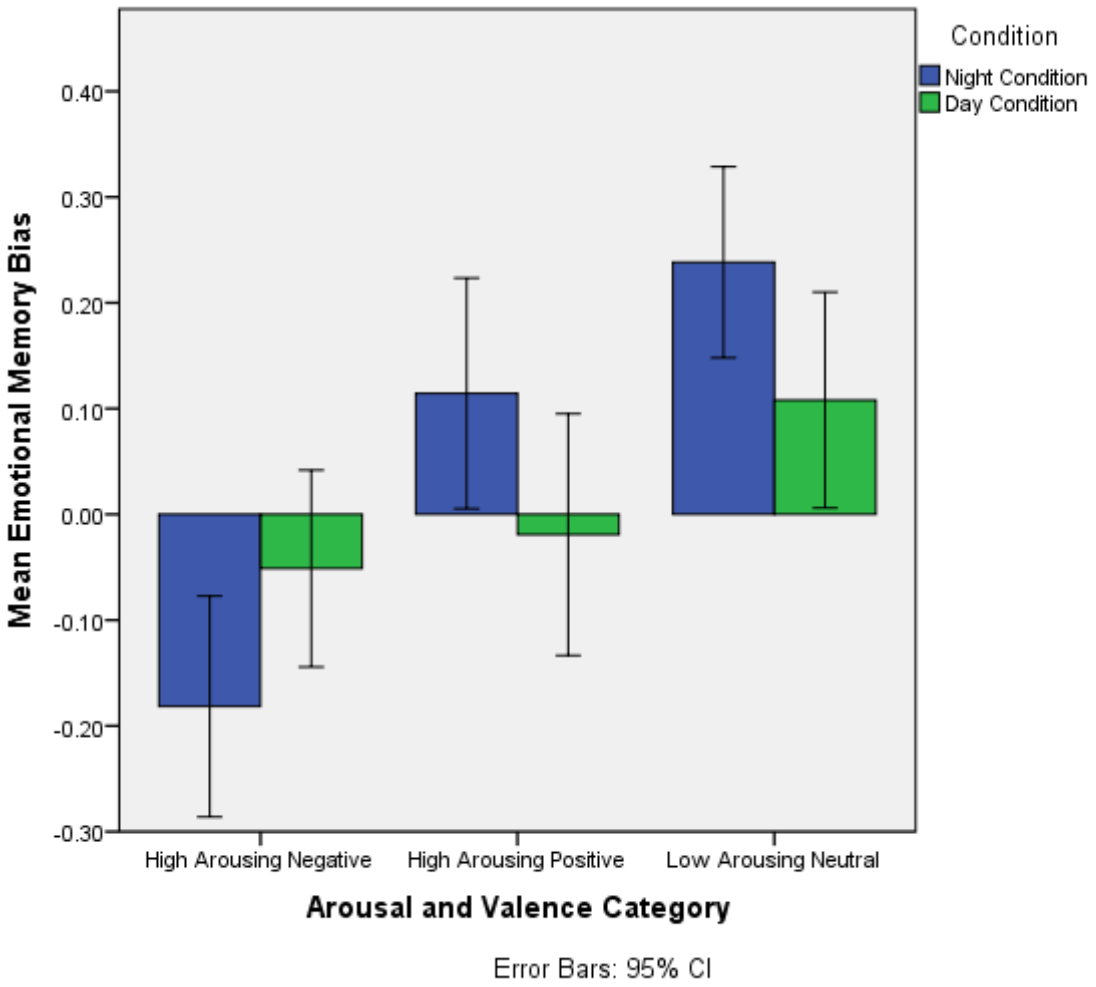

Figure 11 Emotional memory bias: Comparing Picture Type across the Night and Day conditions. Error bars represent 95% confidence intervals.

Interim summary. *Hypothesis 1*, aimed to determine whether PTSD-diagnosed individuals, in comparison with TE and HC individuals, had more accurate recognition memory and greater bias for Negative pictures than for Positive or Neutral pictures, and whether this difference was particularly salient over a sleep-filled delay relative to a wake-filled delay. Both these hypotheses were not confirmed. Analyses detected no between-group differences with regard to recognition accuracy or recognition bias for any particular class of emotional stimulus.

Regarding recognition accuracy, the analyses suggested that, in both the *Night* and *Day* conditions, all participants had greater accuracy scores for Negative pictures than for Neutral pictures. Furthermore, when examining differences between performance within the *Night* and

Day conditions, all participants were equally accurate at recognizing Negative, Positive, and Neutral pictures within the *Night* condition, whereas within the *Day* condition they were significantly more accurate at recognizing Negative pictures than Neutral pictures.

With regard to recognition bias the analyses suggested that, in both the *Night* and *Day* conditions, all participants had a significant liberal bias for Negative pictures, and a significant conservative bias for Neutral pictures. Furthermore, when examining differences between performance within the *Night* and *Day* conditions, all participants showed (a) conservative bias for Neutral pictures within the *Night* condition, suggesting they tended to under-include such pictures on the recognition task, and (b) liberal bias for Negative pictures within the *Night* condition, suggesting they tended to over-include such pictures. Differences in emotional memory bias within the *Day* condition were not as prominent, showing much less variation in bias across the picture types.

Testing Hypothesis 2: Predicting Recognition Accuracy and Recognition Bias After a Sleep-Filled Delay Using Sleep Variables

Because the analyses reported above detected no significant between-group differences in recognition accuracy or bias, my prediction that sleep disruption in PTSD-diagnosed individuals would predict increased accuracy and bias for Negative pictures fell away. However, those analyses did suggest that significant interactions between Picture Type (Negative, Positive and, Neutral) and Condition (*Night* and *Day*) played a role in performance on the recognition task (i.e., that sleep and waking have different associations with stimuli of differing classes of Picture Type in terms of recognition accuracy and bias). In particular, a sleep-filled delay promoted balanced recognition of Negative, Positive and Neutral picture types, although across the same delay participants tended to over-include Negative pictures and under-include Neutral pictures. Because these analyses suggested a clear effect of sleep on recognition accuracy and recognition bias, I decided to investigate whether subjective and objective sleep variables were associated

with these aspects of emotional memory recognition. In other words, I wanted to investigate whether the pattern of recognition accuracy and recognition bias was related to specific elements of sleep rather than general non-specific effects of sleep.

For all subsequent analyses recognition accuracy and recognition bias are related to the *Night* condition only. As a first step in that investigation, I correlated accuracy and bias scores on the emotional memory recognition task with subjective and objective sleep variables, as well as depression severity, as measured by BDI-II scores. I included the latter variable in this analysis because it was the major clinical characteristic, other than those that defined the groups, that varied considerably across groups. I entered all measured subjective and objective sleep variables into the correlation matrix because I was no longer focussing on correlations between variables for which *Investigation 1* had provided evidence of between-group differences. Table 16 presents the correlation matrix.

The analyses detected no significant correlations involving accuracy and bias scores for Negative and Positive pictures, subjective sleep quality, or depression severity. The only significant (or trend-level) correlations that were detected involved objective sleep variables and accuracy and bias scores for Neutral pictures.

Regarding accuracy, the analysis detected a small negative correlation ($p = .04$) between scores for Neutral pictures and REM arousals, suggesting that more frequent REM arousals were associated with poorer accuracy in recognizing such pictures. Correlations between accuracy for Neutral pictures and REM arousals leading to NREM1 or waking, REM latency, and NREM 2 percentage showed trend-level significance.

Regarding bias, the analysis detected a moderate positive correlation between scores for Neutral pictures and the number of spontaneous arousals as well as the number of REM arousals ($p = .02$ and $p = < .01$ respectively), suggesting that increases in both kinds of arousals were associated with a higher degree of conservative emotional memory bias. Furthermore, the

analysis detected a small positive correlation (p = .04) between scores for Neutral pictures and NREM 1 percentage, suggesting that increased light sleep was also associated with a higher degree of conservative emotional memory bias. Finally, the analysis detected a moderate negative correlation (p = < .01) between scores for Neutral pictures and the NREM1 percentage and SWS percentage composite, suggesting that a combination of less SWS percentage and more NREM 1 percentage was associated with a higher degree of conservative emotional memory bias. Correlations between bias for Neutral pictures and REM arousals leading to NREM1 or waking, and SWS percentage, showed trend-level significance.

Table 16 Correlation Matrix: Associations, within the Night condition, between emotional memory recognition task scores, sleep, and depression (N = 58)

	Accuracy scores for the three picture types			Bias scores for the three picture types		
Variable	Negative	Positive	Neutral	Negative	Positive	Neutral
PSQI	-0.03	0.03	0.19	0.09	-0.24	<0.01
Laboratory PSQI	-0.09	0.21	-0.08	0.21	0.14	-0.01
Sleep Latency	0.17	0.17	0.05	0.15	0.23	0.03
Sleep Efficiency	0.02	-0.04	0.06	-0.06	-0.05	-0.01
Awakenings	-0.07	< 0.01	-0.03	< 0.01	0.07	0.15
Spontaneous Arousals	0.07	-0.06	-0.03	0.17	0.21	**0.30***
WASO	-0.19	-0.10	-0.11	-0.09	-0.08	< 0.01
NREM 1 percentage	-0.13	-0.16	-0.16	0.20	0.22	**0.27***
NREM 2 percentage	-0.04	0.10	**0.22**†	0.06	-0.02	0.04
SWS percentage	0.10	0.03	-0.01	-0.03	-0.08	**-0.22**†
REM percentage	-0.02	-0.06	-0.10	-0.19	-0.08	0.09
REM Latency	0.20	0.23	0.24†	0.07	0.12	-0.14
REM Arousal	-0.11	-0.20	**-0.27***	0.07	0.18	**0.38****
REM $\rightarrow$NREM1/W	-0.12	-0.14	**-0.25**†	-0.05	0.02	0.23†
NREM1 + SWS	0.17	0.17	0.13	-0.10	-0.18	**-0.37****
BDI-II	-0.16	-0.10	-0.04	-0.03	-0.16	-0.04

Note. Spearman's *rho* correlation is presented; PSQI = Pittsburgh Sleep Quality Index; WASO = the number of minutes spent awake after sleep onset; REM $\rightarrow$ NREM1/W = REM arousals leading to NREM1 or wake; NREM1 + SWS = composite of NREM1 percentage and SWS percentage; BDI-II = Beck Depression Inventory-Second Edition.

$^{\dagger}p < .1$. *$p < .05$. **$p < .01$.

To follow-up these correlations, I used general-linear modelling to predict recognition accuracy and recognition bias for Neutral pictures using objective sleep measures. To construct the models, I entered significant, or trend-level significant, objective sleep variables (as identified by the correlation analysis) and all two-way interactions associated with these variables. I only entered six variables or associated interactions at a time to ensure that there was no inflation of Type I error as a result of a large number of terms relative to the sample size. After I had entered all the terms, I examined the model for significant contributors as well the overall variance explained. I removed non-contributing variables, starting with two-way interactions. I worked iteratively towards a significant model that explained the largest variance in recognition accuracy and recognition bias.

Regarding accuracy, the model-building process revealed that the variable REM arousals leading to NREM 1 or waking was the best predictor of recognition memory accuracy for Neutral pictures, although the effect size was small (Table 17). Because the correlation between accuracy and this specific form of REM arousals was negative, the analysis suggests that the presence of more such arousals predicts lower accuracy when attempting to recognize Neutral pictures. No other predictor, combination of predictors, or interaction was a significant contributor to this model.

Table 17 General Linear Model: Predicting recognition accuracy related to the Night condition for neutral pictures (N = 58)

	Type III SS	df	MS	F	p	ESE
Corrected Model	3.60	1	3.60	5.10	.03*	0.08
REM → NREM1/W	3.60	1	3.60	5.10	.03*	0.08

Note. SS, sums of square; MS, mean square; REM → NREM1/W = REM arousals leading to NREM1 or wake; ESE, effect size estimate (in this case, η_p^2). For the overall model, $R^2 = 0.08$, adjusted $R^2 = 0.07$.

*$p < .05$.

Table 18 General Linear Model: Predicting recognition bias related to the Night condition for neutral pictures (N = 58)

	Type III SS	df	MS	F	p	ESE
Corrected Model	1.45	2	0.73	7.55	< 0.01**	0.22
REM Arousals	0.59	1	0.59	6.12	.02*	0.10
NREM1 + SWS	0.35	1	0.35	3.67	.06	.06

Note. SS, sums of square; MS, mean square; ESE, effect size estimate (in this case, η_p^2); NREM1 + SWS, composite of NREM1 percentage and SWS percentage. For the overall model, $R^2 = 0.22$, adjusted $R^2 = 0.19$.

*$p < .05$. **$p < .01$.

Regarding bias, the best-fitting model included only REM arousals as a significant predictor, associated with a medium effect size. Furthermore, the NREM1 percentage and SWS percentage composite showed trend-level significance in this model (Table 18).

In summary, general linear modeling revealed that in all participants, regardless of group, REM arousals predicted the accuracy, and the degree of bias, for Neutral pictures on the emotional memory recognition task. More specifically, increased REM arousals leading to NREM1 or waking decreased accuracy in recognizing Neutral pictures, while increased non-specific REM arousals increased conservative bias with regard to those pictures.

Secondary Analyses

I conducted a number of analyses that were not part of the primary set of analyses designed to test the major hypotheses. These secondary analyses sought to clarify relationships between variables based on previous research findings or nuances in the data (described below), although they were not of critical relevance to the current project.

Noradrenergic activity and emotional memory. Previous literature (e.g., Goldstein & Walker, 2014) suggests that nighttime noradrenergic activity may affect sleep-dependent consolidation of emotional memories. Hence, I correlated nighttime noradrenergic activity (as measured by urinary normetadrenaline metabolites) with accuracy scores on for Negative,

Positive, and Neutral pictures, separately. The analyses detected no significant associations, Negative: *r*s < .11, *p*s > .68; Positive: *r*s < .12, *p*s > .65; Neutral: *r*s < -.02, *p*s > .93.

Subjective sleep quality and emotional memory. Based on the improved sleep quality that PTSD-diagnosed individuals reported in the laboratory in comparison to their home environment I wanted to see whether these participants' Laboratory PSQI bore a different association to recognition accuracy and recognition bias than for TE and HC participants. I correlated each group's Laboratory PSQI scores with Negative, Positive and Neutral recognition accuracy and recognition bias.

The analyses detected no significant correlations between each group's Positive or Neutral recognition accuracy scores and their Laboratory PSQI values. However for Negative recognition accuracy, Laboratory PSQI showed a moderate positive correlation for PTSD-diagnosed individuals only, $r(21) = 0.52$, $p = .02$. This finding suggests that, in PTSD-diagnosed individuals, better subjective sleep quality in the laboratory was associated with lower accuracy scores for Negative pictures on the emotional memory task. Interestingly, the opposite association was observed for TE and HC participants, $r(19) = -0.48$, $p = .04$, and $r(18) = -0.31$, $p = .21$, respectively. In other words, for TE and HC participants, better subjective sleep quality in the laboratory was associated with higher accuracy scores for Negative pictures on the emotional memory task (although the correlation for HC participants was non-significant). In summary, these results indicate that better subjective laboratory sleep quality were associated with (a) lower recognition accuracy for Negative pictures in PTSD-diagnosed individuals, but (b) higher recognition accuracy for Negative pictures in both TE and HC participants. In terms of emotional memory bias there were no significant correlations between participants in any group and any Picture Type category.

Summary of Results

In this sample, analyses detected no significant between-group differences in accuracy for, or bias toward, any specific emotional picture type on the recognition memory task. More specifically, PTSD-diagnosed individuals, in comparison with TE and HC individuals, did not show increased recognition accuracy or recognition bias for Negative pictures than for Positive or Neutral pictures, and this difference was not particularly salient over a sleep-filled delay relative to a wake-filled delay. These results disconfirm Hypothesis 1. Because there were no between-group differences in recognition accuracy or recognition bias, *hypothesis 2* fell away.

Although the hypotheses were disconfirmed, the results of *hypothesis 1* suggested that there were prominent differences in participants' recognition accuracy and recognition bias after either a period of waking or a period of sleep. The results revealed that *all* participants tended to have better recognition memory accuracy for Negative pictures than for Neutral pictures. However, after a sleep-filled delay participants remembered all Picture Type categories with a similar degree of accuracy, while after a wake-filled delay they had better recognition for Negative rather than Neutral pictures. The main difference here was that after a sleep-filled delay participants had greater accuracy for Neutral pictures than after a wake-filled delay. This increase in recognition accuracy for Neutral pictures after the sleep-filled delay was responsible for the balance in recognition accuracy for all Picture Type categories in this condition. Furthermore, participants showed conservative recognition bias toward Neutral pictures and liberal recognition bias toward Negative pictures after a sleep-filled delay. These findings are not confirmatory of the primary hypotheses, although they do support the broader objective of the study which is to demonstrate the importance of sleep for emotional memory.

Objective sleep variables contributed to both recognition accuracy and recognition bias for Neutral pictures associated with the *Night* condition. Regarding this category of pictures

increased REM arousals leading to NREM1 or waking decreased recognition accuracy, while increased non-specific REM arousals promoted conservative recognition bias.

CHAPTER SEVEN: INVESTIGATION 4 – EMOTIONAL REACTIVITY REGULATION DURING SLEEP IN PTSD

Emotional reactivity in PTSD-diagnosed individuals, in comparison with controls, is characterized by elevated responses to highly-arousing negative stimuli, both related and unrelated to the precipitant trauma (McTeague et al., 2010; Schmahl et al., 2004). Studies comparing PTSD-diagnosed individuals to controls have assessed emotional reactivity using a number of measures of autonomic arousal such as heart rate, skin conductance level, and blood pressure.

Several studies have shown that healthy sleep is important for the attenuation of emotional reactivity in response to highly-arousing negative stimuli (Gujar, McDonald, Nishida, & Walker, 2011; Pace-Schott et al., 2011). Furthermore, a number of studies have shown that REM sleep is critical to this attenuation process (van der Helm et al., 2011). Walker and Van der Helm (2009) suggested that the centrality of REM sleep to emotional attenuation arises because during waking, emotional experiences are encoded while levels of circulating noradrenaline are high, whereas during REM sleep those same networks that were active during waking encoding are reactivated, but this time in absence of noradrenaline. Therefore, reactivation of networks associated with emotional experiences during sleep in an environment sans noradrenaline may decrease the emotional tone (or emotional reactivity) associated with the experience.

PTSD-diagnosed individuals, in comparison with controls, experience a number of sleep-related alterations that may interrupt the process of attenuation of emotional reactivity. For example, PTSD is characterized by sleep deprivation, which may, within the theoretical framework outlined above, allow less opportunity for attenuation of the emotional tone associated with events encoded during waking, and may, therefore, lead to a situation where already heightened emotional reactivity in the patient is exacerbated. Additionally, and in terms

of more specific mechanisms, PTSD is characterized by elevated nighttime noradrenergic levels at night and by REM sleep alterations (Mellman et al., 1995; Spoormaker & Montgomery, 2008). (Elevated nighttime noradrenergic levels may, in fact, contribute to disrupted REM sleep.) *Investigation 4* aimed to show that PTSD-diagnosed individuals, in comparison with TE and HC participants, experience increased emotional reactivity to highly-arousing negative information and that this increased emotional reactivity was predicted by disordered REM sleep parameters in this group of individuals. These aims are summarised by the following hypotheses:

1. PTSD-diagnosed participants, in comparison with TE and HC participants, will have increased emotional reactivity for negative highly-arousing stimuli (relative to positive highly-arousing or neutral stimuli) across the night and in comparison with the day. In this investigation, emotional reactivity will be indexed by parameters associated with autonomic reactivity (such as heart rate and skin conductance).
2. In all participants, sleep disruption (especially that related to REM sleep alterations) will be associated with elevated emotional reactivity, especially in response to negative and highly-arousing stimuli.
    a. More specifically, PTSD-diagnosed participants with sleep disruption will have elevated emotional reactivity, especially in response to negative and highly-arousing stimuli.

Methods

Study Design

First, I aimed to show that heightened emotional reactivity to highly-arousing negative information experienced by PTSD-diagnosed individuals, in comparison with controls, is particularly salient across a sleep-filled interval in contrast with a wake-filled interval. I used a mixed repeated-measures and between-subjects design for this investigation. Condition (*Night* versus *Day*) and emotional reactivity (to highly-arousing negative (hereafter, simply Negative)

versus highly-arousing positive (hereafter, simply Positive) versus low-arousing neutral (hereafter, simply Neutral) stimuli) were the repeated measures, and group membership was the between-subjects factor. The class of outcome variables was emotional reactivity, indexed by 4 different autonomic arousal variables (viz., heart rate, pre-ejection period, left ventricular ejection time and skin conductance level). Second, I aimed to show that emotional reactivity to negative information in PSTD-diagnosed individuals, in comparison with controls, is predicted by REM sleep parameters, specifically those for which *Investigation 1* provided evidence of between-group difference, or for which previous studies provided empirical associations with emotional regulation.

Experimental Measures

IAPS emotional memory task. The task described in *Investigation 3* provided the stimuli to which emotional reactivity were measured.

Measures of autonomic emotional response. The Vrije Universiteit Ambulatory Monitoring System (VU-AMS; Version 5fs de Geus, Willemsen, Klaver, & van Doornen, 1995; Willemsen, De Geus, Klaver, Van Doornen, & Carroll, 1996) measured autonomic arousal. The VU-AMS took continuous recordings of electrocardiogram (ECG), impedance cardiogram (ICG), and skin conductance level (SCL) data.

I used ECG to calculate heart rate (HR). HR is the most commonly used measure of autonomic reactivity in studies of emotion (Kreibig, 2010). Typically, HR increases for negatively valenced emotions such as fear, sadness, anger, and anxiety, and decreases for positively valenced emotions, such as affection and contentment (although not always for happiness) (Kreibig, 2010). To measure HR, ECG was recorded from three disposable, pre-gelled Ag-AgCl electrodes attached in a triangular, equidistant configuration on the precardium (the area of the chest ventral to the heart), with signals sampled at 500 Hz.

Although many studies examining autonomic responses to emotional stimuli use measures of heart rate variability, I did not take this approach because the stimulus duration was too short in this project (each IAPS picture was presented for 7 s). Measures of heart rate variability require an interval of at least 100 s (de Geus et al., 1995). Furthermore a commonly reported measure of heart rate variability, the low frequency band, has been shown to be an unreliable measure of sympathetic autonomic response (Willemsen et al., 1996).

Instead, I used the ICG to measure variables that are excellent indicators of autonomic reactivity (Willemsen et al., 1996). For the ICG, electrical resistance through the chest is measured as a function of blood volume variation while passing a constant current of 350 mA, 50 kHz through the chest cavity. I measured ICG by placing four spot-electrodes in a configuration consisting of two electrodes on the back that supply high-frequency current, and two measuring electrodes on the chest, to detect the voltage drop over the thorax. To get accurate ICG readings free from artefact, the ICG signal was delivered through a low-pass filter with a cut-off frequency of 60 Hz.

From the ICG, I calculated pre-ejection period (PEP) and left ventricular ejection time (LVET). PEP is a measure of sympathetic activity that is not influenced by the parasympathetic branch of the ANS (Willemsen et al., 1996). This measure is therefore particularly relevant for this research, given that the sympathetic branch of the ANS is activated in response to stress, while the parasympathetic system is activated during times of physiological calmness and digestion (Kreibig, 2010). PEP is described as the interval from left ventricular depolarisation to the opening of the aortic valve. The shorter the PEP value, the higher the degree of sympathetic autonomic reactivity (i.e., the quicker the interval between the electrical signal and aortic opening; Lozano et al., 2007).

LVET, similarly to PEP, is also a measure of the degree of sympathetic autonomic reactivity. LVET represents left ventricular contractility. The lower the LVET value, the higher the degree of autonomic reactivity.

SCL was recorded using the constant voltage method (0.5 V), sampled at 10 Hz. Activity was measured in microSiemens (mS) conductance units, and provided an index of emotional arousal independent of valence (Frazier, Strauss, & Steinhauer, 2004). Ag-AgCl non-polarizable finger electrodes (6 mm diameter contact area) filled with isotonic saline gel were attached to the distal phalanx surfaces of participants' middle and index fingers on the non-dominant hand.

These four indices (HR, PEP, LVET, and SCL) were measured for each IAPS picture presented during the IAPS emotional memory task described in *Investigation 3*. Each measurement began 3 s before the onset of the stimulus, and ended 2 s after the end of the stimulus to allow for a complete physiological response to each stimulus (Cacioppo, Berntson, Larsen, & Ito, 2000). At the start and end of each measurement, the Eprime software (Schneider et al., 2002) sent a marker to the VU-AMS recording to ensure correct time-locking to each picture stimulus. The four physiological indices were measured for all Picture Types (Negative, Positive and Neutral) presented in *Trial 1* (before either a period of sleep or waking) and in *Trial 2* (after either a period of sleep or waking). During the *Night* and *Day* conditions each *Trial 1* consisted of a set of 90 pictures, while each *Trial 2* consisted of a set of 135 pictures. *Trial 2* pictures consisted of 90 pictures from *Trial 1* and 45 new pictures that participants had not seen before. Measures of autonomic reactivity were analysed with respect to the pictures presented in *Trial 1* and the same 90 pictures that were re-presented during *Trial 2*. All four sets of pictures from each trial and condition were balanced for valence and arousal properties (see Appendix F).

Procedure

Figure 12 presents the procedure specific to this investigation. Recall that Figure 3 presented the complete study procedure.

Night condition. Prior to sleep, participants completed the IAPS *Trial 1* emotional memory task described in *Investigation 3*. During this task, the VU-AMS recorded ECG, ICG, and SCL for each picture stimulus. Participants were asked to rest the non-dominant hand, which was attached to the SCL electrodes, on the table in front of them. To ensure that ECG and ICG measures were not affected by varying respiratory behavior, participants were asked to remain seated throughout the procedure and to refrain from using their phones and from making exaggerated body movements. Small movements such as pushing buttons on a keypad do not affect the recording (Porges et al., 2007). Furthermore, participants completed the task on their own to ensure that their responses were not contaminated by emotional contagion from other people or influenced by any social desirability factors associated with the presence of another person. Prior to starting the IAPS task, the VU-AMS recorded 2 minutes of quiet rest to obtain baseline readings of HR, PEP, LVET and SCL.

After the 8-hour sleep period, I administered *Trial 2* of the IAPS task, and recorded ECG, ICG, and SCL in exactly the same way as during the evening pre-sleep procedure.

Day condition. I used the same procedure as for the *Night* condition, except that I used the parallel version of the IAPS emotional memory task (see *Investigation 3*). Participants spent the 8-hour interval awake rather than asleep, and were free to continue with their daily activities, but were reminded not to nap, drink caffeinated or sugary drinks, or exercise excessively.

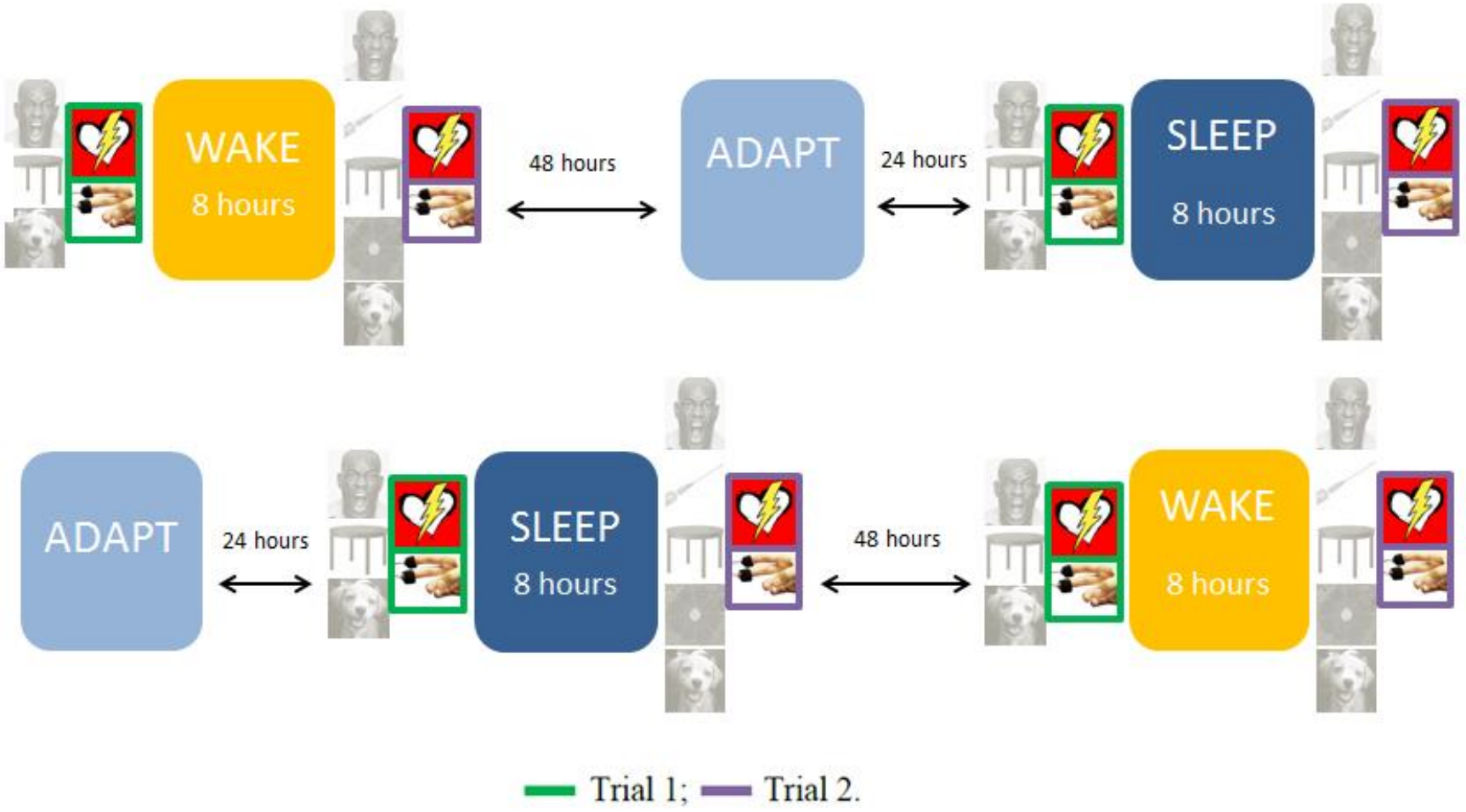

Figure 12 Study procedure for Investigation 4. Participants either completed (a) or (b), in a counterbalanced design.

Statistical Analysis

Before analyzing the VU-AMS data, I employed a number of data cleaning techniques. To ensure the ECG recording was free from artefact, I visually inspected the inter-beat interval (IBI) time series for physiologically implausible readings. Spurious short IBIs or extremely long IBIs were marked as artefact and excluded from the analysis. On average, 1-2 such short or long IBIs were excluded per participant.

Furthermore, to calculate PEP, I manually adjusted critical points on the ECG and ICG waveforms. These points were the Q-point on the ECG waveform and the B-point on the ICG waveform. This procedure is outlined in detail elsewhere (Lozano et al., 2007; Willemsen et al., 1996).

Each measurement of HR, PEP, LVET, and SCL was calculated in relation to baseline measures. That is, the average HR, PEP, LVET, and SCL value for each picture presentation interval was subtracted from the average baseline value for each physiological measure respectively. Each baseline value for all four physiological measures was recorded at the start of each trial.

Testing Hypothesis 1. Here, I tested whether PTSD-diagnosed individuals, in comparison with TE and HC individuals, had increased autonomic reactivity toward Negative pictures rather than toward Positive or Neutral pictures, and whether this effect was particularly salient across a sleep-filled rather than wake-filled delay. Increased autonomic reactivity was defined as increased HR and SCL, and decreased PEP and LVET.

To test the outlined aim, I examined differences with regard to HR, PEP, LVET, and SCL between pictures presented during *Trial 1*, and then re-presented during *Trial 2*. This analysis tested whether PTSD-diagnosed individuals, in comparison with TE and HC individuals, had significant changes (either maintained or enhanced) in emotional reactivity to old pictures (i.e., pictures presented in *Trial 2* that they had already seen in *1*). This maintenance or enhancement

of emotional reactivity for PTSD-diagnosed individuals, specifically, was hypothesized to be stronger for Negative pictures, rather than for Positive or Neutral pictures, and to be stronger within the *Night* condition than the *Day* condition.

For each outcome variable, I used a mixed-design 2 (Picture Presentation: *Trial 1* versus *Trial 2*) x 2 (Condition: Night versus Day) x 3 (Picture Type: Negative versus Positive versus Neutral) x 3 (Group: PTSD versus TE versus HC) repeated-measures ANOVA. Before I began the analyses I first examined the data for deviations from normality, sphericity and homogeneity of variance. If I found any such deviations I have noted them prior to the each results description. If I found no deviations, then I proceeded with the analysis.

Testing Hypothesis 2. Here, I set out to test whether sleep disruption in PTSD-diagnosed individuals was associated with increased autonomic reactivity, following a period of sleep, toward Negative pictures. First, I correlated REM sleep variables on which there were significant between-group differences in *Investigation 1* or that were empirically associated with emotional regulation during sleep, with autonomic reactivity variables related to Negative pictures. I then ran a series of general linear models to explore whether the sleep variables that were involved in significant correlational relationships predicted, either individually or in interaction with each other or with group membership, autonomic reactivity toward Negative pictures.

Results

Testing Hypothesis 1: Between-group differences in emotional reactivity

I began the analyses as described above, by inspecting normality for each autonomic arousal variable (HR, PEP, LVET and SCL). I examined each of those outcome variables with respect to the factors of interest (Picture Presentation, Condition, Picture Type, and Group). Several variables violated the assumption of normality – Appendix H details the results of the Shapiro-Wilk tests. I attempted to correct each violation using conventional transformations (log, square root, etc.). However, because for any particular variable normality was usually violated

for the data emerging from one group, but not for those emerging from the other groups, transformations corrected the data for the non-normally distributed group, while negatively affecting those groups that were initially normally distributed. Furthermore, there is no non-parametric substitute for mixed-design ANOVA (Field, 2009). I therefore proceeded with the conventional analysis of the untransformed, interpreting significant results with caution.

Table 19 Emotional Reactivity, Night Condition: Comparing Pictures Presented in Both Trial 1 and Trial 2

	Trial 1			Trial 2		
	PTSD	TE	HC	PTSD	TE	HC
Variable	(*n* = 21)	(*n* = 18)	(*n* = 20)	(*n* = 21)	(*n* = 18)	(*n* = 20)
ΔHR						
Negative	1.70 (3.83)	0.16 (2.50)	0.91 (4.54)	-0.22 (9.17)	3.54 (5.84)	1.33 (5.33)
Positive	1.90 (3.87)	0.88 (2.77)	1.59 (4.38)	0.26 (9.00)	4.42 (6.06)	1.66 (5.04)
Neutral	2.28 (3.69)	0.94 (2.66)	1.94 (4.64)	0.29 (8.88)	4.47 (6.02)	2.13 (7.02)
ΔPEP[a]						
Negative	1.19 (5.67)	0.10 (6.64)	2.12 (13.10)	5.03 (15.93)	7.30 (11.81)	14.61 (17.50)
Positive	1.69 (5.49)	0.31 (4.74)	1.87 (14.72)	5.59 (15.64)	8.10 (12.46)	14.23 (18.37)
Neutral	1.71 (6.23)	-0.18 (4.78)	2.03 (13.86)	6.05 (15.87)	7.44 (12.58)	14.34 (18.67)
ΔLVET[a]						
Negative	5.65 (44.75)	11.98 (55.40)	-12.00 (50.27)	28.57 (51.02)	19.29 (65.07)	-4.51 (59.15)
Positive	4.44 (42.32)	8.01 (52.55)	-12.42 (49.08)	29.65 (51.41)	19.44 (64.43)	-0.40 (62.24)
Neutral	3.83 (41.98)	6.88 (54.24)	-10.79 (46.55)	28.72 (50.67)	19.80 (67.72)	-6.20 (63.31)
ΔSCL						
Negative	-0.25 (0.53)	-0.17 (0.68)	-0.15 (0.46)	0.38 (2.46)	0.79 (2.17)	0.64 (1.91)
Positive	-0.25 (0.52)	-0.18 (0.61)	-0.15 (0.46)	0.34 (2.42)	0.80 (2.14)	0.64 (1.89)
Neutral	-0.26 (0.54)	-0.18 (0.61)	-0.15 (0.47)	0.32 (2.44)	0.83 (2.14)	0.63 (1.90)

Note. Means are presented with standard deviations in parentheses. ΔHR = heart rate, change from baseline; ΔPEP = pre-ejection period, change from baseline; ΔLVET = left ventricular ejection time change from baseline; ΔSCL = skin conductance level, change from baseline

[a]For the TE group, *n* = 16, due to equipment failure.

Table 20 Emotional Reactivity, Day Condition: Comparing Pictures Presented in Both Trial 1 and Trial 2

	Trial 1			Trial 2		
	PTSD	TE	HC	PTSD	TE	HC
Variable	(*n* = 21)	(*n* = 18)	(*n* = 20)	(*n* = 21)	(*n* = 18)	(*n* = 20)
ΔHR						
Negative	1.56 (3.38)	0.96 (2.78)	0.06 (4.03)	7.97 (8.47)	4.89 (5.76)	4.33 (11.97)
Positive	1.96 (3.18)	1.72 (2.79)	0.89 (3.66)	8.60 (8.61)	5.75 (5.33)	4.93(12.52)
Neutral	1.90 (3.46)	1.85 (3.02)	1.14 (3.45)	8.54 (8.37)	5.55 (5.44)	4.93 (12.01)
ΔPEP[a]						
Negative	1.13 (6.53)	0.00 (3.90)	2.52 (13.03)	-0.49 (11.66)	-2.13 (9.27)	1.42 (21.59)
Positive	0.83 (6.44)	-0.03 (4.03)	2.41 (12.45)	-0.57 (10.95)	-1.20 (8.78)	1.67 (21.02)
Neutral	1.00 (5.92)	-0.44 (4.48)	3.24 (12.51)	-0.50 (11.50)	-1.58 (9.18)	0.93 (21.48)
ΔLVET[a]						
Negative	5.70 (54.41)	4.22 (34.53)	-5.85 (47.18)	-5.61 (60.86)	-18.47 (39.05)	-16.16 (63.57)
Positive	7.99 (55.62)	2.23 (34.79)	-5.51 (46.52)	-3.70 (64.01)	-18.65 (33.68)	-18.44 (66.83)
Neutral	4.99 (52.89)	3.90 (35.17)	-4.54 (50.98)	-5.58 (66.27)	-18.69 (33.65)	-14.80 (65.23)
ΔSCL						
Negative	-0.17 (0.67)	-0.06 (0.45)	-0.06 (0.60)	1.71 (2.37)	0.96 (2.14)	1.07 (1.28)
Positive	-0.18 (0.68)	-0.06 (0.45)	-0.55 (0.62)	1.71 (2.32)	1.00 (2.17)	1.06 (1.28)
Neutral	-0.18 (0.68)	-0.08 (0.45)	-0.06 (0.61)	1.73 (2.33)	1.01 (2.15)	1.05 (1.27)

Note. Means are presented with standard deviations in parentheses. ΔHR = heart rate, change from baseline; ΔPEP = pre-ejection period, change from baseline; ΔLVET = left ventricular ejection time change from baseline; ΔSCL = skin conductance level, change from baseline

[a]For the TE group, *n* = 16, due to equipment failure.

Table 19 and Table 20 show the descriptive statistics related to HR, PEP, LVET and SCL for pictures presented in *Trial 1* and re-presented in *Trial 2*.

HR. Table 21 presents the results of the 2 x 2 x 3 x 3 ANOVA examining HR change in response to the same picture presented in *Trial 1* and *Trial 2*. One dataset, from a participant in the TE group, was lost because she accidentally knocked over the VU-AMS device during both the *Night* and *Day* conditions. The final sample analyzed here was therefore: PTSD, $n = 21$; TE, $n = 18$; and HC, $n = 20$.

I comment here on the four statistically significant results shown in the Table. First, the analysis detected a significant main effect of Picture Presentation. Perusal of the relevant descriptive statistics (average HR change in response to the *Trial 1* pictures = 1.35+-0.34, and to the *Trial 2* pictures = 4.08+-0.67) suggested that participants were less responsive on initial presentation than on repeat presentation.

Second, the analysis detected a significant main effect of Condition. Perusal of the relevant descriptive statistics (average HR change in response to pictures presented in the *Night* condition = 1.68+-0.62, and in the *Day* condition = 3.75+-0.71) suggested that, regardless of picture type, participants were less responsive after a sleep-filled delay than after a wake-filled delay.

Third, the analysis detected a significant main effect of Picture Type. A series of post-hoc planned contrasts suggested that (a) the HR change associated with Negative pictures was significantly lower than that associated with Neutral pictures (Negative = 2.27+-0.44; Positive = 2.88+-0.44; Neutral = 3.00+-0.43), but that (b) there was no significant difference between the HR changes associated with Positive and Neutral pictures.

Table 21 Heart Rate, Comparing Pictures Presented in Both Trial 1 and Trial 2: Results of the 2x2x3x3 mixed-design repeated-measures ANOVA (N = 59)

Variable/Effect	F	p	ESE
Main Effects			
Picture Presentation	20.51	< .001***	.27
Condition	4.17	.04*	.07
Picture Type	37.74	< .001***	.40
Contrast 1	58.58	< .001***	0.51
Contrast 2	2.02	.16	0.04
Group	0.43	.65	.02
Interaction Effects			
Picture Presentation x Condition	8.41	< .01**	.13
Picture Presentation x Picture Type	0.47	.63	.01
Picture Presentation x Group	0.62	.54	.02
Condition x Picture Type	1.16	.32	.02
Condition x Group	0.98	.38	.03
Picture Type x Group	1.30	.28	.04
Picture Presentation x Condition x Picture Type	0.10	.90	< .01
Picture Presentation x Condition x Group	2.56	.09	.08
Picture Presentation x Picture Type x Group	0.72	.58	.03
Condition x Picture Type x Group	0.13	.97	< .01
Picture Presentation x Condition x Picture Type x Group	0.41	.80	.01

Note. Contrast 1: Negative pictures vs Neutral pictures; Contrast 2: Positive pictures vs Neutral pictures. Degrees of freedom were: Picture Presentation (1, 56); Condition (1, 56); Picture Type (2, 112); Group (2, 56); Picture Presentation x Condition (1, 56); Picture Presentation x Picture Type (2, 112); Picture Presentation x Group (2, 112); Condition x Picture Type (2, 112); Condition x Group (2,112); Picture Type x Group (4, 224); Picture Presentation x Condition x Picture Type (2, 112); Picture Presentation x Condition x Group (2, 112); Picture Presentation x Picture Type x Group (4; 224); Picture Presentation x Condition x Picture Type x Group (4, 224). ESE = effect size estimate (in this case, η^2).

*p < .05. **p < .01. ***p < .001.

Fourth, the analysis detected a significant Picture Presentation x Condition interaction effect (see Figure 13 for a graphic depiction). Post-hoc planned contrasts suggested that autonomic reactivity, as indexed by change in HR, (a) was relatively similar across conditions for the initial (*Trial 1*) presentation of the pictures, but (b) was significantly larger for repeat

(*Trial 2*) presentation of the pictures within the *Day* condition than within the *Night* condition. Indeed, in the *Night* condition HR change in response to the *Trial 1* pictures was not significantly different to that for the *Trial 2* pictures, whereas in the *Day* condition participants experienced a significantly larger response to the *Trial 2* pictures.

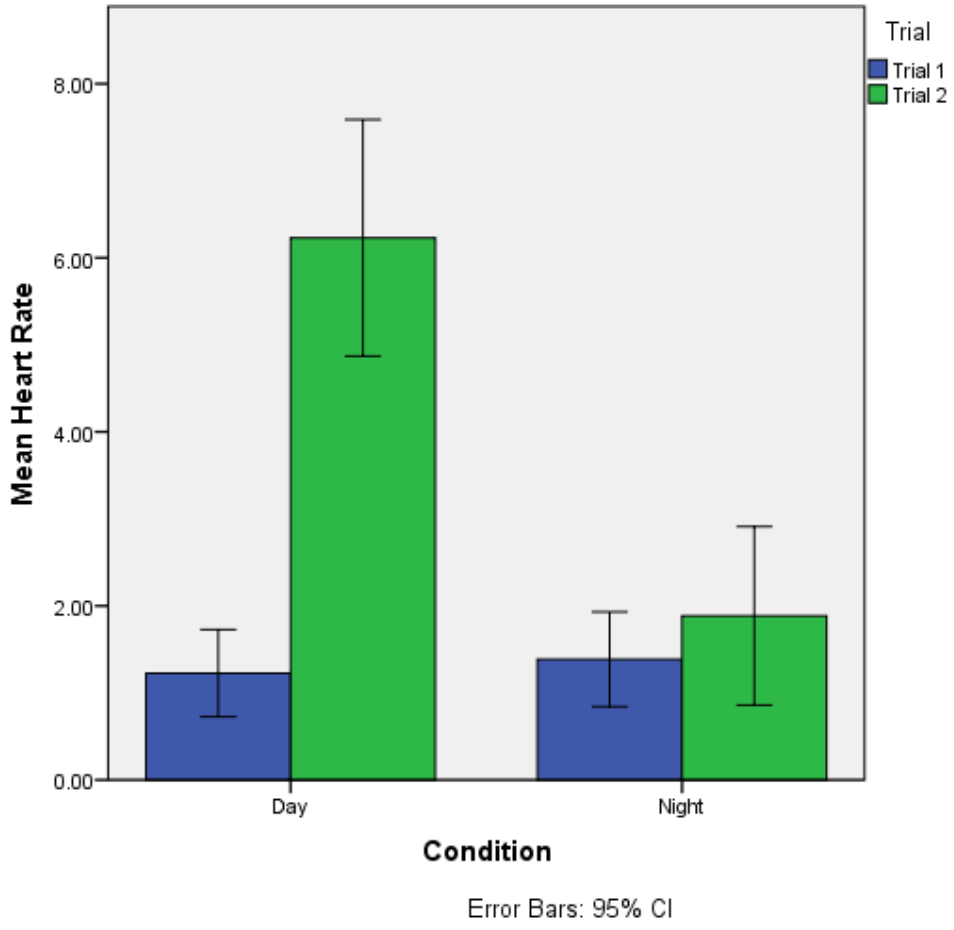

Figure 13 Heart Rate Change: Comparing autonomic reactivity to the initial presentation of a picture (on Trial 1) to the repeat presentation of that picture (Trial 2), within each of the Night and Day conditions. Error bars represent the 95% confidence interval.

Together, these results showed that PTSD-diagnosed individuals, in comparison with TE and HC individuals, did not have increased HR toward Negative pictures rather than toward Positive or Neutral pictures, and this effect was not particularly salient across the *Night* condition rather than the *Day* condition.

Although the analysis did detect main effects of Picture Presentation, Condition, and Picture Type, the significant interaction between Picture Presentation and Condition was perhaps the most informative in terms of describing participants' emotional reactivity, as indexed by a change in HR. That interaction suggested that significantly larger values of HR change in response to the second (post-delay) presentation of the pictures occurred after a wake-filled delay, but not a sleep-filled delay. One interpretation of this pattern of data, then, is that, in all participants, regardless of group assignment, and for all picture types, regardless of valence and arousal characteristics, sleep maintained a low level of emotional reactivity whereas waking activity significantly increased it.

PEP. Table 22 describes the results of the 2 x 2 x 3 x 3 ANOVA examining PEP change in response to the same picture presented in *Trial 1* and *Trial 2*. Increases in PEP reflect decreased autonomic reactivity, while decreases reflect increased autonomic reactivity. In addition to the single participant in the TE group whose data was lost due to participant error, there were technical difficulties with PEP recordings for an additional 2 participants in the TE group. The sample was therefore PTSD: $n = 21$; TE: $n = 16$; and HC: $n = 20$. In this analysis the assumption of sphericity was violated for the interaction of Condition x Picture Type. For this interaction the Greenhouse-Geisser statistic is reported.

I comment here on the three statistically significant results shown in the Table. First, the analysis detected a significant main effect of Picture Presentation. The relevant descriptive statistics (average PEP change in response to the *Trial 1* pictures = 1.19+-0.86, and to the *Trial 2* pictures = 4.46+-1.57) revealed that all participants had significantly increased PEP during *Trial 2* in comparison with *Trial 1*. This finding suggests that when the same pictures were presented a second time, participants had were less responsive.

Second, the analysis detected a significant main effect of Condition. The relevant descriptive statistics (average PEP change in response to pictures presented in the *Night*

condition =5.20+-1.57, and in the *Day* condition = 0.47+-1.45) showed that all participants had increased PEP during the *Night* condition in comparison with the *Day* condition. This finding suggests that, regardless of picture type, participants were less responsive after a sleep-filled delay than after a wake-filled delay.

Table 22 Pre-Ejection Period, Comparing Pictures Presented in Both Trial 1 and Trial 2: Results of the 2x2x3x3 mixed-design repeated-measures ANOVA (N = 57)

Variable/Effect	F	p	ESE
Main Effects			
Picture Presentation	8.52	< .01**	.14
Condition	5.70	.02*	.10
Picture Type	0.99	.37	.02
Group	1.05	.36	.04
Interaction Effects			
Picture Presentation x Condition	21.04	< .001***	.28
Picture Presentation x Picture Type	0.79	.46	.01
Picture Presentation x Group	1.32	.28	.05
Condition x Picture Type[a]	0.14	.84	< .01
Condition x Group	0.19	.83	< .01
Picture Type x Group	1.86	.12	.06
Picture Presentation x Condition x Picture Type	0.52	.59	.01
Picture Presentation x Condition x Group	1.47	.24	.05
Picture Presentation x Picture Type x Group	1.37	.25	.05
Condition x Picture Type x Group	0.97	.43	.04
Picture Presentation x Condition x Picture Type x Group	0.41	.80	.02

Note. Degrees of freedom were: Picture Presentation (1, 54); Condition (1, 54); Picture Type (2, 108); Group (2, 54); Condition x Picture Presentation (1,54); Picture Presentation x Picture Type (2, 108); Picture Presentation x Group (2, 108); Condition x Picture Type (1.71, 92.05); Condition x Group (2,108); Picture Type x Group (4, 216); Picture Presentation x Condition x Picture Type (2, 108); Picture Presentation x Condition x Group (2, 108); Picture Presentation x Picture Type x Group (4; 216); Picture Presentation x Condition x Picture Type x Group (4, 216). ESE = effect size estimate (in this case, η^2).[a] Greenhouse-Geisser statistic reported;

* $p < .05$, ** $p < .01$, *** $p < .001$

Thirdly, the analysis detected a significant Picture Presentation x Condition interaction effect (see Figure 14 for a graphical depiction). Post-hoc planned contrasts revealed that although participants' had similar PEP measurements during *Trial 1* across both the *Night* and *Day* condition, during *Trial 2* participants experienced a significant increase in PEP across the *Night* condition. During *Trial 2* of the *Day* condition PEP was slightly negative in comparison with baseline. These results suggest that after a sleep-filled delay participants experienced a significantly attenuated response to *Trial 2* pictures, while after a wake-filled delay they experienced a slight increase in response.

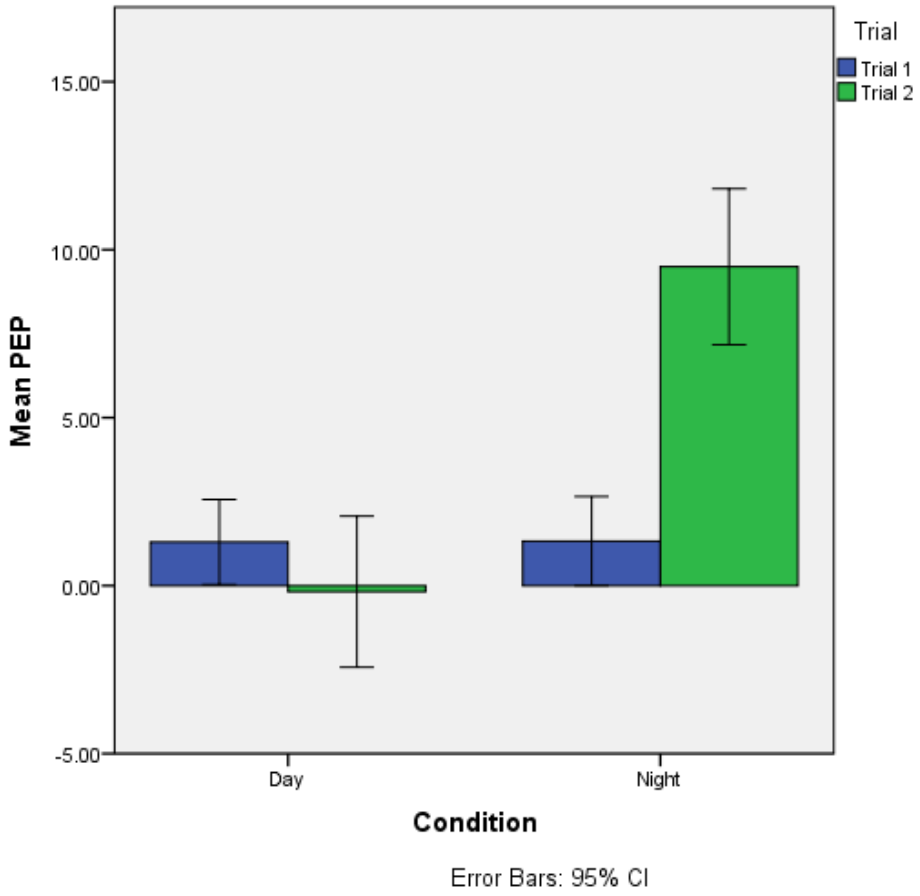

Figure 14 Pre-Ejection Period Change: Comparing autonomic reactivity to the initial presentation of a picture (on Trial 1) to the repeat presentation of that picture (Trial 2), within each of the Night and Day conditions. Error bars represent the 95% confidence interval.

Taken together these results corroborate the findings related to HR, showing that PTSD-diagnosed individuals, in comparison with TE and HC individuals, did not have decreased PEP for Negative pictures rather than Positive or Neutral pictures, and this effect was not particularly salient across the *Night* condition rather than the *Day* condition. Rather, increased autonomic reactivity, indexed by decreased PEP, was greatest across waking, rather than sleep and across *Trial 1*, rather than *Trial 2*. Furthermore the interaction between Picture Presentation and Condition revealed that while participants had similar PEP during *Trial 1* irrespective of Condition, in relation to *Trial 2* they had somewhat decreased PEP after a wake-filled delay, and significantly increased PEP after a sleep-filled delay. This result suggests that sleep attenuated autonomic reactivity to pictures of all valence and arousal categories and for all participants.

Table 23 Left Ventricular Ejection Time, Comparing Pictures Presented in Both Trial 1 and Trial 2: Results of the 2x2x3x3 mixed-design repeated-measures ANOVA (N = 57)

Variable/Effect	F	p	ESE
Main Effects			
Picture Presentation	0.01	.94	< .01
Condition	1.99	.16	.04
Picture Type	0.36	.70	.01
Group	1.51	.23	.05
Interaction Effects			
Picture Presentation x Condition	13.27	< 0.01**	.20
Picture Presentation x Picture Type	0.66	.52	.01
Picture Presentation x Group	1.43	.25	.05
Condition x Picture Type	0.63	.53	.01
Condition x Group	0.32	.73	.01
Picture Type x Group	1.14	.34	.04
Picture Presentation x Condition x Picture Type	1.48	.23	.03
Picture Presentation x Condition x Group	0.42	.66	.02
Picture Presentation x Picture Type x Group	0.46	.77	.02
Condition x Picture Type x Group	1.05	.38	.04
Picture Presentation x Condition x Picture Type x Group	1.33	.26	.05

Note. Degrees of freedom were: Picture Presentation (1, 54); Condition (1, 54); Picture Type (2, 108); Group (2, 54); Condition x Picture Presentation (1,54); Picture Presentation x Picture Type (2, 108); Picture Presentation x Group (2, 108); Condition x Picture Type (2, 108); Condition x Group (2,108); Picture Type x Group (4, 216); Picture Presentation x Condition x Picture Type (2, 108); Picture Presentation x Condition x Group (2, 108); Picture Presentation x Picture Type x Group (4; 216); Picture Presentation x Condition x Picture Type x Group (4, 216). ESE = effect size estimate (in this case, η^2).

** $p < .01$

LVET. Table 23 describes the results of the 2 x 2 x 3 x 3 ANOVA examining LVET change in response to the same picture presented in *Trial 1* and *Trial 2*. As for PEP increases in LVET reflect decreased autonomic reactivity, while decreases reflect increased autonomic reactivity. As for PEP, participant error and recording error reduced the number of participants in the TE group with the final sample related to LVET detailed as PTSD: $n = 21$; TE: $n = 16$; and HC: $n = 20$.

I comment here on the one statistically significant result shown in the Table. This analysis detected a significant Picture Presentation x Condition interaction effect (see Figure 15 for a graphic depiction). Post-hoc planned contrasts revealed that although participants' had similar LVET measurements during *Trial 1* across both the *Night* and *Day* condition, during *Trial 2* participants experienced a significant increase in LVET after the *Night* condition. During *Trial 2* of the *Day* condition LVET was strongly negative in comparison with baseline. These results suggest that after a sleep-filled delay participants experienced a significantly attenuated response to *Trial 2* pictures, while after a wake-filled delay they experienced a significant increase in response.

Taken together these results corroborate the findings related to HR and PEP, showing that PTSD-diagnosed individuals, in comparison with TE and HC individuals, did not have decreased LVET for Negative pictures rather than Positive or Neutral pictures, and this effect was not particularly salient across the *Night* condition rather than the *Day* conditio. Most importantly, and in line with HR and PEP measures, the significant interaction between Picture Presentation and Condition revealed that while participants had similar LVET during *Trial 1* irrespective of condition, during *Trial 2* participants experienced strongly negative LVET after a wake-filled delay and strongly positive LVET after a sleep-filled delay. This finding suggests that participants in this study experienced increased autonomic reactivity after a period of waking and decreased autonomic reactivity after a period of sleep in response to pictures of all valence and arousal categories.

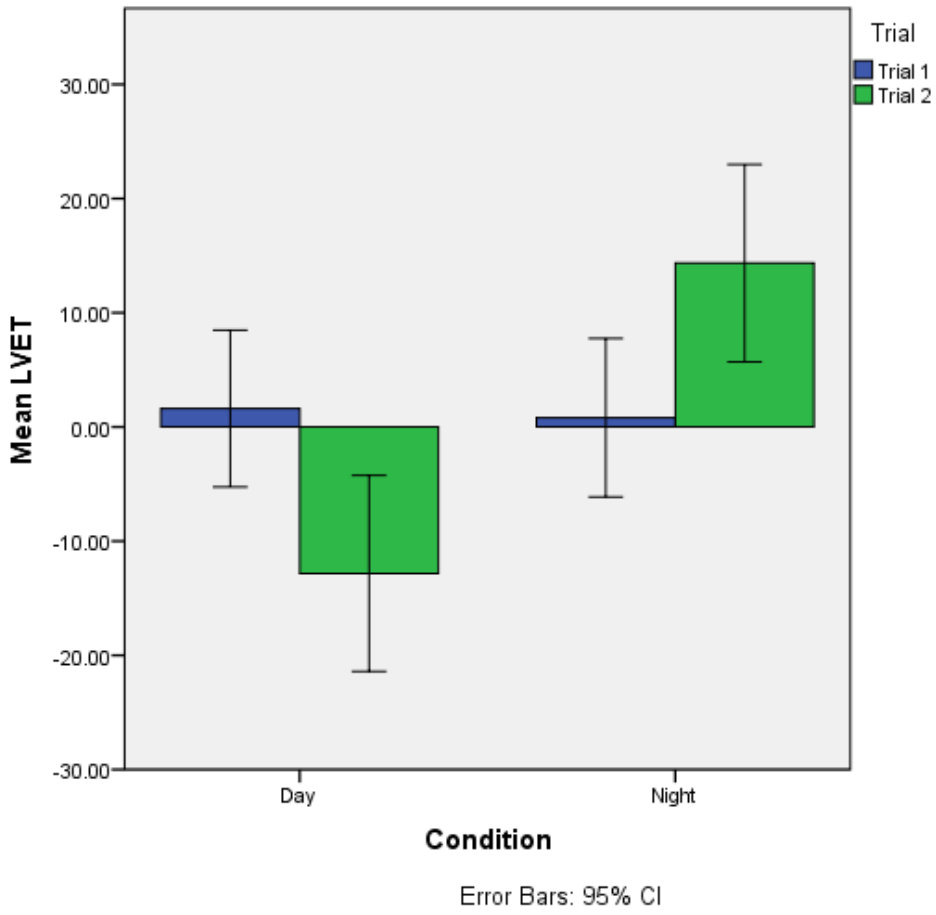

Figure 15 Left Ventricular Ejection Time Change: Comparing autonomic reactivity to the initial presentation of a picture (on Trial 1) to the repeat presentation of that picture (Trial 2), within each of the Night and Day conditions. Error bars represent the 95% confidence interval.

SCL. Table 24 describes the results of the 2 x 2 x 3 ANOVA examining SCL change in response to the same picture presented in Trial 1 and Trial 2. There was only participant in the TE group whose data was lost due to participant error, as for HR measures. The sample was therefore PTSD: n = 21; TE: n = 18; and HC: n = 20. The assumption of sphericity was violated for the interaction of Condition x Picture Type. For this interaction the Greenhouse-Geisser statistic is reported.

I comment here on the one statistically significant result shown in the Table. The analysis detected a significant main effect of Picture Presentation. The relevant descriptive statistics (average SCL change in response to the *Trial 1* pictures = -0.15+-0.06, and to the *Trial 2* pictures

= 0.93+-0.18) revealed that all participants had significantly increased SCL during *Trial 2* in comparison with *Trial 1*. This finding suggests that when the same pictures were presented a second time, participants were more responsive.

There were no significant interactions between any factors. However when examining the means associated with the Picture Presentation and Condition interaction, which was significant with respect to HR, PEP and LVET, the means showed a similar trend as the other variables of autonomic reactivity, despite not reaching statistical significance and having a small effect size, *Night* condition, *Trial 1*: M = -0.19, SE = 0.07; *Night* condition, *Trial 2*: M = 0.60, SE = 0.28; *Day* condition, *Trial 1*: M = -0.10, SE = 0.8; *Day* condition, *Trial 2*: M = 1.26, SE = 0.26. The pattern of means suggested that while participants had approximately similar SCL during *Trial 1*, the increase in SCL from *Trial 1* was greater during *Trial 2* after a wake-filled delay in comparison with a sleep-filled delay.

Taken together these results corroborate the findings related to HR, PEP and LVET showing that PTSD-diagnosed individuals, in comparison with TE and HC individuals, did not have decreased SCL for Negative pictures rather than Positive or Neutral pictures, and this effect was not particularly salient across the *Night* condition rather than the *Day* condition. The only significant result related to SCL showed that participants had greater SCL when re-exposed to the same pictures during *Trial 2* in comparison with *Trial 1*. There were no significant interactions between any variables, including Picture Presentation and Condition which showed significant interactions for HR, PEP and LVET. However for SCL the means related to this interaction showed a similar pattern as for the other variables of autonomic reactivity.

Table 24 Skin Conductance Level, Comparing Pictures Presented in Both Trial 1 and Trial 2: Results of the 2x2x3x3 mixed-design repeated-measures ANOVA (N = 59)

Variable/Effect	F	p	ESE
Main Effects			
Picture Presentation	42.96	< 0.001***	.43
Condition	3.03	.09	.05
Picture Type	0.20	.82	< .01
Group	0.10	.99	< .01
Interaction Effects			
Picture Presentation x Condition	2.14	.15	.04
Picture Presentation x Picture Type	0.38	.68	.01
Picture Presentation x Group	0.31	.74	.01
Condition x Picture Type[a]	0.94	.38	.02
Condition x Group	0.67	.52	.02
Picture Type x Group	1.90	.12	.06
Picture Presentation x Condition x Picture Type	0.59	.56	.01
Picture Presentation x Condition x Group	0.94	.40	.03
Picture Presentation x Picture Type x Group	1.77	.14	.06
Condition x Picture Type x Group	0.86	.49	.03
Picture Presentation x Condition x Picture Type x Group	0.63	.64	.02

Note. Degrees of freedom were: Picture Presentation (1, 56); Condition (1, 56); Picture Type (2, 112); Group (2, 56); Picture Presentation x Condition (1, 56); Picture Presentation x Picture Type (2, 112); Picture Presentation x Group (2, 112); Condition x Picture Type (2, 112); Condition x Group (2,112); Picture Type x Group (4, 224); Picture Presentation x Condition x Picture Type (2, 112); Picture Presentation x Condition x Group (2, 112); Picture Presentation x Picture Type x Group (4; 224); Picture Presentation x Condition x Picture Type x Group (4, 224). ESE = effect size estimate (in this case, η^2).

[a] Greenhouse-Geisser statistic reported; *** $p < .001$

Testing Hypothesis 2: Predicting emotional reactivity across a sleep-filled delay using sleep variables

Although *Hypothesis 1* was disconfirmed, the results of several analyses testing that hypothesis allowed the interpretation that sleep attenuated emotional reactivity in response to all

picture types, for all participants. I therefore conducted correlations to further describe any associations between emotional reactivity and sleep.

Regarding the emotional reactivity variables that were involved in the correlational analyses, I selected these based on the results of the analyses, described above, that tested Hypothesis 1. Specifically, these were the outcome variables for which the analyses detected (a) statistically significant main effects of Condition, or (b) statistically significant Condition-related interaction effects. In other words, because the focus here was on examining the effects of sleep versus waking on emotional reactivity, the Condition factor was of prime importance. Hence, the variables were HR, PEP, and LVET. For more detail regarding the variable selection process and the composition of those variables, please see Appendix I.

Regarding the sleep variables that were involved in the correlational analyses, because *hypothesis 1* in the current investigation did not demonstrate between-group differences in emotional reactivity, it was no longer relevant to include sleep variables that showed between-group differences in the correlation analysis. There are still relatively few studies examining the relationship between sleep and emotional reactivity, so I correlated all subjective and objective sleep variables with measures of emotional reactivity. I also included depression severity as a correlate, given that the groups were not matched with respect to depression severity. Table 25 shows the resulting correlation matrix.

HR in response to Negative, Positive and Neutral pictures showed significant but small positive correlations with subjective sleep quality (PSQI) indicating that increased HR was associated with greater disruptions in subjective sleep quality. There was a significant but small positive correlation between HR in response to Negative pictures and depression severity indicating that increased HR was associated with greater depression severity.

LVET related to a comparison of the same pictures presented during *Trial 1* and *Trial 2* showed a significant but small positive correlation with NREM 2 percentage, indicating that

higher LVET values were associated with increased NREM 2 percentage. Higher LVET values indicate decreased autonomic reactivity. Furthermore, surprisingly there was a significant but small negative correlation between LVET and SWS percentage, indicating that increased autonomic reactivity (signalled by decreased LVET) was associated with increased SWS percentage.

Table 25 Correlation Matrix: Associations between Emotional Reactivity, Sleep Outcome Variables, and Depression Severity (N =56)

	HR			PEP	LVET
Variable	Negative	Positive	Neutral		
Subjective Sleep					
PSQI	**0.27***	**0.27***	-0.04	-0.03	0.04
Laboratory PSQI	0.09	0.01	< 0.01	0.12	-0.05
Objective Sleep					
Sleep Latency	-0.06	-0.20	-0.10	0.14	0.02
Sleep Efficiency	-0.06	0.09	0.04	0.06	-0.03
Awakenings	0.08	-0.01	-0.01	-0.08	0.12
Spontaneous Arousals	0.04	0.04	0.05	0.08	-0.03
WASO	0.18	0.06	0.09	-0.15	0.02
NREM 1 percentage	-0.03	-0.09	-0.07	0.05	0.14
NREM 2 percentage	0.04	-0.04	-0.03	-0.18	**0.27***
SWS percentage	-0.02	0.07	0.09	0.19	**-0.26***
REM percentage	-0.02	0.01	-0.06	-0.12	0.05
REM Latency	0.13	0.10	0.18	0.13	-0.08
REM Arousal	0.05	0.05	0.02	-0.07	0.07
REM→ NREM1/W	-0.03	0.02	-0.05	0.09	0.15
NREM1 + SWS	< 0.01	0.08	0.08	0.11	**-0.24**†
BDI-II	**0.29***	0.23†	**0.24**†	0.12	0.09

Note. Data are for Spearman's *rho* correlation coefficient. HR = heart rate; PEP = pre-ejection period; LVET = left ventricular ejection time; PSQI = Pittsburgh Sleep Quality Index; WASO = the number of minutes spent awake after sleep onset; REM → NREM1/W = REM arousals leading to NREM1 or wake; NREM1 + SWS = composite of NREM1 percentage and SWS percentage; BDI-II = Beck Depression Inventory – second edition.

$^{\dagger}p < .10$. *$p < .05$. **$p < .01$.

Building on these correlational findings, and using the statistically significant associations as a guide, I used 4 separate general linear models to assess the influence of the relevant sleep outcome variables and depression severity on emotional reactivity following a sleep-filled delay. I constructed these models with (a) change in HR (in response to Negative, Positive, or Neutral pictures), and (b) change in LVET (from pictures presented initially on *Trial*

1 to their re-presentation on *Trial 2*) as outcome variables. To construct the models, I entered as predictors all sleep outcome variables that correlated at $p \leq .10$ with the emotional reactivity outcome variable in question as well as depression severity, and all two-way interactions featuring these variables. I only entered 6 variables or associated interactions at a time, so as to ensure there was no inflation of Type I error as a result of a large number of terms in comparison with the sample size. After I had entered all the terms, I examined the model for significant contributors to the outcome as well the overall variance explained. I removed non-contributing variables, starting with two-way interactions, working iteratively toward a significant model that explained the largest amount of variance in emotional reactivity following a period of sleep.

The model building process revealed only one statistically significant model. This model showed that NREM 2 percentage was a significant predictor of the change in LVET from initial picture presentation on *Trial 1* to re-presentation of that picture on *Trial 2*, $F(1) = 4.31$, $p = .04$, $R^2 = .07$ (adjusted $R^2 = .05$). This was the only significant predictor, and it was associated with a small effect size.

Secondary analyses. I conducted a number of analyses that were not part of the primary set of analyses designed to test the major hypotheses. These secondary analyses sought to clarify relationships between variables based on previous research findings although they were not of critical relevance to the current project.

Noradrenergic activity and emotional reactivity. Previous literature suggests that nighttime noradrenergic activity may impact the processing of emotional tone during sleep (e.g., Goldstein & Walker, 2014). Based on this literature I correlated nighttime urinary normetadrenaline metabolite values (representing noradrenergic activity) with emotional reactivity for Negative, Positive and Neutral pictures. No significant correlations emerged between nighttime normetadrenaline values and variables of autonomic arousal.

Summary of Results

Both *hypothesis 1* and *hypothesis 2* were disconfirmed. The analyses suggested that PTSD-diagnosed participants, in comparison with TE and HC participants, did not have increased emotional reactivity, indexed by autonomic reactivity, for highly-arousing negatively-valenced pictures when a period of sleep filled the delay between initial picture presentation and repeat presentation. Because there were no-between group differences I could not test *hypothesis 2* which posited that between-group differences would be predicted by sleep variables.

Irrespective of findings related to between-group differences, the analyses also demonstrated no differences in participants' responses to pictures of different valence and arousal categories. The only exception here was related to HR measures when comparing Negative, Positive and Neutral pictures. Here the results surprisingly indicated that HR in response to Negative pictures was associated with a smaller change from baseline than for Neutral pictures.

Although the hypotheses were disconfirmed, the results of *hypothesis 1* suggested that there were prominent differences in participants' responses to all pictures after either a period of waking or a period of sleep. Overall, the attenuation of emotional reactivity was evident and consistent for pictures initially presented before bedtime and then re-presented after a period of sleep. For three of the four autonomic arousal variables, outcome was predicted by an interaction between Picture Presentation (i.e., when the picture was presented, *Trial 1* or *Trial 2*) and Condition (i.e., *Night* versus *Day*), showing that autonomic arousal was either maintained at a low level or attenuated when a period of sleep, but not waking, filled the delay between picture presentations. The re-presentation of pictures after a period of waking was associated with elevated emotional reactivity. These findings are not confirmatory of the primary hypotheses, although they do support the broader objective of the study which is to demonstrate the importance of sleep for emotional reactivity, measured here by variables of autonomic reactivity.

Although there was a consistent reduction in emotional reactivity after sleep, none of the models I tested made a persuasive argument that specific elements of sleep were responsible for this attenuation. The only model that included a significant predictor was one where, for LVET related to a comparison of the same pictures first presented before sleep and re-presented after sleep, increased NREM 2 percentage predicted decreased autonomic reactivity. Subjective sleep variables and depression severity, although associated with measures of HR, did not predict any variable of emotional reactivity.

CHAPTER EIGHT: DISCUSSION

This research project set out to investigate the characteristics and mechanisms of sleep disruption in PTSD-diagnosed individuals. Based on the findings from the first investigation, I aimed to evaluate whether, and how, sleep disruption in PTSD-diagnosed individuals impacted neutral declarative memory performance, emotional memory performance, and emotional reactivity. This series of investigations was based on findings related to sleep in healthy individuals, which show that sleep is vital for neutral declarative and emotional memory consolidation, as well as attenuation of emotional reactivity.

In this concluding chapter of the dissertation, I will discuss the findings related to each investigation (*Investigations 1-4*) separately before I comment on how the findings from the investigations are related to one another.

Investigation 1: Describing Disordered Sleep in PTSD

Investigation 1 had two aims. First, it aimed to clarify (given the inconsistencies reported in the literature) the characteristics of sleep disruption in PTSD-diagnosed individuals, relative to the observed sleep architecture in TE and HC individuals. Second, it aimed to examine whether PTSD-diagnosed individuals had elevated levels of nighttime noradrenaline and whether this elevation disrupted sleep in this clinical population, in comparison with participants in the other groups. Overall, then, this investigation sought to test the proposal that elevated nighttime noradrenaline is a mechanism that might explain patterns of sleep disruption in PTSD.

Objective and subjective sleep disruption in PTSD. Regarding the first aim, the analyses of objective sleep measures revealed that, on average, PTSD-diagnosed individuals spent a larger percentage of sleep time in light sleep than the average participant in the other two groups. Spending relatively more time in light sleep is therefore associated with a PTSD

diagnosis, rather than with trauma exposure per se. Indeed, the analyses detected no differences in NREM 1 percentage between TE and HC participants.

Both PTSD and TE participants spent less time in SWS than HC participants, indicating that sleep depth was compromised in these two groups. The findings demonstrated no difference between PTSD and TE participants with respect to the time spent in SWS. These results indicate that there is a clear difference in SWS percentage between those who have experienced trauma and those who have not. Interestingly, however, a PTSD diagnosis alone is not associated with an individual being less likely to spend time in SWS, over and above the experience of trauma.

Considering that Kobayashi et al. (2007) found that two of the main differences between PTSD-diagnosed individuals and control participants were increased NREM 1 percentage and decreased SWS percentage, I created a composite of those two variables. The findings with respect to this composite variable revealed that PTSD-diagnosed participants had decreased sleep depth (a combination of more NREM 1 percentage and decreased SWS percentage) in comparison with both TE and HC participants. Furthermore TE participants showed the same pattern of decreased sleep depth in relation to HC participants. Furthermore, when examining sleep depth as a single concept comprised of measures of NREM 1 percentage and SWS percentage, the findings showed that differences were observed between PTSD and the other groups as well as between TE and HC participants. Between-group differences in NREM 1 percentage only or SWS percentage only were evident between (a) PTSD-diagnosed participants and all control participants, or between (b) participants in both trauma groups and healthy controls, respectively. Thus, using a single variable to capture sleep depth may provide greater sensitivity in measuring graded sleep disruption between those with a formal PTSD diagnosis, those who experience trauma but who do not develop PTSD, and healthy individuals without any significant trauma experience and psychiatric diagnoses.

The analyses detected no between-group differences in any of the other sleep variables. Hence, in this sample it appears that, for example, PTSD-diagnosed individuals, relative to controls, took on average a similar amount of time to fall asleep, had a similar amount of sleep in comparison to time in bed, had a similar amount of awakenings and arousals, had a similar amount of NREM 2 percentage and REM percentage, and experienced a similar number of arousals from REM sleep (both non-specific and leading to NREM 1 or waking).

Collectively, these results suggest that those in the PTSD, TE, and HC groups experienced relatively similar patterns of sleep, when indexed by PSG measures. Where PTSD-diagnosed individuals did experience relative sleep disruptions, these were related to sleep-stage specific disturbances, rather than gross disturbances in their sleep architecture.

These findings are congruent, to some extent, with the current literature. Certainly, they are consistent with the meta-analysis by Kobayashi et al. (2007), who also found increased NREM 1 percentage and decreased SWS percentage in PTSD-diagnosed individuals compared to controls. However, most of the studies included in that meta-analysis used samples of male war veterans. Out of 20 studies, 13 had a male war veteran only sample, with another 6 studies having largely male samples with mixed trauma etiology and only 1 study having a female-only sample (with unknown trauma aetiology). Because female participants with non-war related trauma etiologies are underrepresented in the literature, it has not been clear whether their sleep patterns are similar to those exhibited by male war veterans. The results of this study suggest that although it is important to consider sex and trauma aetiology in any study, participants of both sexes and different trauma etiologies may experience increased NREM 1 percentage and decreased SWS percentage. These findings are corroborated by a study examining sex differences in sleep in participants with and without PTSD (Kobayashi & Mellman, 2012). The authors found no differences in NREM 1 percentage or SWS percentage between men and

women, but did find that women with PTSD had greater difficulties with sleep maintenance, spending more time awake after sleep onset than women without PTSD or men.

Since the publication of the Kobayashi et al. (2007) meta-analysis, several other studies examining sleep in PTSD-diagnosed individuals have entered the literature. However, no updated systematic review or meta-analysis incorporates these newer studies, except for a general meta-analysis of sleep in the context of several psychiatric disorders (Baglioni et al., 2016). This latter meta-analysis, with stringent inclusion and exclusion criteria, found that sleep in PTSD is characterised primarily by deficits in sleep continuity (defined by a combination of less sleep efficiency, longer sleep latency, and increased awakenings) and decreased sleep depth (defined by a combination of increased NREM 1 percentage and decreased SWS percentage).

In contrast to Kobayashi et al. (2007), Baglioni et al. (2016) found that deficits in sleep continuity were the most prominent deficit in PTSD (effect size g = - 0.72, in comparison to sleep depth where g = - 0.23). However, because of the stringent inclusion and exclusion criteria (such as excluding studies where psychoactive medication was not discontinued and only including studies that had a healthy control group), only 13 studies were included in this analysis. Only 7 of the 20 studies that had been included in the Kobayashi et al. (2007) meta-analysis were included, and several new studies that did not meet the study criteria were also excluded (e.g., Germain et al., 2013; Kobayashi et al., 2014; Lipinska, Timol, Kaminer, & Thomas, 2014; Mellman et al., 2014; van Liempt, Vermetten, Lentjes, Arends, & Westenberg, 2011). Baglioni et al. (2016) excluded studies that recorded only 1 night of PSG data, despite the fact that PTSD-diagnosed individuals do not show altered sleep patterns on the first night in the sleep laboratory in comparison with a subsequent night (Herbst et al., 2010). Baglioni et al. (2016) also only included studies that used a healthy control group, whereas some otherwise excellent studies only used a trauma-exposed control group. From this point of view, the meta-analysis by Baglioni et al. (2016) excludes a very large amount of data relevant to the study of

sleep in PTSD. In mitigation, of course, is the fact that the intention of those authors was to compare the sleep profiles of several psychiatric disorders, rather than to provide a detailed analysis of the data relevant to PTSD. Therefore, a more updated meta-analysis is required to provide a state-of-the-science examination of the literature on sleep and PTSD. At this point the most comprehensive results regarding sleep characteristics in PTSD-diagnosed individuals are still provided by Kobayashi et al. (2007), and the findings presented here are largely consistent with those presented in that meta-analysis.

The results reported in *Investigation 1* differ from the extant literature in that they showed no between-group differences on any REM sleep parameters. Although I did not measure REM density because of limitations associated with our recording software, PTSD-diagnosed individuals did not experience relative alterations in REM percentage, increased REM arousals, or increased REM arousals leading to NREM 1 or waking.

Data from previously published studies suggest that PTSD is characterised by a number of REM sleep alterations. In fact, some studies have reported increased REM percentage (e.g., Engdahl et al., 2000), whereas others have reported decreased REM percentage (Lavie, Hefez, Halperin, & Enoch, 1979; Lipinska et al., 2014). Furthermore, several studies report increased REM density (e.g., Dow, Kelsoe, & Gillin, 1996; Raboni, Alonso, Tufik, & Suchecki, 2014), a finding that is supported by both of the abovementioned meta-analyses. Kobayashi et al. (2007) found increased REM density in all but one of the studies they reviewed, with a cumulative effect of $d = 0.43$, while Baglioni et al. (2016) found increased REM pressure (defined by shorter REM latency, increased REM density, and increased REM percentage) with a cumulative effect size of $g = 0.54$. Furthermore, many authors have shown that REM fragmentation, measured as arousals from REM sleep or as the average duration of a REM segment, is increased in PTSD-diagnosed individuals in comparison with controls (e.g., Breslau et al., 2004; Habukawa, Uchimura, Maeda, Kotorii, & Maeda, 2007; Mellman et al., 2014). Mellman (2002) showed that

increased REM fragmentation in the aftermath of a trauma predicted subsequent PTSD diagnosis. Together, these findings related to REM sleep have led some authors to believe that sleep disruption in PTSD is characterised primarily by REM alterations, even though disruptions in sleep continuity and depth are also evident in PTSD-diagnosed individuals (Spoormaker & Montgomery, 2008).

Clearly, however, not all PTSD studies report REM sleep abnormalities. A recent study by Mellman et al. (2014) demonstrated that there is a progression of REM-associated symptoms from early diagnosis to chronic PTSD, which may explain why, across studies, different results are reported regarding REM-related symptoms. In that study, 80 individuals in the PTSD group had carried the diagnosis between 11 and 75 months. The results showed that REM sleep was decreased and fragmented, with longer REM latency, for those participants with a recent diagnosis of PTSD (from several months to a few years) compared to those with long-standing PTSD (several years). Participants with long-standing PTSD tended to have unchanged or increased REM sleep with shorter REM latency. These results suggest that the chronicity of the condition is an important factor to consider when examining the presentation of sleep disruption.

In the current study, the time between trauma experience and study participation (and therefore PTSD duration), was tightly controlled, with a relatively short duration (M = 1.30, SD = 1.02 years). Given that most participants had experienced trauma relatively recently, it is not clear why this study failed to demonstrate between-group differences in REM-related parameters, while Mellman et al. (2014) found that short trauma duration was significantly associated with the presentation of REM-related disruptions.

Subjective sleep quality and the sleep laboratory environment. The importance, generalizability, and overall validity of the results related to objective measures of sleep are contingent on the assumption that sleep in the laboratory is a fair (although admittedly imperfect) approximation of sleep in the home environment. However, an unfamiliar environment, such as a

sleep laboratory, can impact sleep quality negatively, especially on the first night in that environment. This is known as the first night effect (Tamaki, Bang, Watanabe, & Sasaki, 2016). Although sleep researchers attempt to correct for the first night effect by including an adaptation night (see, e.g., Herbst et al., 2010; Lorenzo & Barbanoj, 2002), for some individuals the disparity between many aspects of the sleep environment and the home environment remains substantial.

For instance, the participants in this study all lived in low-SES communities. Many lived in shanty towns, in over-crowded houses, with constant all-night activity on the roads outside. Participants often co-slept with other family members. Nighttime criminal activities, such as house break-ins, are common in their communities. Therefore, the quiet single-occupant environment of the sleep laboratory differed substantially from their home sleep environments. Given this disparity in environments, it is plausible that participants' sleep quality differs between the two environments, and sleep in the laboratory is not a good approximation of everyday sleep in the home environment.

One obvious solution that would counteract the disparity between home and laboratory environments, would be to take PSG recordings in the home environment. Such recording is, however, technologically impractical for many laboratories (including ours, currently), and is particularly challenging when participants are drawn from communities where their, and the researchers', safety at night cannot be guaranteed. Furthermore, the introduction of a device, a particular new set of behaviours and the knowledge of external monitoring into the home sleep environment may not guarantee a valid representation of everyday sleep.

Instead of overcoming the confound of different sleep environments, researchers can measure whether the same sleep quality is achieved in both environments by recording subjective sleep experiences. Such a contingency measure would allow researchers to understand whether the objective sleep measures they obtain are likely to represent everyday sleep quality.

For example, if laboratory objective and laboratory subjective measures correlate strongly, and, simultaneously, subjective (and independent) measures of sleep quality in the laboratory and in the home also correlate strongly, then objective measures of sleep are more likely to represent everyday sleep accurately. However, although several studies record subjective sleep experiences in the laboratory using visual analog scales, sleep diaries or unstandardized questionnaires, the vast majority of studies do not control for the difference between laboratory subjective and home subjective sleep quality (for exceptions see, Herbst et al., 2010; Kobayashi, Huntley, Lavela, & Mellman, 2012).

In this study, I administered the PSQI to measure recent (past month) sleep quality in the home environment, and an adapted version of the PSQI to measure sleep quality in the laboratory environment. The results suggested that, on average, PTSD-diagnosed participants reported significantly poorer subjective sleep quality in their home environment. However, these significant between-group differences disappeared when examining subjective sleep quality in the laboratory. Furthermore, according to the recommendations regarding PSQI interpretation, a cut-off score of 5 indicates clinical sleep disruption. With the exception of one individual PTSD-diagnosed participants scored well above this cut-off when rating their home sleep quality. However their mean laboratory sleep quality score was marginally greater than 5, indicating very minimal sleep disruption in that environment.

These results suggest that, on average, PTSD-diagnosed individuals slept better in the sleep laboratory than in their home environment, whereas participants in the TE and HC groups experienced similar sleep quality across the two environments. Furthermore, these results are not likely explained by the electrodes and equipment that participants slept with, because there were no between-group differences in how participants perceived the equipment to impact on their sleep quality. The vast majority of participants (52 of 60) indicated that the equipment did not influence their sleep quality at all. These results indicate that other factors related to the sleep

environment must account, at least partially, for the disparity between sleep quality at home and in the laboratory with respect to PTSD-diagnosed individuals.

Despite the lack of routine measurement of subjective sleep quality comparing the two environments, several studies have noted that PTSD-diagnosed individuals may sleep better in the laboratory than at home, because such participants may perceive the former environment as safe (Hurwitz, Mahowald, Kuskowski, & Engdahl, 1998; Kobayashi et al., 2012; Spoormaker & Montgomery, 2008). The authors of those studies speculate that a perception of safety may lead to decreased overall anxiety and hyperarousal, and therefore increased sleep quality. In the present study, participants' qualitative responses regarding the difference in their sleep quality between the two environments (see Appendix E) suggests that many participants attribute their improved sleep quality to a perception that the laboratory environment was safer, quieter, and more comfortable than their home environment.

Comparing objective and subjective sleep quality measures. Many studies have noted that there is a discrepancy between subjective and objective measures of sleep in PTSD-diagnosed individuals (see, e.g., Klein, Koren, Arnon, & Lavie, 2003; Woodward, Friedman, & Bliwise, 1996). Studies using subjective measures consistently report a variety of sleep complaints associated with PTSD (see, e.g., Chakravorty et al., 2014; Giosan et al., 2015; Werner, Griffin, & Galovski, 2016; Pigeon et al., 2011). In contrast, studies using objective measures, such as polysomnography, report inconsistent findings (see, e.g., Calhoun et al., 2007; Engdahl et al., 2000; Yetkin et al., 2010). Consequently, the suggestion has emerged that PTSD diagnosed individuals demonstrate sleep-state misperception – that is, they over-report their sleep difficulties, which in reality are smaller than they perceive them to be (Lavie, 2001).

In the current sample of PTSD-diagnosed individuals, in comparison to participants in the TE and HC groups, subjective measures of sleep in the home environment showed clear clinical sleep disruption, while objective measures showed relatively few indications of sleep disruption.

One possible conclusion from this set of results is that PTSD-diagnosed individuals have sleep-state misperception. An alternative explanation, however, is that these participants do experience poor sleep in their home environment, but that their sleep quality is improved when they sleep in the laboratory.

The latter explanation is more likely. In this sample, objective sleep measures were correlated with participants' subjective sleep quality in the laboratory; this statement is especially true for PTSD-diagnosed individuals. For example, in those individuals, poor laboratory subjective sleep quality was associated with less sleep efficiency, more time spent awake after sleep onset, and more frequent awakenings. However, this significant association between objective and subjective sleep measures was not present for subjective sleep measures of everyday sleep, which showed significant sleep disruption in PTSD-diagnosed individuals. Because objective measures of sleep in PTSD-diagnosed individuals showed some, but relatively little, sleep disruption, and there is congruency between laboratory-based objective and subjective sleep measures in this clinical group, it is likely that PTSD-diagnosed individuals did experience some improvement in their sleep quality in the laboratory.

Other authors have also noted evidence contradicting the sleep-state misperception in PTSD. Kobayashi et al. (2012) directly examined the validity of the sleep-state misperception in PTSD-diagnosed individuals (with either current or a recovered lifetime diagnosis) in comparison with TE and HC participants. They measured sleep quality using two objective measures (polysomnography and actigraphy) and two subjective measures (self-report questionnaire and sleep diary). Actigraphs were used for home recording, while polysomnography was used in the laboratory. They found that PTSD-diagnosed individuals with current symptoms did not over-report their sleep disturbance. Instead, all participants over-reported their total sleep time using sleep diaries in comparison with actigraphy, except for participants with current PTSD symptoms. These latter participants were accurate about the

length of time they slept. However, PTSD-diagnosed participants were not accurate at estimating total sleep time when comparing sleep diaries to PSG measures recorded in the laboratory. Kobayashi et al. (2012) speculated that perhaps individuals with current PTSD symptoms were more vigilant in their home environment, and therefore more accurate about their sleep duration, than participants in the other groups. However, in the sleep laboratory individuals with current PTSD symptoms may have felt safer than in their home environment and may therefore have been less vigilant.

Herbst et al. (2010) compared 2 nights of PSG recording in two settings – in the laboratory and at home. They found that when PTSD-diagnosed participants, in comparison with healthy controls, experienced their first recording night at home, they had higher REM density, which is a sign of REM dysregulation. However, this effect was not observed when PTSD-diagnosed participants spent their first night in the sleep laboratory. These results suggest that the home environment, rather than the laboratory environment, may be associated with a greater degree of sleep disruption in PTSD.

With respect to the improvement in sleep quality experienced by PTSD-diagnosed individuals in the laboratory, the observation that participants with current PTSD symptoms may feel less safe and more vigilant in their home environment is made in both this study and that of Kobayashi et al. (2012). Overall, then, I suggest that PTSD-diagnosed participants may have better sleep quality in the laboratory than in the home environment. Furthermore, in some studies, particularly those that compare everyday subjective sleep quality (e.g. measured by the PSQI) with objective PSG measures, notions of sleep-state misperception in PTSD may be an artefact of environment.

Noradrenergic activity at night does not predict sleep disruption in PTSD.

Regarding the second objective of this investigation, I aimed to test the hypothesis that elevated noradrenergic activity at night may be one mechanism explaining sleep disruption in

PTSD-diagnosed individuals. I specifically measured noradrenergic activity because it is an index of autonomic arousal. PTSD is characterised by increased hyperarousal, which from a neurobiological point of view can be measured by different indicators of autonomic arousal.

There were no between-group differences in noradrenergic measures, either overall or specifically over the night rather than across waking. This result indicates that PTSD diagnosed individuals did not have elevated noradrenergic activity at night and subsequently I was not able to investigate a relationship between elevated nighttime noradrenergic activity and sleep disruption in PTSD.

However, previously published studies have shown, using a variety of measures, that PTSD-diagnosed individuals have elevated autonomic arousal at night. For example, Mellman, Kumar, et al. (1995) showed that urinary noradrenergic measures were elevated in PTSD diagnosed individuals at night in comparison with control participants. Furthermore, in that study the degree of noradrenergic activity was correlated with the degree of sleep disruption.

A more recent study showed that a heart rate variability measure, which indicates parasympathetic activity, was lower at night in PTSD-diagnosed individuals than in controls (Kobayashi et al., 2014). Activity in the parasympathetic nervous system is associated with calmness, digestion, and sleep. Hence, when the activity of this system is attenuated, this indicates activation of autonomic systems. These results therefore suggest that sleep in PTSD-diagnosed individuals is associated with greater autonomic activity. Furthermore, the findings indicated that that in relation to sleep duration, PTSD-diagnosed individuals showed dysregulated autonomic activity, while TE participants showed regulated autonomic activity. In a follow-up study, Kobayashi, Lavela, Bell, and Mellman (2016) showed that the dysregulation of autonomic activity during sleep in PTSD-diagnosed participants in comparison to TE participants, may be related to decreased REM percentage. Van Liempt et al. (2013) also showed that PTSD diagnosed individuals in comparison with control participants have increased HR

during sleep, although Bertram et al. (2014) found that PTSD diagnosed individuals have increased HR during both waking and sleep.

Despite this rapidly growing thread in the literature suggesting that, in comparison with controls, nighttime autonomic activity is increased in PTSD-diagnosed individuals during sleep, there is still little direct evidence that increased autonomic activity during sleep is a causal mechanism underlying sleep disruption in this clinical population. The current findings do not provide clarity with respect to this hypothesised causal mechanism.

There are a number of possible explanations as to why the current analyses did not detect between-group differences in nighttime autonomic activity, as measured by urinary metabolites of noradrenaline. One possibility is that PTSD-diagnosed individuals do not actually have elevated autonomic reactivity at night and that the other research studies have spurious findings. However, because the studies have reported different measures of autonomic activity and still come to a similar conclusion, this possibility is unlikely. Furthermore, it is difficult to directly compare the findings reported in this study with those of Mellman, Kumar, et al. (1995), Kobayashi et al. (2014), Kobayashi, Lavela, Bell, and Mellman (2016), and Van Liempt et al. (2013), because each study measured a different aspect of autonomic arousal or used different metabolite measures.

Another possible explanation for a lack of significant findings with respect to noradrenergic activity is that all participants in this sample had elevated noradrenergic activity. Although participants had normetadrenaline metabolite values in the normal range, all participants in this study come from areas of Cape Town that have high poverty and crime statistics. Given the environments participants live in, all of them might have experienced some degree of long-standing increased autonomic arousal. Animal models have shown that rats living in environments that promote chronic stress do experience chronically elevated and aberrant noradrenergic activity (Morilak et al., 2005).

Yet another possibility is that inferring centrally produced noradrenergic activity from urinary measures can be unreliable (Hinz, Stein, & Uncini, 2011). However, I used this method because previous studies had demonstrated that PTSD-diagnosed individuals did have elevated noradrenergic activity using urinary measures (Mellman et al., 1995; Yehuda, Southwick, Giller, Ma, & Mason, 1992).Despite these confirmatory findings there are some inconsistencies in the literature - some other studies have not found that urinary metabolites of noradrenaline are elevated during sleep in PTSD-diagnosed individuals (see, e.g.,Yehuda et al., 1998). Furthermore, one study showed that while noradrenergic activity was elevated in PTSD-diagnosed individuals in comparison with healthy controls when measuring cerebrospinal fluid concentrations (CSF; the only true way to measure brain-derived noradrenergic concentrations), measurement of peripheral plasma-based noradrenergic activity did not corroborate the findings from CSF measurements (Geracioti et al., 2001). In summary, although urinary measures have, on occasion, yielded results that confirm elevations in noradrenergic activity in PTSD, peripheral measures derived from urine or plasma may not always be aligned accurately to the production of noradrenaline in the brain.

Summary of Investigation 1. The results of *Investigation 1* show that PTSD diagnosed participants experienced few objectively measured sleep disruptions. The disruption they do experience are characterised by a combination of more NREM 1 percentage and less SWS percentage, in comparison to both TE and HC participants. Furthermore TE participants showed the same pattern of sleep disruption in comparison with HC participants. These results are congruent with past research. There were no observable between-group differences in REM parameters, although other studies have demonstrated a variety of REM sleep abnormalities in PTSD diagnosed individuals.

The analysis of participants' subjective sleep revealed that PTSD diagnosed individuals had poorer subjective sleep in their home environment in comparison with both TE and HC

individuals. However in the sleep laboratory their self-rated sleep was equivalent to TE and HC participants. Furthermore, objective measures of sleep correlated with subjective laboratory sleep quality rather than subjective home sleep quality. This relationship was particularly evident for PTSD-diagnosed participants rather than participants in the other two groups, highlighting that sleep quality in the laboratory is different, and likely improved, than sleep quality in the home environment for this clinical group. These findings may account for the observation in some studies that PTSD-diagnosed individuals have better objective sleep quality in the laboratory than their reported subjective sleep quality, especially in instances where studies have not compared self-reported laboratory and home sleep quality.

Furthermore in this study I did not demonstrate between-group differences in nighttime noradrenergic function in PTSD diagnosed individuals in comparison with control participants. Noradrenergic measures were obtained to indicate the level of autonomic activity. Other studies have shown that PTSD diagnosed individuals have increased autonomic activity at night, measured by a variety of measures such as noradrenaline, heart rate variability and HR. The lack of findings in the present study may be because all participants had elevated noradrenergic activity. An alternative explanation is that using urinary noradrenergic measures as a proxy for centrally produced noradrenaline is not always accurate.

Investigation 2: Neutral Declarative Memory Processing During Sleep in PTSD

This investigation I aimed to test the hypothesis that PTSD-diagnosed individuals, in comparison with TE and HC participants, have specific deficits in nighttime neutral declarative memory consolidation. The investigation also aimed to test the hypothesis that daytime measures of memory performance in PTSD would be characterised by the widely reported impairments in immediate and delayed recall. Finally, the investigation aimed to examine whether sleep disruption in PTSD-diagnosed individuals predicted nighttime neutral declarative memory deficits.

Neutral declarative retention is impaired across a sleep-filled delay in PTSD. The results of the current investigation showed that during waking hours PTSD diagnosed individuals in comparison with both TE and HC participants had deficits in neutral declarative immediate recall and delayed recall but not retention. However, after a sleep-filled delay, PTSD-diagnosed individuals, in comparison with HC participants, showed impaired performance on recall and retention measures of previously-learned neutral declarative information. These results suggest that deficits in retention of such information might be traced to specific sleep-related mechanisms. The analyses detected no differences in memory performance between TE and HC participants. Hence, it appears that mere trauma exposure is not enough to affect memory performance, although the fairly small sample in this study would fail to detect small effect sizes. Therefore, the relationship between those with and without trauma exposure remains unclear.

To my knowledge, this is the first study in PTSD to demonstrate a different pattern of neutral declarative memory deficits related to sleep and waking. Whereas three other published studies have investigated the association between sleep disruption and neutral declarative memory performance in PTSD-diagnosed individuals (Brownlow, Brown, & Mellman, 2014; Lipinska et al., 2014; van Liempt et al., 2011), none have included a daytime control condition. The inclusion of this condition is important for two reasons. First, without a daytime control condition one cannot infer that the neutral declarative memory deficits that manifest in PTSD-diagnosed individuals after a period of sleep are specific to the effects of sleep, or merely reflect the passage of time. The current investigation demonstrated that retention (i.e., a comparison of what was recalled after a delay to what was learned initially) is impaired in PTSD-diagnosed individuals when the delay is filled with sleep but not when it is filled with waking activity. This finding suggests that the retention deficit might be traced to some sleep-specific mechanism.

Second, the inclusion of a daytime control condition, and the subsequent observations made in this investigation, may shed light on a long-standing conundrum related to the kinds of

memory deficits, and associated neuroanatomical findings, reported in PTSD-diagnosed individuals. Regarding neutral declarative memory performance during waking, many studies, including this one, have demonstrated that PTSD is characterized by deficits in immediate and delayed recall, but not retention (Johnsen & Asbjornsen, 2008). That is, PTSD-diagnosed individuals, in comparison with controls, may initially encode less information, and may later recall less information, but they do not retain less information over time (i.e., in PTSD-diagnosed individuals, the percentage of encoded information recalled after a waking delay is similar to that of controls; (Vasterling & Brailey, 2005)).

With respect to the measurement of neutral declarative memory, memory retention, in contrast with immediate and delayed recall, is the measure of memory most reliant on the hippocampus (Kramer et al., 2004; Samuelson, 2011; Sass et al., 1992). This is because one critical memory function associated with the hippocampus is that of consolidation of newly acquired information. This consolidation process is most reliably measured by a comparison of initial learning and subsequent recall after a delay (i.e. retention; Kramer et al., 2004). However, many studies have demonstrated that PTSD-diagnosed individuals do not have deficits in neutral declarative memory retention despite having smaller hippocampi than controls. Furthermore, some, but not all, studies investigating associations between abnormalities in hippocampal size/function and memory performance have shown positive correlations; several studies have not reported such a relationship (Woodward et al., 2009). Taken together, these findings highlight a disjuncture between cognitive performance and neuroanatomical findings in PTSD: At the cognitive level PTSD diagnosed individuals have neutral declarative memory deficits; at the neuroanatomical level they have smaller hippocampi than control participants. Although the hippocampus has a well-established role in memory functioning, memory deficits ordinarily observed in PTSD are not the kind that are the most reliant or associated with hippocampal functioning in these individuals. Together, these findings characterize an uneven literature, and

suggest that another factor plays a role in the relationship between deficits in memory performance and the size and functioning of the hippocampus in PTSD-diagnosed individuals.

Despite the fact that I did not measure hippocampal volume or functioning, the findings of this investigation suggest that sleep may play a connecting role between neutral declarative memory deficits and hippocampal functioning in PTSD. The data reported here indicate that PTSD-diagnosed individuals do have deficits in retention of neutral declarative information, but that this deficit occurs only in the presence of a sleep-filled delay, and not in the presence of a wake-filled delay. The inference one might make, then, is that these individuals experience disruptions of sleep-dependent consolidation. These consolidation processes involve hippocampal activation. Speculatively, the smaller hippocampi that characterize PTSD-diagnosed individuals may not function adequately during sleep-dependent consolidation processes, resulting in relatively poor performance on measures of retention administered the following day. Furthermore, and equally speculatively, if adequate consolidation does not occur during sleep, brain networks may be saturated for next-day encoding, resulting in deficits on next-day tests of immediate and delayed recall in this clinical population.

Sleep disruption in PTSD predicts neutral declarative retention deficits. The initial part of this investigation's analysis, summarized above, suggested that PTSD-diagnosed individuals retained less information over a sleep-filled delay – the same pattern of retention deficits was not observed over a wake-filled delay. These findings suggest that sleep-dependent memory consolidation is impaired in this group of participants. To examine this inference further, I examined whether certain sleep parameters were associated with the observed retention deficit in in PTSD-diagnosed. I first correlated sleep variables for which *Investigation 1* provided evidence of between-group differences, or for which previous studies provide evidence of potential implication in the relationship between sleep and memory. Having thus identified the sleep variables that were, in this sample, significantly associated with retention scores after a

sleep-filled delay, I built a series of general linear models that would delineate more clearly the relationship between group membership, objectively measured sleep, depressive symptomatology, and retention.

The models suggested that neither SWS percentage nor a combination of NREM 1 percentage and SWS percentage predicted the amount of information that was retained over a sleep-filled delay. This finding stands in contrast to those from many previously published studies that have demonstrated the importance of SWS for consolidation of neutral declarative material (Feld & Diekelmann, 2015; Genzel, Kroes, Dresler, & Battaglia, 2014; Marshall et al., 2006; Walker, 2009b). Those studies show that SWS consolidates memory through two complementary processes: (i) *active systems consolidation* refers to the distribution of memories from hippocampal networks to neocortical areas, and (ii) *synaptic homeostasis* refers to the removal of synapses that are weakly potentiated, leaving only strongly potentiated synapses behind (Diekelmann & Born, 2010). Considering those data, and the fact that PTSD in this sample is characterized by neutral declarative retention deficits over a sleep-filled delay and a combination of more NREM 1 percentage and less SWS percentage, it is surprising that this retention deficit and that aspect of sleep disruption are not related.

One possible explanation that may account for the lack of association described above is related to the fact that SWS is not the only sleep stage associated with memory consolidation. While earlier work on sleep-dependent memory consolidation emphasised the role of SWS, several studies have demonstrated that REM sleep is also vital to the memory consolidation process. A number of electrophysiological markers that are present during REM sleep are theorized to represent processes of learning and memory consolidation. Theta activity during REM, both in animal models and human studies, is associated with improved memory consolidation (Boyce et al., 2016; Fogel, Smith, & Cote, 2007). Furthermore, silencing REM-specific theta activity in rats suppresses memory consolidation (Boyce et al., 2016).

Consistent with these studies, my findings revealed that REM arousals leading to NREM 1 or waking predicted retention scores after a sleep-filled delay. Apart from this main effect, the analyses also detected that the interaction between group membership and REM arousals leading to NREM 1 or waking was a significant predictor of retention. This interaction suggested that PTSD-diagnosed individuals who have more REM arousals leading to NREM 1 or waking have poorer retention, while TE and HC participants who have fewer such arousals have better retention. Furthermore, this interaction was associated with a medium-to-large effect size.

Interestingly, this set of findings was specific to REM arousals that led to a lighter stage of sleep or to awakening; the number of non-specific REM arousals was not a significant predictor of retention deficits. This finding highlights that disruptions in REM continuity (REM fragmentation) are key in predicting neutral declarative retention deficits, rather than temporary arousals that may not affect the continuity of this sleep stage.

REM fragmentation in PTSD-diagnosed individuals may lead to discontinuity of the normal consolidation processes that occur during REM sleep. Current evidence suggests that theta rhythm may be central to REM-related memory consolidation. This is because theta rhythm entrains ponto-geniculo-occipital (PGO) waves. PGO waves, which are not reported in PSG studies because they are impossible to measure via surface EEG in humans, play a critical role in the expression of immediate early genes (IEGs; Hutchison & Rathore, 2015). It is the expression of these genes, according to animal models, that is critical to REM-related memory consolidation as their expression leads to LTP, which ensures that synapses are strengthened to form long-lasting connections (Ribeiro et al., 2002).

Speculatively, one possible mechanism explaining the association between REM disruption and decreased neutral declarative memory consolidation in PTSD is that fragmented REM disrupts the continuity of the theta rhythm. Disrupted theta rhythm may, via its association to PGO waves, result in decreased IEG expression and an inability to form long-lasting memory

representations as demonstrated in this study by decreased delayed recall on waking and a subsequent retention deficit in PTSD diagnosed individuals. This speculation is supported by a recent study comparing PTSD-diagnosed individuals to TE participants that showed that during REM sleep, specifically, those participants carrying a PTSD diagnosis had less theta power over right prefrontal regions.

Although this explanation is appealing, it does not account for the finding in this study, and in many others (e.g., Brewin et al., 2007; Johnsen & Asbjornsen, 2008), that PTSD-diagnosed individuals have impaired performance on tests of immediate and delayed recall, but not on tests of retention, when tested during normal waking hours, and when the delay is filled with waking activity. That pattern of memory deficits is more consistent with an account suggesting that memory networks are saturated and unable to perform successful next-day encoding after unsuccessful consolidation during sleep. Although SWS is strongly associated with the restoration of memory networks through *active system consolidation* and *synaptic homeostasis* that leave hippocampal and other brain networks refreshed for next-day encoding, a recent study showed that REM sleep is also implicated in restorative processes. Grosmark, Mizuseki, Pastalkova, Diba, and Buzsaki (2012) showed that firing rates are unexpectedly decreased during REM sleep in contrast with NREM sleep in the rat hippocampus, suggesting a downscaling of neuronal activity in preparation for next-day encoding (Feld & Diekelmann, 2015). These results suggest that restorative processes leaving the hippocampus refreshed for next-day encoding might not be isolated to SWS, and that REM sleep may also play a role in such restoration.

Furthermore, Blanco et al. (2015) showed that REM-related processes of (1) gene expression leading to localised strengthening of synapses, and (2) downscaling leading to networks that are ready for next-day encoding, are not mutually exclusive. Those authors suggested that, instead, those two processes may work together to optimise memory

consolidation. The data reported here suggest, indirectly, that both processes are interrupted. That is, memory retention across a sleep-filled delay is impaired, suggesting that IEG expression is disrupted; daytime encoding and subsequent retrieval after a wake-filled delay are impaired, suggesting a failure of downscaling.

These findings illustrate the importance of examining, delineating, and measuring the cognitive, affective, and behavioural consequences of different sleep-stage impairments in PTSD-diagnosed individuals. Furthermore, the significance of the current study is that it presents data congruent with previous research showing SWS disruption in PTSD, but simultaneously illustrates that it is the more subtle REM-related disruptions that contribute to functional impairment. This finding is consistent with the observation that sleep disruption in PTSD is characterised primarily by REM sleep abnormalities (Spoormaker & Montgomery, 2008).

This is the fourth study, to my knowledge, investigating the relationship between sleep disruption and neutral declarative memory performance in PTSD-diagnosed individuals. The results of three of those studies, including the current one, suggest a relationship between REM sleep and consolidation of neutral declarative memories consolidation in this clinical population (Brownlow et al., 2014; Lipinska et al., 2014). In contrast, Van Liempt et al. (2011), studying PTSD, TE, and HC participants, found that sleep fragmentation in the first, SWS-rich, half of the night, predicted delayed recall after sleep in all participants. PTSD-diagnosed participants had significantly poorer recall after sleep than HC participants. However, those authors did not report REM-related parameters in their study, so it is unclear whether measures of REM fragmentation were investigated. Although further research is needed to delineate the contributions of SWS and REM sleep to neutral declarative memory deficits, the current study corroborates previous findings that highlight REM disruption as central.

Furthermore I also examined whether depression severity had any impact in its own right, or in interaction with sleep variables and/or group membership, in predicting neutral declarative

retention deficits following a sleep-filled delay. The findings demonstrated that this clinical feature did not, as a stand-alone clinical characteristic, or in combination with any other variable, have any such predictive value. This result suggests that PTSD diagnosis, over and above depression severity, is predictive of such deficits.

Broader considerations regarding sleep-dependent memory consolidation. Related to broader examinations of the role of sleep in memory consolidation unrelated to specific sleep-stage investigations, some authors have suggested that sleep-dependent consolidation functions because there is no interference during the sleep period, whereas waking life is characterised by continued encoding, which may act to erode memories (see e.g., Feld & Diekelmann, 2015; Walker, 2009a). Within that theoretical perspective, sleep merely protects memories from eroding, rather than actively consolidates them. The current findings stand in contrast to predictions emerging from that theory. Instead, they demonstrate that in a population that may be vulnerable to consolidation deficits, disrupted sleep is associated with a loss of information over time. If sleep functioned only to protect memories from eroding, the prediction would be that PTSD-diagnosed individuals would not show a specific retention deficit across sleep, unless there was evidence that during sleep their brains were actively encoding or processing information in such a way as to erode memories. There is no evidence of these processes during sleep in PTSD-diagnosed or any other individuals, and in the current study PTSD-diagnosed participants did not spend more time awake, or have more spontaneous arousals, than TE or HC participants. These findings therefore strengthen the body of evidence suggesting that consolidation is an active process that needs to occur in order for memories to strengthen over time. Without active sleep-dependent consolidation, the strength of memory traces is lost, an effect that is not demonstrated, even in vulnerable individuals, across wake-filled intervals.

Summary of Investigation 2. This investigation showed, consistent with previous research, that PTSD-diagnosed individuals, in comparison with HC participants, have deficits in

immediate and delayed recall of neutral declarative information across waking. Across a sleep-filled interval, however, PTSD-diagnosed participants showed deficits in both delayed recall and retention, suggesting that, in comparison with HC participants, their sleep-dependent memory consolidation is impaired. Furthermore, the degree of this impairment was predicted by degree of REM fragmentation. That is, PTSD-diagnosed participants who experienced more REM arousals leading to a discontinuity of REM sleep also had impaired memory retention, likely representing impaired memory consolidation. In contrast to predictions emerging from previous studies, SWS was not associated with or predictive of the amount of information retained after a sleep-filled delay. Although PTSD-diagnosed individuals had decreased SWS percentage in comparison with HC participants, only REM fragmentation was associated with cognitive impairment.

Investigation 3: Emotional Memory Processing During Sleep in PTSD

In *Investigation 3*, I tested the prediction that PTSD-diagnosed individuals, in comparison with TE and HC participants, would demonstrate increased recognition accuracy and recognition bias for highly-arousing negative information, rather than highly-arousing positive or low-arousing neutral information. I also tested the prediction that this pattern of recognition accuracy and recognition bias would be particularly prominent when a sleep-filled delay, rather than a wake-filled delay, separated learning from recall. Furthermore, I also set out to test the proposition that sleep disruption, particularly that related to REM sleep parameters, predicted increased recognition accuracy and recognition bias towards highly-arousing negative information in PTSD-diagnosed individuals.

No increase in recognition accuracy or recognition bias for negative information across sleep in PTSD. The results of the analysis showed that PTSD-diagnosed individuals did not have greater recognition accuracy or recognition bias towards highly-arousing negative pictures, either after a sleep-filled or wake-filled delay, in comparison with TE and HC participants. The first observation generated by these findings, is that they are in contrast to the

results reported in *Investigation 2*, where I demonstrated that PTSD-diagnosed individuals retained less neutral declarative information over a sleep-filled delay and that this retention deficit was predicted by a higher degree of REM fragmentation experienced by these individuals. The findings reported here demonstrate no between-group differences and consequently I could not investigate whether sleep disruption was related to the hypothesised between-group differences. I will discuss this discrepancy between *Investigations 2* and *3* in greater detail in the last section of the *Discussion*. I discuss subsequent observations emerging from findings related to *Investigation 3* in the sections below.

Recognition accuracy. The results suggested that all participants, regardless of group assignment, and across both sleep and waking delays, recognized highly-arousing negative pictures significantly more accurately than both highly-arousing positive and low-arousing neutral pictures. Based on previous findings, I would have expected PTSD-diagnosed individuals and to a lesser extent TE participants to have greater recognition accuracy for highly-arousing negative pictures (Golier et al., 2003; McNally et al., 1998). However, research indicates that individuals free from psychopathology have better memory for both highly-arousing negative and highly-arousing positive information than for neutral information (Buchanan & Lovallo, 2001; Walker & van der Helm, 2009). Therefore, I would have expected participants in the HC group, to remember both highly-arousing negative and highly-arousing positive information better than low-arousing neutral information.

One possible explanation for this result is imbedded in the participants' daily environment. All the women who participated in this study lived in low-SES urban neighborhoods. Whereas most adults in South Africa will experience at least one traumatic event in their lifetimes (Koen et al., 2016), rates of exposure to violence are substantially higher in low-SES urban areas (Seedat, Van Niekerk, Jewkes, Suffla, & Ratele, 2009). These areas have some of the highest crime rates in the world with respect to murder, sexual assault, and intimate

partner violence (Prinsloo, Matzopoulos, Laubscher, Myers, & Bradshaw, 2016). Although participants in the HC group had not personally witnessed or experienced a DSM-IV traumatic event, their awareness of such events would likely be heightened given that such crimes and their subsequent traumatic repercussions are ubiquitous in low-SES South African environments. Research demonstrates that in contexts where security needs are prioritized, individuals are highly sensitive to highly-arousing negative stimuli (Higgins, 1997; Sassenberg, Sassenrath, & Fetterman, 2015). Hence HC participants, who are likely to prioritise security given their threat-salient environments, may have heightened sensitivity to highly-arousing negative stimuli. This heightened sensitivity to highly-arousing negative stimuli may lead to better memory for such information, at the expense of highly-arousing positive information, which may not be prioritised to the same extent.

So, when data from the *Night* and *Day* conditions were analyzed together, participants' performance on the recognition task suggested significantly better accuracy when dealing with highly-arousing negative pictures than with either highly-arousing positive or low-arousing neutral pictures. When data from the *Night* and *Day* conditions were considered separately, however, a different pattern of results emerged: Participants' accuracy when dealing with low-arousing neutral pictures was significantly different depending on whether a period of sleep or a period of waking filled the delay between initial exposure and recognition testing. In the *Day* condition, accuracy for low-arousing neutral pictures was worse than for highly-arousing negative or highly-arousing positive pictures. In the *Night* condition, however, accuracy for low-arousing neutral pictures was equivalent to that for the other two picture types. This set of results suggests that sleep consolidated stimuli from all valence and arousal categories in a balanced way, whereas waking was associated higher recognition accuracy for highly-arousing negative pictures rather than pictures in the other categories.

These results stand in contrast to several studies which show that sleep preferentially consolidates valenced and arousing information over neutral information (Groch, Zinke, Wilhelm, & Born, 2015; Morgenthaler et al., 2014; Nishida et al., 2009; Wagner, Hallschmid, Rasch, & Born, 2006). For example, Walker and Tharani (2009) showed that participants who experienced normal sleep after learning negative, positive, and neutral information, had superior retention for both negative and positive information over neutral information.

In another study, Atienza and Cantero (2008), examining emotional memory retention using a sleep deprivation paradigm, found similar results. In this study all participants were exposed to negative, positive and neutral pictures that ranged in arousal rating from high to medium arousal. After encoding the pictures, half of the participants were sleep deprived, while the other half experienced normal sleep (controls). After a 1 week delay that allowed for the effects of sleep deprivation to wear off, participants were asked to differentiate between pictures from the original set and those from a new set that were interspersed with the original pictures (recognition memory task). Their results showed that participants in the sleep deprivation group had intact recognition for negative, but not positive, information. Similarly, those participants showed intact recognition for highly-arousing information, but controls showed better retention of information with medium arousal ratings. Furthermore, those participants that had normal sleep after encoding had better recognition accuracy for negative, positive, and highly-arousing information than for neutral and low-arousing information. The results of this study, then, suggested that sleep deprivation enhances recognition accuracy towards negative and highly-arousing information over positive and medium-arousing information, and confirmed that healthy sleep consolidates valenced (both negative and positive) and highly-arousing information over neutral and low-arousing information.

In this study, unlike in that by Atienza and Cantero (2008), participants were not sleep deprived. Indeed, the PSG results (reported in detail in *Investigation 1*) indicated that there were

no significant between group-differences in sleep efficiency, and that participants, regardless of group assignment, spent approximately equivalent amounts of time awake after sleep onset. Furthermore, both sleep efficiency and WASO values were generally in the normal range. Given this set of sleep circumstances, one might have predicted, given the findings of previously published studies, that all participants (again, regardless of group assignment) would have greater recognition memory accuracy for valenced and arousing pictures than for neutral and low-arousing pictures. However, the observed data did not confirm this prediction, instead showing that, after a sleep-filled delay, there were no differences in recognition accuracy for highly-arousing negative, highly-arousing positive, and low-arousing neutral pictures. In other words, in these participants there was no preferential sleep-based consolidation of valenced and arousing information over neutral and low-arousing information. Instead the data suggest that sleep preferentially consolidated memory for low-arousing neutral information in such a way that recognition accuracy was balanced across valence and arousal dimensions. Furthermore, after a wake-filled delay participants had greater recognition accuracy for highly-arousing negative pictures. Taken together, these data from the *Night* and *Day* conditions suggest that sleep may reset recognition accuracy from waking which is characterised by disproportionate recognition accuracy for highly-arousing negative information. This interpretation is tentative at this stage because my study design did not specifically test for this relationship between waking and sleep (i.e. I did not test all participants first across a period of waking followed directly by a period of sleep).

Regarding the finding that sleep preferentially consolidated neutral pictures, several explanatory possibilities exist. One possibility is that previous studies have found spurious results regarding sleep-dependent consolidation of emotional material over neutral material. Perhaps no such consolidation benefit for emotional material over neutral material exists. For example, Cairney et al. (2014) examined emotional memory recall (for highly-arousing negative

vs low-arousing neutral information) in 15 male participants using a nap paradigm. They found no difference in memory accuracy across dimensions of valence and arousal. However, the sample in that study was very small, and the researchers did not include a waking control condition.

Another possibility with respect to the finding that sleep preferentially consolidated recognition memory for low-arousing neutral pictures is that sleep performed a regulatory function in individuals who are ordinarily exposed to high levels of environmental danger. Speculatively, sleep in all participants, but especially in those with a history of trauma exposure, may have helped promote resilience and restored balance with respect to the increased recognition accuracy participants demonstrated for information with highly-arousing negative valence and high arousal through waking experiences[1]. Although individuals in the PTSD and TE groups had varying levels of trauma symptomology, all individuals were functioning within their communities. None of these individuals had symptoms severe enough for them to be institutionalised, or admitted into hospital care. In the face of psychopathology and traumatic experience it is possible that sleep played a regulatory function to enable such individuals to not be functionally incapacitated by their tendency to remember highly-arousing negative information.

The finding that waking is associated with an increase in recognition accuracy toward highly-arousing negative information is somewhat consistent with results by Gujar et al (2011). Although the focus of their study was on emotional reactivity and not emotional memory, they demonstrated that participants had increasingly negative emotion in response to face stimuli

[1] Here I note that this interpretation is in contrast to the results of Investigation 1 that showed that there were between-group differences in sleep quality, which demonstrated some level of sleep disruption in PTSD-diagnosed individuals. Furthermore findings from Investigation 2 demonstrated that sleep disruption in PTSD-diagnosed individuals predicted neutral declarative memory deficits on a free recall task. I comment on the contrast between the finding reported in Investigations 1-2 and Investigation 3 (which suggests that sleep in PTSD-diagnosed individuals may promote resilience), in greater detail at the end of the Discussion.

across waking. Speculatively, increased negative emotion that builds through the day may facilitate accuracy in recognising such stimuli. Several studies have shown that current mood state influences memory retrieval, so that memories that are mood-congruent are more likely to be retrieved (Isen, Shalker, Clark, & Karp, 1978; Riskind, Rholes, & Eggers, 1982).

Recognition bias. Regarding recognition bias, the findings showed that all participants, regardless of group assignment and across both the *Night* and *Day* conditions, had a liberal recognition bias for highly-arousing negative pictures (i.e., were over-inclusive when faced with a forced-choice recognition task as to whether they had seen the pictures once or twice before) and a conservative recognition bias for low-arousing neutral pictures (i.e., were under-inclusive on the same task). Memory for high-arousing positive pictures was relatively unbiased.

However, when considering the influence of sleep and waking on recognition bias a different pattern of results emerged. When waking activity filled the delay between picture exposure and the recognition task, all participants, regardless of group assignment, did not show any significant bias, one way or another, for either valenced and arousing or low-arousing neutral pictures. When sleep filled the delay, however, all participants, again regardless of group assignment, tended to demonstrate a liberal (over-inclusive) bias toward highly-arousing negative pictures, a conservative (under-inclusive) bias toward low-arousing neutral pictures, and no detectable bias toward highly-arousing positive pictures.

Although many sleep studies report on data regarding recognition accuracy in healthy individuals, few report on data regarding recognition bias. Two studies that did report on the latter showed that healthy participants tended to show liberal bias for highly-arousing negative material, while low-arousing neutral material was characterised by a more conservative bias (Atienza & Cantero, 2008; Baran, Pace-Schott, Ericson, & Spencer, 2012). However, Baran et al. (2012) observed no significant difference in recognition bias across sleep or waking. One study examined recognition bias in healthy participants under conditions of normal sleep and sleep

deprivation using negative, positive, and neutral stimuli (Sterpenich et al., 2009). They found that there was no difference in recognition bias across the three valence categories, and that there were no performance differences between the two different experimental conditions.

Viewing this literature as a whole, there is no clear consensus regarding whether recognition bias after a sleep-filled delay is different than after a wake-filled delay or whether there are different kinds of recognition bias after sleep related to highly-arousing negative, highly-arousing positive or low-arousing neutral information. The findings presented here are consistent with those presented by Atienza and Cantero (2008). These authors also reported that recognition bias after a sleep-filled delay was liberal for highly-arousing negative stimuli and conservative for low-arousing neutral stimuli. However future studies should confirm whether this pattern is indeed consistent across studies, since other studies have found discrepant results. To further understand the relevance of recognition bias for participants in this study, I compare the results reported here with those related to recognition accuracy.

Understanding recognition bias in relation to recognition accuracy. In the present study, all participants demonstrated increased recognition accuracy towards information bearing negative valence and high arousal in comparison with positive highly-arousing and neutral low-arousing information after a wake-filled delay. However, sleep promoted equal recognition of information across the valence and arousal spectrums. These results tentatively suggest that sleep may reset recognition accuracy from waking which is characterised by disproportionate recognition accuracy for highly-arousing negative information.

With respect to recognition bias, the opposite pattern was observed in comparison with recognition accuracy: Experiencing a wake-filled interval between stimulus exposure and the recognition task was associated with an approximately equivalent low level of bias in relation to each stimulus type, whereas experiencing a sleep-filled interval was associated with liberal recognition bias for highly-arousing negative information and conservative bias for low-arousing

neutral information. Speculatively, while sleep may reset recognition accuracy in this sample of participants, it may prime participants towards highly-arousing negative information in preparation for next-day experiences. For participants coming from environments containing a high level of objective threat, such a pattern of emotional memory processing may be adaptive. Participants need to be vigilant and sensitive towards highly-arousing negative information (with a tendency to remember stimuli from this category more strongly) to anticipate threatening situations. This pattern of sensitivity towards highly-arousing negative information may lead to increased recognition accuracy for such information during the day, which after a period of sleep may be reset. Such recalibration of recognition accuracy may prevent individuals from becoming overwhelmed by highly-arousing negative information. Over-consolidation of negative content is associated with depression (Liu, Wang, Zhao, Ning, & Chan, 2012; MacLeod, Mathews, & Tata, 1986; Mathews & MacLeod, 1994), and consistent heightened sensitivity to arousing information is associated with anxiety disorders (Eden et al., 2015; Hagemann, Straube, & Schulz, 2016).

Although such adaptive functioning may be expected from HC participants and perhaps to some extent from TE individuals, it is surprising in this study that all participants evidenced this pattern of emotional memory processing. Two factors may account for an adaptive pattern of emotional memory processing in this sample of PTSD-diagnosed individuals[2].

The first is that these participants reported qualitatively that their sleep quality in the laboratory was fairly good; recall, in fact, that they reported sleeping better in the laboratory than in their home environments. Further evidence supporting the assertion that their reported improved subjective sleep quality may have adaptively influenced their emotional memory is demonstrated by the fact that subjective sleep quality in the laboratory was correlated with

[2] Again I discuss the discrepancy between *Investigation 1-2* and *Investigation 3* in greater detail towards the end of the *Discussion*.

recognition accuracy. However, more notably, while for TE and HC participants better subjective sleep quality was associated with greater recognition memory accuracy for highly-arousing negative pictures, in PTSD-diagnosed individuals greater subjective sleep quality was significantly associated with lower accuracy for the same stimuli, with a moderate effect size. This result suggests that although, overall, there were no between-group differences in recognition accuracy, PTSD-diagnosed individuals achieved fairly equal recognition accuracy for all valence and arousal categories after sleep via a different mechanism to TE and HC participants. Specifically reasonably healthy sleep in PTSD may have resulted in a reduction in recognition accuracy towards highly-arousing negative information, which may have allowed for other valence and arousal categories to achieve relatively equal consolidation. Furthermore, when examining the clinical significance of objective sleep disruption in PTSD-diagnosed individuals, these measures of sleep demonstrated fairly minimal sleep disruption in comparison to TE and HC participants. These results suggest that all groups of participants had reasonable sleep quality which may have promoted adaptive emotional processing, although via different mechanisms for participants from different groups.

Second, although participants in the PTSD and TE groups experience symptoms related to trauma, they are functioning capably, to at least some extent, in their everyday lives (e.g., no participant had been admitted to a psychiatric centre with severe functional impairment). This functional capability suggests they may be experiencing some level of regulation with regard to emotional memory processing. Next, I consider the relationship between sleep and emotional memory processing to further clarify this relationship.

Frequency of REM arousals predicts recognition accuracy and recognition bias for low arousing neutral information. Surprisingly, the results showed that (a) the number of REM arousals leading to NREM 1 or waking predicted recognition accuracy for low-arousing neutral

pictures, and (b) non-specific REM arousals predicted recognition bias for the same category of stimuli. No sleep variables predicted recognition accuracy or bias for valenced pictures.

Regarding participants' accuracy for low-arousing neutral information, the analysis revealed that participants (regardless of group assignment) who had greater REM fragmentation had significantly poorer recognition accuracy than those with less REM fragmentation, for this category of picture. These results are very similar to those reported in *Investigation 2*, which demonstrated that participants who had greater frequency of the same kind of REM fragmentation had poorer retention of low-arousing neutral declarative information across sleep but not waking. There are at least two explanations for the similarity between the result presented here and those presented in *Investigation 2*. The first explanation is that perhaps uninterrupted REM, which is not marked by frequent REM arousals that lead to a sleep stage shift, specifically consolidates low-arousing neutral information (i.e. neutral declarative information) and has no role in the consolidation of highly-arousing and/or valenced information. This explanation, however, is not consistent with many studies that suggest REM sleep makes a unique contribution to the consolidation of emotional information. These studies have shown that emotional information is remembered better than low-arousing neutral information over a period of sleep rather than waking, and that the strength of emotional memories is associated with the amount of REM sleep (Nishida et al., 2009; Wagner et al., 2001; Wiesner et al., 2015).

Another possible explanation is that REM sleep has a primary emotional memory regulation function that is flexible depending on an individual's circumstances and daily waking experiences. In a context where participants tend to have disproportionally better recognition accuracy for highly-arousing negative information in contrast with highly-arousing positive and low-arousing neutral information across waking, uninterrupted REM sleep may reset this pattern. Considering the overwhelming evidence that REM sleep is involved in the consolidation of

emotional memory, I favor this explanation over an explanation which suggests that REM sleep only consolidates neutral declarative information. Speculatively, this finding may indicate that REM sleep makes different contributions to recognition accuracy depending on the waking experiences of individuals and that its primary role with respect to emotional memory is regulatory in nature.

With respect to recognition bias for neutral and low-arousing information, the analysis revealed that participants who had greater frequency of non-specific REM arousals had greater conservative bias than those with a lower frequency of these REM arousals. This finding suggests that REM fragmentation, irrespective of whether it leads to a sleep stage shift or not, prompts participants to under-include low arousing neutral information. This finding also suggests that uninterrupted REM sleep is associated with less conservative bias. However, REM fragmentation had no impact on the liberal bias associated with highly-arousing negative information. Previous studies have not reported on the association between REM sleep and stimuli related to recognition bias. For example, although Baran et al. (2012) reported recognition bias for highly-arousing negative and low-arousing neutral pictures across sleep and waking, they did not examine the relationship between these biases and various REM sleep parameters. The findings in this study regarding REM sleep parameters and recognition bias are preliminary – it is unclear why REM sleep fragmentation may heighten bias for low-arousing neutral but not highly-arousing negative information. The findings do, however, highlight that uninterrupted REM sleep is important for unbiased emotional memory.

Summary of Investigation 3. Here I tested the two main sets of predictions. Firstly I examined whether PTSD-diagnosed individuals, in comparison with participants in the other groups, would demonstrate increased recognition accuracy and recognition bias for highly-arousing negative information, rather than highly-arousing positive or low-arousing neutral information. I also tested whether this pattern would hold more strongly when a sleep-filled

rather than wake-filled delay separated learning from recall. Secondly I investigated the proposition that sleep disruption, particularly that related to REM sleep parameters, would predict increased recognition accuracy and recognition bias towards highly-arousing negative information in PTSD-diagnosed individuals. The results disconfirmed both sets of predictions.

However, the results pointed to several other effects related to sleep and recognition accuracy and recognition bias. In the *Day* condition, all participants, regardless of group assignment, demonstrated disproportionally greater recognition memory accuracy for highly-arousing negative pictures in contrast with highly-arousing positive pictures and low-arousing neutral pictures. However the results tentatively suggested that sleep reset this pattern of recognition accuracy, so that all information, whether highly-arousing and/or valenced or not, was remembered equally well after sleep.

However, the opposite pattern was observed with respect to recognition bias. In the *Day* condition, all participants, again regardless of group assignment, experienced relatively little recognition bias across waking, whereas in the *Night* condition highly-arousing negative pictures were over-included and low-arousing neutral pictures were under-included.

The contrast between recognition accuracy and recognition bias in this sample may be understood by considering the context in which participants lived. Their environments are characterized by high levels of objective threat. Sleep may reset recognition accuracy from waking, which is dominated by recognition accuracy for highly-arousing negative information, to recognition accuracy that is approximately equivalent for all valence and arousal categories after sleep. However, the results related to recognition bias indicate that sleep may also prime participants towards being over-inclusive in recognising highly-arousing negative information during the day. Such priming may be beneficial for identifying threat during waking experiences.

Furthermore, in this study, uninterrupted REM sleep predicted greater recognition accuracy and lower conservative recognition bias for low-arousing neutral information. There

were no associations between REM sleep parameters and highly-arousing negative or highly-arousing positive information. One interpretation of this finding is that uninterrupted REM sleep is important for processing only low-arousing neutral information (that is, neutral declarative information). An alternative explanation suggests that when participants are exposed to emotional information carrying a variety of valence and arousal properties, uninterrupted REM sleep plays a regulatory function in ensuring that individuals are left with a balance of emotional information that is most adaptive to their waking experiences. In summary I favor the explanation that continuity of REM may be integral to the regulation of emotional memory processes during sleep.

Investigation 4: Emotional Reactivity Regulation During Sleep in PTSD

This investigation tested the prediction that PTSD-diagnosed participants, in comparison with TE and HC participants, would experience increased emotional reactivity to highly-arousing negative information in comparison with highly-arousing positive or low-arousing neutral information. Furthermore, the investigation aimed to test the prediction that this bias toward negatively valenced information would be particularly salient when stimuli were presented after a period of sleep compared to a period of waking activity. Finally, the investigation tested the prediction that sleep disruption, particularly that related to REM sleep parameters, would be associated with heightened emotional reactivity towards highly-arousing negative information in PTSD-diagnosed individuals.

No heightened emotional reactivity towards highly-arousing negatively valenced information after sleep in PTSD. In this investigation, emotional reactivity was indexed by four separate autonomic arousal variables: HR, PEP, LVET and SCL. Increased HR and SCL, and decreased PEP and LVET, indicate increased autonomic activity. Circadian effects did not explain the results described below because participants had similar degrees of emotional reactivity during the initial presentation of emotional stimuli before either sleep or waking.

The results of the analyses disconfirmed the predictions: PTSD-diagnosed participants, in comparison with TE and HC participants, did not maintain or have greater emotional reactivity in response to highly-arousing negatively valenced pictures and this effect was not more prominent after a sleep-filled rather than a wake-filled delay. Furthermore, during the *Day* condition, PTSD-diagnosed participants also did not have greater emotional reactivity in response to highly-arousing negatively valenced pictures. Regarding this *Day* condition finding, this result is in contrast to many other studies which report that PTSD-diagnosed individuals, in comparison with controls, tend to have greater emotional reactivity towards highly-arousing negative stimuli (Ben-Amitay, Kimchi, Wolmer, & Toren, 2016; Fitzgerald et al., 2016; Fonzo, Huemer, & Etkin, 2016; Liberzon, Abelson, Flagel, Raz, & Young, 1999; Schmahl et al., 2004).

It is currently unclear why PTSD diagnosed individuals did not evidence this relationship since other studies have demonstrated this effect. However one study found that participants who had experienced multiple traumas and had severe PTSD had blunted autonomic responses (measured by startle response and SCL) to highly-arousing negative scripts, in comparison with participants with single traumas and moderate PTSD (McTeague et al., 2010). Those in the multiple trauma and severe PTSD group had responses to the emotive scripts that were similar to healthy controls, despite having severe PTSD symptomology. However, the participants in this study experienced a single event of sexual assault and had moderate PTSD severity (M_{CAPS} = 67.67, SD_{CAPS} = 14.12; Weathers et al., 2001), although the environments where participants lived were characterised by continuous violence and exposure to danger (e.g., gang shootings in their areas, frequent burglaries; Williams et al., 2007). It is currently unknown whether such pervasive and continuous exposure to violence and danger results in blunted autonomic responses.

Another possible explanation for the lack of findings related to the *Day* condition in PTSD is related to methodological considerations regarding the IAPS. Perhaps the IAPS pictures

were not effective in eliciting autonomic responses in PTSD-diagnosed individuals or perhaps South African participants did not understand the picture series in the same way as US participants (where the study was normed) and therefore did not respond in the expected way. Neither of these explanations is likely. In the former case another study found that PTSD-diagnosed participants did have increased autonomic reactivity to negative in comparison to neutral pictures drawn from the IAPS, demonstrating that the IAPS is effective in eliciting different autonomic responses to different categories of pictures in PTSD (Fitzgerald et al., 2016). In the latter case a study in our laboratory showed that South African participants rated IAPS pictures of all valence and arousal properties in a very similar way to the US norms (r = .913; Nestadt & Kantoor, 2015). This finding shows that the IAPS is likely to elicit expected emotional responses and consequently expected autonomic responses.

Attenuation or maintenance of low emotional reactivity after a sleep-filled delay in comparison with a wake-filled delay. Although the major hypotheses were disconfirmed, the analyses detected some interesting relationships that, upon interpretation, might advance a broader understanding of the relationship between emotional reactivity and sleep.

Specifically, the analyses detected a main effect of Condition on both HR and PEP values. These analyses revealed that autonomic arousal was significantly decreased during sleep in comparison with waking, irrespective of group membership, picture type or when the pictures were presented (either before or after either sleep or waking). Furthermore, the analyses detected a significant interaction between Condition and Picture Presentation with respect to HR, PEP and LVET values. That is to say, regardless of group membership or picture type, the analyses generally detected significant increases in autonomic arousal from the first to the second presentation of the pictures in the *Day* condition, but significant decreases in the *Night* condition. However, more notably participants' HR, PEP and LVET measures all indicated that although the initial presentation of the stimuli was associated with approximately equal degrees of

autonomic arousal across both sleep and waking, the second presentation after either 8 hours of sleep or waking showed divergent degrees of autonomic arousal. These results, therefore, suggest that sleep is associated with attenuation of autonomic arousal whereas waking is not.

Although this overall tenor of this result was consistent across HR, PEP, and LVET, there were subtle differences in the presentation of this attenuation between the three measures. For example, participants' HR in response to the picture stimuli increased sharply from the first to the second presentation in the *Day* condition (i.e., there was significantly higher HR on *Trial 2* than on *Trial 1*, with 8 hours of regular waking activity separating the two), while it remained stable from the first to the second presentation in the *Night* condition (i.e., there was neither a significant increase or decrease from *Trial 1* to *Trial 2*, with 8 hours of sleep separating the two). Together, these results suggest that a period sleep helped participants to maintain a relatively low heart rate when faced with pictures of varying arousal and valence qualities.

Regarding PEP (which, recall, decreases as a marker of increasing autonomic arousal), participants' responses to the picture stimuli increased markedly from the first to the second presentation in the *Night* condition, whereas responses decreased marginally from the first to the second presentation in the *Day* condition. Hence, this finding suggests that sleep, in comparison to waking, markedly lowered autonomic arousal, and as such is consistent with the finding regarding HR.

Regarding LVET (which, recall, decreases as a marker of increasing autonomic arousal), participants' responses to the picture stimuli increased markedly from the first to the second presentation in the *Night* condition, whereas responses decreased significantly from the first to the second presentation in the *Day* condition. Hence, this finding suggests that sleep, in comparison to waking, markedly lowered autonomic arousal, and as such is consistent with the finding regarding PEP and HR.

Regarding SCL (which, recall, increases as a marker of increasing autonomic arousal) participants' responses to the picture stimuli increased marginally from the first to the second presentation in the *Night* condition, whereas responses increased greatly from the first to the second presentation in the *Day* condition. Hence, this finding follows a similar pattern to the results presented for HR, that is a period sleep helped participants to maintain a relatively low SCL in comparison to waking, when faced with pictures of varying arousal and valence qualities. However this result was not statistically significant.

Together, these findings regarding HR, PEP, and LVET present a consistent picture: A period of sleep in between the first and second picture presentations helped participants either (a) maintain a low level of autonomic arousal in response to those pictures, or (b) decrease their levels of autonomic arousal in comparison to the second presentation of the stimuli during the day. Hence, the suggestion here is that there is a consistent pattern of generalised attenuation of emotional reactivity across sleep, but not across waking. This pattern was present across all participants, regardless of group membership, and for all picture types, regardless of arousal and valence properties. That this effect was statistically significant for multiple measures of autonomic arousal (HR, PEP and LVET) suggests it is robust across several modes of physiological reactivity.

These results are consistent with those presented by Cunningham et al. (2014). They also demonstrated generalised attenuation of emotional reactivity after sleep, irrespective of the arousal and valence properties of stimuli. In their study, participants viewed highly-arousing negatively valenced pictures and low-arousing neutral pictures before and after an intervening period of either sleep (n = 18) or waking (n = 21). Measure of heart rate deceleration and skin conductance response both showed a decrease in autonomic arousal after sleep but not after waking. van der Helm et al. (2011) corroborated these results. They demonstrated that subjective ratings of both negative and positive pictures decreased in intensity across sleep but not across

waking. Interestingly, pictures with the highest valence and arousal ratings (both positive and negative) showed the most attenuation of emotional reactivity. Furthermore, this study also showed that the amygdala, a brain structure critical for regulation of autonomic arousal, is less reactive and demonstrates stronger connectivity to the ventromedial prefrontal cortex (vmPFC) after a period of sleep rather than waking. These findings are also consistent with studies using sleep-deprivation paradigms. The latter report that sleep-deprived participants, in comparison to those who have slept normally, show increased emotional reactivity (indexed by both subjective rating and physiological measures) to both highly-arousing negatively and positively valenced stimuli (Mauss, Troy, & LeBourgeois, 2013; Sauvet et al., 2010).

Several other studies, however, present data with a contrasting pattern: these studies show that sleep may protect or promote emotional reactivity, rather than attenuate it. For example, Baran et al. (2012) studied self-reported emotional reactivity in response to negative and neutral pictures across sleep and waking. They found that emotional reactivity to negative pictures, but not neutral pictures, was reduced across waking, but preserved across sleep. Hence, they concluded that sleep served to protect emotional reactivity. Groch, Wilhelm, Diekelmann and Born (2013) replicated these findings, using event-related potentials to measure emotional reactivity. Finally, Wagner et al. (2002) showed using self-report ratings, that REM-rich sleep, in particular, was associated with enhanced emotional reactivity.

Together, the studies reviewed above suggest that sleep modulates emotional reactivity. However, the literature is equivocal about direction of that modulation. Whereas some studies, including this one, suggest that sleep attenuates emotional reactivity, others suggest that it protects or enhances emotional reactivity. Furthermore, some studies, including this one, suggest that sleep modulates emotional reactivity irrespective of the arousal/valence properties of the stimuli, whereas others suggest selective modulation of negatively and positively valenced stimuli.

One possible explanation for these divergent findings is that sleep plays a flexible and context-specific role in modulating emotional reactivity depending on prior waking experiences. As I described in *Investigation 3*, participants in this study live in environments where they are exposed to high levels of objective danger on a daily basis. In this context, waking events may lead to increased emotional reactivity, as demonstrated by the current findings of elevated HR and decreased LVET after a wake-filled delay. The global attenuation of emotional reactivity that participants experienced after a sleep-filled delay may be adaptive for next-day functioning, where participants may face objective danger again. Studies show that heightened baseline emotional reactivity is non-adaptive in that it leads to indiscriminate reactivity to highly-arousing negative stimuli and poor discrimination between what is actually threatening and what is non-threatening in the environment (Goldstein & Walker, 2014). Although my study design did not allow me to determine a causal relationship between waking- and sleep-related emotional processing, the findings allow for the speculation that sleep may reduce heightened emotional reactivity accumulated during waking experiences so as to promote adaptive responses to threat the next day.

Of course, not all individuals find themselves in contexts marked by high levels of objective danger. For instance, college students may require heightened post-sleep emotional reactivity for effective learning, since emotion facilitates learning (Phelps, 2004). For such individuals, within such contexts, it might be more adaptive for sleep to preserve or enhance emotional reactivity so as to promote more effective next-day functioning. This effect is demonstrated by studies that used college students or healthy young adults as participants, that is, sleep either preserved or enhanced emotional reactivity, whereas waking activity did not (Baran et al., 2012; Gilson et al., 2015; Groch et al., 2013; Lara-Carrasco, Nielsen, Solomonova, Levrier, & Popova, 2009; Wagner et al., 2002). However other studies using young adults or students have also found that sleep attenuates emotional reactivity in comparison to waking (e.g.,

Cunningham et al., 2014). However none of these studies - showing attenuation, preservation or enhancement of emotional reactivity - controlled for the kinds of waking experiences participants had during the day (e.g. daily stressors, exam periods, living environments). Future research should test this speculation directly: Does the effect of sleep on emotional reactivity depend, at least partially, on the everyday environmental context within which participants live, and on their usual waking experiences?

The findings and interpretations presented above relate to the function of sleep for processes of emotional regulation in all participants. Here I explore how these findings may be relevant to PTSD-diagnosed individuals.

Similar to the argument presented in *Investigation 3*, a sleep-based adaptive emotional regulatory response to emotional stimuli would be expected from HC participants, but not from PTSD-diagnosed participants. The reasons for successful attenuation of emotional reactivity across sleep in PTSD in this study may be accounted for by two divergent explanations. First, perhaps PTSD-diagnosed participants do not have difficulty attenuating elevated waking emotional reactivity after a period of sleep, congruent with the findings in this study. However, previous literature suggests that PTSD is characterized by elevated emotional reactivity and by an inability to successfully attenuate emotional reactivity back to baseline (Pace-Schott, Germain, & Milad, 2015). An alternative to the first explanation may follow similar lines as one given in the Discussion section for *Investigation 3*. To wit: PTSD-diagnosed participants reported that they slept much better in the sleep laboratory than at home. Their subjective sleep quality in the laboratory was equivalent to that reported by TE and HC participants. Furthermore, analyses detected few between-group differences with regard to objective measures of sleep quality[3]. Together, these results suggest that PTSD-diagnosed participants had reasonable sleep

[3] Here I note that this interpretation is in contrast to the results of *Investigation 1* that showed that there were between-group differences in sleep quality, which demonstrated some level of sleep disruption in PTSD-

quality, which may have promoted adaptive emotional regulation (demonstrated by attenuated emotional reactivity after a sleep-filled delay). Mechanisms explaining attenuation of emotional reactivity across sleep in PTSD remains unknown, however.

Although this conclusion is tentative and preliminary, it does allow the hypothesis that improved sleep quality in PTSD-diagnosed individuals promotes resilience and adaptive functioning. Support for this hypothesis comes from research that has used targeted sleep therapies to treat sleep disruption in PTSD. Such research indicates that other symptoms of the disorder are minimized as sleep disruption is treated successfully. These therapies include both pharmacological and behavioral interventions. For example, the drug prazosin reduces both nightmares and insomnia symptoms, and also decreases overall symptom prevalence and improves daytime functioning (Germain et al., 2012; Kung, Espinel, & Lapid, 2012; Lipinska, Baldwin, & Thomas, 2016; Raskind et al., 2013). Cognitive-behavioral therapy for insomnia and image rehearsal therapy also have similar efficacy profiles (Davis & Wright, 2007; Krakow et al., 2001; Talbot et al., 2014). The findings from such intervention studies, together with the preliminary findings from this study, suggest that improving sleep quality may be a novel and useful method of enhancing daytime functioning (including emotion regulation) in PTSD.

Few predictive relationships between measures of sleep and emotional reactivity. Because there was no evidence that PTSD-diagnosed individuals showed heightened emotional reactivity toward highly-arousing negative pictures after either a sleep-filled or a wake-filled delay, I was not able to investigate whether sleep disruption predicted this phenomenon. However, because the analyses showed, across several measures of autonomic arousal, that

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diagnosed individuals. Furthermore findings from *Investigation 2* demonstrated that sleep disruption in PTSD-diagnosed individuals predicted neutral declarative memory deficits on a free recall task. I comment on the contrast between the finding reported in *Investigations 1-2* and *Investigation 3* (which suggests that sleep in PTSD-diagnosed individuals may promote resilience), in greater detail at the end of the *Discussion*.

emotional reactivity was attenuated across sleep but not across waking, I examined whether subjective and objective measures of sleep predicted this attenuation effect.

To examine the relationship, I first examined whether each measure of autonomic arousal and each measure of objective and subjective sleep quality were correlated. Then, I examined whether any single sleep measure, or any combination of sleep measures, predicted any single index of autonomic arousal.

Regarding HR, the findings showed that individuals who reported poor subjective sleep quality in their home environment also showed increased HR for highly-arousing negative and highly-arousing positive stimuli, but not for low-arousing neutral stimuli, suggesting that this relationship was demonstrated for stimuli with high arousal (irrespective of valence) rather than stimuli with low arousal properties. Furthermore, individuals with greater depression severity also had higher HR in response to highly-arousing negative pictures. However, when subjective sleep quality and depression severity variables were applied as predictors during general linear modelling neither predicted HR related to each respective valence and arousal category, indicating that initial correlational relationships are associative rather than predictive. One possible explanation for these associative relationships is that a third variable (e.g., neurotransmitter or hormone level) may mediate the relationship between subjective sleep quality or depression severity and HR.

For example, regarding the association between poor sleep quality and increased HR in response to arousing stimuli, research shows that individuals who are sleep deprived are more reactive in response to arousing stimuli (irrespective of valence) rather than low-arousing stimuli (Gujar, Yoo, Hu, & Walker, 2011; Yoo, Gujar, Hu, Jolesz, & Walker, 2007). This increased reactivity to such stimuli is characterised by increased activity in limbic areas such as the amygdala and diminished activity and connectivity between frontal and limbic circuits (Yoo et al., 2007). Disinhibition of the amygdala can lead to increased HR, because the amygdala

projects to areas of the brain such as the medulla which is directly responsible for HR regulation (Barbas, Saha, Rempel-Clower, & Ghashghaei, 2003; Sgoifo, Carnevali, Alfonso Mde, & Amore, 2015). However these circuits are regulated by a complex array of neurotransmitters and hormones such as noradrenaline, adrenocorticotropin and cortisol (McEwen, Gray, & Nasca, 2015). The activity of these hormones may therefore mediate the relationship between poor sleep characterised by sleep deprivation and HR in response to arousing stimuli.

With respect to the association between increased depression severity and increased HR in response to highly-arousing negative stimuli, endocrinological factors may similarly mediate this relationship. Depression is associated with increased resting-state sympathetic activation and decreased resting-state parasympathetic activation measured by HR, SCL and heart rate variability (Sgoifo et al., 2015; Waugh, Muhtadie, Thompson, Joormann, & Gotlib, 2012). During presentation of highly-arousing negative or stressful stimuli depression is associated with dysregulation of the ANS, with studies showing either decreased or increased sympathetic and parasympathetic reactivity (Hamilton & Alloy, 2016). However, autonomic reactivity to highly-arousing negative stimuli or stressful stimuli is also modulated by an array of neurotransmitters and hormones such as noradrenaline, adrenaline and cortisol (McEwen et al., 2015). These neuroendocrinological markers may therefore also mediate the relationship between increased depression severity and HR rate in response to highly-arousing negative stimuli.

Regarding PEP, the analysis detected no significant associations with subjective and objective sleep. Regarding LVET, the analysis detected only one significant relationship with a measure of sleep quality: NREM 2 percentage predicted the change in LVET across an intervening period of sleep, albeit with a very small effect size. This analysis revealed that participants who had greater NREM 2 percentage had greater LVET responses to the picture stimuli, and therefore attenuated autonomic arousal. Within the current literature, there is no theorized role for NREM 2 in emotional reactivity. Hence, possible reasons for this result remain

unclear. Furthermore, this relationship was not replicated with any other variables of autonomic arousal including PEP, which in comparison to LVET is a better indicator of sympathetic activation of the ANS (Imrich et al., 2009), suggesting that the relationship between NREM2 percentage and autonomic arousal is tentative at best.

Surprisingly, the current data provided no evidence for an associative or predictive role for REM sleep in the attenuation of overnight emotional reactivity. Several other studies have shown that REM sleep is important for the attenuation of emotional reactivity (Cunningham et al., 2014; Gujar, McDonald, et al., 2011; Pace-Schott et al., 2011; Rosales-Lagarde et al., 2012; van der Helm et al., 2011). Furthermore, some studies have suggested that REM sleep disruption may contribute to an inability to attenuate emotional reactivity in PTSD. Using classical conditioning paradigms, a number of studies have demonstrated that extinction of a previously conditioned stimulus and the generalisation of extinction from one stimulus to another is reliant on intact REM sleep in healthy individuals (Pace-Schott et al., 2009; Spoormaker et al., 2010). In PTSD, the inability to extinguish previously conditioned fear responses, or to generalise an extinction response from one stimulus to another, are core symptoms of the disorder. These authors hypothesize that the commonly observed REM sleep disruptions in PTSD may contribute to the pathophysiology of these core symptoms. However, because the current study did not use a classical conditioning paradigm, I could not explore this specific aspect of emotional reactivity. Future studies may benefit from using such a paradigm to directly assess the relationship between REM sleep and fear extinction in PTSD-diagnosed individuals.

Summary of Investigation 4. Here I tested the two main sets of predictions. Firstly I examined whether PTSD-diagnosed individuals, in comparison with participants in the other groups, would demonstrate increased emotional reactivity in response to highly-arousing negative information, rather than highly-arousing positive or low-arousing neutral information. I also tested whether this pattern would hold more strongly when a sleep-filled rather than wake-

filled delay separated the initial presentation from the second presentation. Secondly I investigated the proposition that sleep disruption, particularly that related to REM sleep parameters, would predict increased emotional reactivity towards highly-arousing negative information in PTSD-diagnosed individuals. The results disconfirmed both sets of predictions.

However, the results pointed to several other effects related to sleep and emotional reactivity. I showed that emotional reactivity, irrespective of the arousal and valence properties of the stimuli or of the group membership of the responders, was generally attenuated across sleep, whereas it was elevated across waking. This effect was robust in that it was evident for three of the four indices of autonomic arousal. This result suggests a global attenuation of emotional reactivity across sleep that may be adaptive for individuals who live in a high-threat environment. However, previously published studies have found divergent results regarding the attenuation of emotional reactivity after sleep, although these studies have not investigated individuals that come from high-threat environments. These results allow the speculation that such attenuation of emotional reactivity could prevent participants from becoming overwhelmed by highly-arousing negative content during next-day waking experiences.

Furthermore, contrary to previous research, I did not demonstrate that REM-related variables predicted emotional reactivity. In fact there was only one predictive relationship demonstrated between NREM 2 percentage and LVET, which suggested that having a larger percentage of this stage of sleep was associated with less emotional reactivity. However the effect size here was small and this result was not replicated in any of the other variables that were indices of emotional reactivity. Hence although there was a clear attenuation of emotional reactivity after a sleep-filled rather than wake-filled delay, this effect seems to be unrelated to sleep stages. Future studies are needed to clarify whether this effect is related to the general effects of rest associated with sleep, some other aspect of sleep that is not captured by PSG sleep stages or REM sleep, in keeping with results from previous research.

Comparing findings related to neutral declarative memory, emotional memory, and emotional reactivity after a sleep-filled delay in PTSD-diagnosed individuals

Investigation 2 demonstrated that PTSD-diagnosed individuals, in comparison with TE and HC participants, retained less neutral declarative information after a sleep-filled, but not a wake-filled, delay. This pattern of post-sleep retention difficulties in PTSD-diagnosed individuals was predicted by the degree of REM fragmentation that these individuals experienced.

Investigations 3 and *4*, which examined emotional memory and emotional reactivity respectively, found no significant between-group differences. Specifically, the analyses in those investigation disconfirmed the predictions that PTSD-diagnosed individuals would show (a) more accurate recognition of highly-arousing negative stimuli than of highly-arousing positive stimuli and low-around neutral stimuli, (b) a bias toward recognizing negative stimuli over positive and neutral stimuli, and (c) increased emotional reactivity in response to highly-arousing negative stimuli, but not to highly-arousing positive or low-arousing neutral stimuli. The analyses also disconfirmed the prediction that the latter pattern of increased emotional reactivity to negative stimuli would be prominent after a sleep-filled, but not a wake-filled, delay.

Investigations 3 and *4* did, however, find that all participants, including those carrying a PTSD diagnosis, benefitted from sleep in a manner that they did not from waking. Specifically, in *Investigation 3*, after a sleep-filled delay all participants were able to accurately identify highly-arousing negative, highly-arousing positive and low-arousing neutral picture with equal accuracy, whereas after a wake-filled delay their accuracy was heightened for highly-arousing negative pictures specifically. In *Investigation 4*, after a sleep-filled delay all participants had lower emotional reactivity (in comparison with baseline measures) to pictures of all valence and arousal categories, whereas after a wake-filled delay they displayed an increase in reactivity to pictures of all valence and arousal categories.

Viewed side-by-side, the results of *Investigations 2-4* seem contradictory: In PTSD-diagnosed individuals, the same night of sleep seems to have resulted in neutral declarative retention deficits, on the one hand, and a combination of balanced retrieval of emotional and neutral information and an attenuation of emotional reactivity, on the other.

One possible explanation for these divergent results may arise from the different kinds of tasks employed in *Investigations 2-4*, and, more specifically, the different brain structures these tasks are known to activate. The neutral declarative memory tasks required free recall, which is heavily dependent on the hippocampus (Korte & Schmitz, 2016; Squire & Dede, 2015). Furthermore, although the hippocampus is activated during free recall tasks (both immediately following learning, and after a delay), studies have shown that its volume is most closely associated with measures of information retention related to new learning (Kramer et al., 2004; Sass et al., 1992). For example Kramer et al. (2004) investigated neutral declarative immediate recall, delayed recall and retention of information over a short delay in patients with Alzheimer's disease. All participants also had a structural MRI brain scan. The authors showed that while immediate recall and delayed recall were predicted by cortical gray matter volume, retention was predicted by hippocampal volume, even after controlling for the amount of information that participants initially learnt. The authors concluded that hippocampus has a fairly specific role in the consolidation of new memories.

In contrast, the emotional memory task was dependent on recognition memory, which is less reliant on the hippocampus and more reliant on frontal memory circuits (Squire & Dede, 2015). Similarly, emotional reactivity (as measured by indices of autonomic arousal) in response to the emotional memory stimuli, is not dependent on hippocampal structures (Macey, Ogren, Kumar, & Harper, 2015).

Also, recall that PTSD-diagnosed individuals reported that their sleep quality in the laboratory was better than their sleep quality at home. Furthermore, although they did have some

PSG sleep disruption, this disruption was fairly minimal (e.g., their sleep efficiency, number of awakenings, time spent awake, and REM percentage values were all similar to participants in the other group) – they only experienced less sleep depth than participants in the other groups. This decrease in sleep depth was not associated with any aspect of neutral declarative memory, emotional memory, or emotional reactivity. Instead, the degree of REM fragmentation that PTSD-diagnosed individuals experienced predicted their ability to retain neutral declarative information across a sleep-filled delay, explaining a significant proportion of the variance related to neutral declarative memory retention (interaction between group membership and the degree of REM fragmentation: η^2 = .22, large effect size). However, the actual between-group differences in REM fragmentation were very small (η^2 = .04, small effect size). Together, these findings suggest that a small and relatively circumscribed disruption of sleep quality in the laboratory made a substantial impact on neutral declarative memory retention.

That a fairly minimal increase in REM fragmentation may result in substantial impairment in memory retention in PTSD is consistent with studies showing that hippocampus function, which is particularly important for memory retention, is especially sensitive and vulnerable to change in hippocampal structure or connectivity (Harry & Lefebvre d'Hellencourt, 2003; Schreiber & Baudry, 1995). For example, Lowenstein, Thomas, Smith, and McIntosh (1992) demonstrated that rats that received a momentary impact to the surface of the brain had cellular alteration to the hippocampus and associated structures, but not to any other parts of the brain. The same study showed that the resulting structural changes to the hippocampus were associated with abnormal firing of hippocampal cells. In humans, hippocampal damage has been documented after only brief general tonic clonic seizures, corroborating animals studies which identify the hippocampus as vulnerable to injury (Briellmann, Newton, Wellard, & Jackson, 2001). Hence, and because the hippocampus is already compromised in PTSD-diagnosed individuals (Woon et al., 2010), one might speculate that the fairly minimal objective sleep

disruptions in PTSD-diagnosed individuals in comparison to TE and HC participants may have affected nighttime hippocampal activation. This pattern of altered activation may, in turn, have affected retention of information but not recognition memory or emotional reactivity. This speculation is strengthened by the fact that REM fragmentation was strongly negatively correlated with neutral declarative memory retention after a sleep-filled interval in PTSD-diagnosed individuals (r = -.50, p = .03), an effect which was not demonstrated in TE (r = -.13, p = .60) and HC (r = .17, p = .47) participants.

Speculatively in PTSD-diagnosed individuals the brain circuits recruited for emotional memory processing and for emotional reactivity, may have responded to better sleep in the laboratory (in comparison with sleep in their home environment), in such a way that participants in this clinical group benefitted from sleep in the same way that TE and HC participants did. Emotional memory recognition is predominantly reliant on activation of the prefrontal cortex and amygdala, although activation of the hippocampus is also demonstrated in some studies (Buchanan, 2007). Emotional reactivity defined by autonomic activation is reliant on brain structures such as the prefrontal cortex (medial prefrontal cortex and orbitofrontal cortex), insular cortex, amygdala, hypothalamus, and medullary structures (Sgoifo et al., 2015). Of these different brain areas associated with emotional memory recognition and emotional reactivity, structural MRI studies show that the amygdala has reduced volume (O'Doherty, Chitty, Saddiqui, Bennett, & Lagopoulos, 2015), but hyperactivation in PTSD-diagnosed individuals (Fragkaki, Thomaes, & Sijbrandij, 2016).

However, some studies indicate that the amygdala is relatively less sensitive to brain insult than the hippocampus. For example in temporal lobe epilepsy, seizure activity affects both hippocampal and amygdalar structures equally, however damage to the hippocampus is more commonly reported than amygdalar damage (Hermann et al., 2003; Wieser & Epilepsy, 2004). Furthermore, clinically, patients with circumscribed mesial temporal lobe epileptic focus have

difficulty with memory tasks associated with hippocampal function, rather than affect regulation associated with amygdalar function (Ozkara et al., 2004; Wieser & Epilepsy, 2004). Furthermore hyperactivation of the amygdala under conditions of sleep deprivation ceases after a recovery night of sleep (Beattie, Kyle, Espie, & Biello, 2015; Yoo et al., 2007). Together these studies suggest that the amygdala may be less sensitive and vulnerable to change and that its abnormal activation may return to normal after a night of recovery sleep. Because of these factors, although the amygdala is already compromised in PTSD-diagnosed individuals, one might speculate that the fairly minimal objective sleep disruptions in PTSD-diagnosed individuals may not have affected nighttime amygdalar activation. Relatively normal amygdalar activation during sleep in PTSD-diagnosed individuals may have contributed to a pattern of emotional memory performance and emotional reactivity that was approximately equivalent to TE and HC participants.

Limitations and Avenues for Future Research

One must consider the following limitations of the current project when evaluating its significance, weighing interpretations of its data, and planning future research based on its findings.

First, participants in the PTSD and TE groups had significant comorbid symptoms of depression, and PTSD-diagnosed participants had greater depression severity than TE participants. This situation presents a confound that must be taken into account when interpreting findings with respect to sleep, neutral declarative memory, emotional memory, and emotional reactivity. However, depression severity (as measured by BDI-II scores) did not prove to be a significant predictor when it was included in the various general linear models described in *Investigations 1-4*. Hence, I suggest that depression severity did not have a significant impact on the data trends, and that its interpretive value has been properly weighted. Furthermore, because

major depressive disorder is especially comorbid with PTSD in sexual assault survivors, as compared to PTSD occurring in the context of other trauma etiologies (Au, Dickstein, Comer, Salters-Pedneault, & Litz, 2013), the ecological validity of using a depression-free cohort is questionable.

Second, the fact that the current study used a female-only sample of sexual assault survivors might limit the generalisability of these findings. Men and individuals who experienced traumas of different aetiologies may have different sleep, neutral declarative memory, emotional memory and emotional reactivity profiles (see, e.g., Kobayashi & Mellman, 2012). However, because most PTSD studies, including those examining sleep, memory, and emotion, have been conducted using samples of male war veterans, the present study adds diversity to the field as a whole.

Third, regarding the subjective measurement of sleep, the findings demonstrated that for PTSD-diagnosed individuals in comparison with TE and HC participants, sleep quality in the laboratory was improved in comparison with sleep quality in the home environment. Objective measures of sleep were congruent with subjective measures of sleep in the laboratory but not in the home environment. Because of the congruence between subjective and objective measures of sleep in the laboratory and the relatively few objective sleep difficulties experienced by PTSD-diagnosed individuals, the findings suggest that PTSD diagnosed individuals experience improved sleep in the laboratory. However the difference in sleep quality between the two subject measures of sleep as well as between subjective sleep quality in the home environment and objective sleep quality in the laboratory may be attributable to measure variance. This finding limits the current project's ability to examine the full spectrum of neutral declarative memory, emotional memory and emotional reactivity difficulties that may arise in association with impaired sleep in this clinical population. Future studies should endeavour to use portable

EEG devices that can be used in the home environment, to get a relatively accurate representation of everyday sleep in PTSD-diagnosed individuals.

Fourth, I used urinary metabolites as a proxy for central noradrenergic action, even though some authors suggest that using such metabolites to represent centrally produced neurotransmitters is not very accurate (Hinz et al., 2011). Although this is not necessarily the reason why the analyses detected no significant role for noradrenaline in regulating sleep, neutral declarative memory, emotional memory, or emotional reactivity, future studies should use other biological markers, such as noradrenergic indicators derived from blood, either to replace or supplement urinary metabolites. Alternatively, studies might use measures of other hormones (e.g., adrenocorticotropic hormone or cortisol) in attempts to usefully describe the association between autonomic arousal and sleep, memory, and emotional functioning in PTSD.

Aside from the directions for future research suggested by these limitations, other such directions are suggested by the fact that a number of the current findings would benefit from clarifying follow-up studies. For instance, *Investigation 3* demonstrated that all participants, regardless of group assignment, were able to recognise all categories of previously-presented pictures (highly-arousing negatively valenced, highly-arousing positively valenced, and low-arousing neutral) with equal accuracy after a sleep-filled delay. After a wake-filled delay, however, recognition accuracy was higher for highly-arousing negatively valenced pictures only. Then, *Investigation 4* demonstrated that all participants, again regardless of group assignment, maintained low, or had attenuated, emotional reactivity in response to pictures of all valence and arousal categories after a sleep-filled delay. After a wake-filled delay, however, they showed increased emotional reactivity in response to an equivalent set of stimuli. Together, these sets of results tentatively suggest that a period of sleep had a regulatory function in response to participants' waking experiences. Whether that regulatory function is in direct response to the quality of participants' waking experiences remains unknown, however: the current design does

not allow for any direct inference about the relationship between sleep and waking, because half of the participants experienced the *Night* condition first, while the other half experienced the *Day* condition first, and there were at least 48 hours separating the two conditions. A future study might test the hypothesis that the regulatory function of sleep processes are directly related to waking experiences by observing and recording all participants' experiences during waking hours first, followed immediately by the experimental night of sleep.

Furthermore, as stated above, *Investigation 3* found that all participants, regardless of group assignment, recognized previously presented pictures with various valence and arousal properties equally accurately after a sleep-filled delay. This finding stands in contrast to those from previously published studies, which suggest that sleep consolidates valenced and arousing information preferentially over low-arousing and neutral information. In *Investigation 4*, I showed that all participants maintained low or had attenuated emotional reactivity after a period of sleep, while other studies have found that sleep protects or promotes emotional reactivity. In my findings I argue that sleep may play a flexible role in regulating emotional memory or emotional reactivity depending on the individual context of participants, related to their waking experiences. That is I argue not only that sleep regulates emotional memory and emotional reactivity based on waking experiences, but that the kind of regulatory process may differ depending on the context and environment individuals find themselves in. A follow-up study could establish the validity of this claim by inviting participants to take part in various experimental arms, where the nature of their waking experiences would be manipulated (stressful versus pleasant versus filled with new learning etc).

Finally, regarding emotional reactivity, the IAPS task allowed for a basic comparison of emotional reactivity to previously presented pictures after a period of sleep or a period of waking. However, a number of studies suggest that sleep is important for a specific kind of emotional regulation, namely the extinction of a previously conditioned fear response and the

generalization of extinction from one stimulus to another (Pace-Schott et al., 2009; Spoormaker et al., 2010). The lack of fear extinction and the lack of generalization of the extinction effect from one stimulus to another, are core symptoms of PTSD. However, in this study I did not employ a classical conditioning paradigm, because my study design did not allow for the inclusion of a fear conditioning protocol in addition to the measurement of neutral declarative memory and emotional memory before and after a sleep-filled or wake-filled delay. Future studies should investigate directly whether disrupted sleep in PTSD diagnosed individuals is related to the failure to (a) extinguish previously conditioned fear responses and (b) generalise the extinction effect from one stimulus to another.

CHAPTER NINE: SUMMARY AND CONCLUSION

The current research project set out to demonstrate that the sleep disruption commonly experienced by PTSD-diagnosed individuals has significant impact on their neutral declarative memory, emotional memory, and emotional reactivity. *Investigation 1* examined whether PTSD-diagnosed participants, in comparison with TE and HC participants, experienced more subjectively and objectively measured sleep disruption. In this investigation I also explored whether subjective and objective sleep disruption in PTSD-diagnosed individuals was predicted by elevated autonomic activity at night, indexed by noradrenergic activity. The findings demonstrated that PTSD-diagnosed individuals reported improved subjective sleep quality in the laboratory in comparison to their sleep quality in their home environments. Objective measures of sleep showed that they experienced limited PSG sleep disruption, characterized by greater NREM 1 sleep percentage and less SWS percentage, in comparison with TE and HC participants. These particular sleep disruptions did not contribute significantly to any aspect of neutral declarative memory or emotional memory performance, or emotional reactivity, in PTSD-diagnosed individuals. Furthermore, PTSD-diagnosed individuals did not have elevated noradrenergic activity at night, and nighttime noradrenergic levels were not associated with participants' subjective or objective sleep quality.

Investigation 2 examined whether PTSD-diagnosed participants, in comparison with TE and HC participants, had neutral declarative memory deficits in immediate and delayed recall during the day, and neutral declarative memory deficits in retention (a measure of memory consolidation) across the night. Furthermore I tested the prediction that subjective and objective measures of sleep would predict the amount of information participants retained after a sleep-filled delay. The findings confirmed both hypotheses. PTSD-diagnosed individuals performed more poorly than TE and HC participants on a test assessing retention of previously-learned

neutral declarative information across a sleep-filled delay. (There were no between-group differences when retention was measured across a wake-filled delay; instead PTSD-diagnosed participants had deficits in immediate and delayed recall during the day.) Despite the few between-group differences in objective sleep parameters, the retention deficit was predicted by increased REM fragmentation, rather than decreased SWS percentage, in PTSD-diagnosed individuals. This finding demonstrates that, although PTSD-diagnosed individuals may experience relatively decreased SWS, the REM fragmentation that they experience is likely to have more significant implications for their performance on tasks assessing neutral declarative memory.

Regarding *Investigations 3-4*, the analyses did not confirm my predictions. That is, PTSD-diagnosed individuals, in comparison with TE and HC participants, did not demonstrate increased accuracy and bias, or increased emotional reactivity, towards highly-arousing negatively valenced information after a sleep-filled delay. Instead they, together with TE and HC participants, recognized highly-arousing negatively valenced, highly-arousing positively valenced, and low-arousing neutral pictures with equal accuracy after a sleep-filled delay. Furthermore, all participants, regardless of group assignment, showed attenuated emotional reactivity to previously-presented stimuli after a sleep-filled delay, irrespective of the valence and arousal properties of those stimuli. In contrast, after a wake-filled delay all participants, regardless of group assignment, showed increased recognition accuracy for highly-arousing negatively valenced information in comparison with highly-arousing positively valenced and low-arousing neutral information. Also after a wake-filled delay, all participants showed elevated emotional reactivity in response to previously-presented stimuli, regardless of the valence and arousal properties of those stimuli. Together, these results allow the tentative suggestion that a period of sleep has a regulatory function with respect to emotional memory and emotional reactivity in response to participants' waking experiences. This suggestion supports the argument

that the kind of regulatory processes that individuals experience during sleep may differ depending on their everyday context and environmental experiences. Future studies should be designed to test this hypothesis.

I also examined whether specific aspects of subjective or PSG sleep predicted the pattern of emotional memory accuracy/bias and emotional reactivity demonstrated in this study. With respect to emotional memory, better REM continuity predicted higher recognition accuracy for low-arousing neutral information. With respect to emotional reactivity, the analyses detected no significant associations between subjective or PSG aspects of sleep and emotional reactivity. Hence, although there was a clear attenuation of emotional reactivity after a sleep-filled, rather than a wake-filled, delay, this effect appeared to be unrelated to sleep stages. This result stands in contrast to those from previously published studies suggesting that REM sleep plays a role in regulating emotional reactivity during sleep. Future studies might clarify the source of this disparity, and might also explore whether the effect observed here is related to the general effects of rest associated with sleep, or is related to some other aspect of sleep not captured by PSG analyses conducted here.

There is a distinct contrast in the results from *Investigations 2-4*: Whereas neutral declarative memory processing after sleep was impaired in PTSD-diagnosed participants, these individuals had relatively intact emotional memory processing and emotional regulation after a sleep-filled delay. This contrast may be explained by considering the kinds of tasks employed in the different investigations, and the brain structures these tasks may activate. Small disruptions in REM continuity may have affected hippocampal-dependent neutral declarative memory in PTSD-diagnosed individuals because hippocampal structures are sensitive to disruptions in circuitry. However, these sleep disturbances may not have affected PTSD-diagnosed participants' emotional memory (based on a recognition task) and emotional reactivity, because these functions are not predominantly reliant on hippocampal structures.

Aside from being methodologically robust (e.g., I measured sleep parameters using both subjective (self-report) and objective (PSG) means, and recruited, alongside PTSD-diagnosed individuals, both HC and TE individuals), the research contributes to knowledge in a number of significant ways. First, it demonstrates that in PTSD-diagnosed individuals, sleep disruption co-exists with other memory-based symptoms, and demonstrates that the co-occurrence of these symptoms is neither incidental nor accidental. That is, symptoms in PTSD are not isolated from one another, but rather meaningfully related. This finding also suggests that sleep disruption is an active component of PTSD psychopathology, rather than a passive symptom, which has treatment implications. If sleep disruption in PTSD drives other symptoms of the disorder, then treating sleep disruption can alleviate these symptoms. Sleep focused treatments may offer a unique addition to the arsenal of PTSD therapies, especially given that many PTSD-diagnosed individuals do not respond to pharmacological or behavioural intervention. With respect to emotional memory and emotional reactivity the results showed that PTSD-diagnosed participants benefitted from sleep in the same way as TE and HC participants. This finding suggests that a reasonable, although not perfect, night of sleep in this clinical population is associated with intact functioning for certain cognitive and emotional domains. Thus overall, the research bolsters the neuroscientific view of sleep as a critical biological process linked integrally to psychological well-being.

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Appendix A

Participant Information Sheet

(All information provided is treated confidentially)

1.Participant's demographic details

Name:……..
Age:…… DOB:…….
Gender (Male or female):…….
First language:……..
Years of schooling (incl. primary, secondary and tertiary education if applicable):….....
Telephone:…….
Email address:……
Postal Address:……..
……
……

What kind of traumatic events have you experienced?
.....

When did this/these traumatic event occur?
……

2. Medical history

2.1. Do you smoke? YES/NO

2.2. Do you consume any recreational drug? (**This information is for the purposes of this research simply because the effects of certain psychotropic drugs may interfere with the results**)

……

If yes, how frequently do you use this or these drugs? When was the last time you used the drug in question?

……

2.3. Are you taking any medication to help you sleep better? If so please provide the name.

……

2.4. Are you suffering from any medical condition we should be aware of (heart condition, HIV, high blood pressure, diabetes, cancer, epilepsy etc.)? Have you had a head injury?

…….

2.5. (i) Are you on any anti-depressants or psycho-tropic medication? Please provide the name of your medication.

……...

(ii) How long have you been taking this medication?

……

(iii) Are you partaking in any therapy/ seeing a psychologist or counselor?

……

2.6. Do you suffer from any sleep disorder (E.g. sleep apnea, insomnia, narcolepsy) YES/NO; if YES please state the disorder that applies to you:

……

What is your bed-time?

……

GP's or specialist's name:
.....
Address: .....
Telephone: .....

I, ……., confirm that the information contained on this form are correct.

Signed:..... Name: ..... Date: .....

Socio- Economic Status and Demographic Questionnaire

1. Age: _____

2. Sex (circle one): Male Female

3. What is your home language? (Please circle only *one* option)

   English Afrikaans Xhosa Zulu Pedi

   Other (please specify _____

4. What is the total monthly income of the household in which you live? If you are a student please take care to put your immediate caregiver's monthly income, not your own. (Please circle only *one* option):

   R0 – R499 R500 – R999 R1000 - R2499

   R2500 – R5499 R5500 – R9999 R10 000+

5. Occupation (please circle appropriate letter):
   (a) Unemployed
   (b) Self-employed
   (c) Business employed
   (d) Student/pupil
   (e) Other (*Specify*) _____

6. Education: Highest degree or grade completed: _____

Appendix B

Informed consent document

Informed Consent to Participate in Research and Authorization for Collection, Use, and Disclosure of Sleep Patterns, Performance on Memory tasks and Other Personal Data

You are being asked to take part in a research study. This form provides you with information about the study and seeks your authorization for the collection, use and disclosure of your sleep architecture patterns, cognitive performance data, autonomic arousal data and urine samples as well as other information necessary for the study. The Principal Investigator (the person in charge of this research) or a representative of the Principal Investigator will also describe this study to you and answer all of your questions. Your participation is entirely voluntary. Before you decide whether or not to take part, read the information below and ask questions about anything you do not understand. For your information – this study is covered by UCT's No Fault Insurance Policy.

1. Name of Participant

_____

2. Title of Research Study
"Neutral Declarative Memory, Emotional Memory and Emotional Regulation during Sleep in Posttraumatic Stress Disorder"

3. Principal Investigator and Telephone Number(s)

Malgorzata (Gosia) Lipinska
University of Cape Town (UCT)
Contact number: 084 621 0683

4. What is the purpose of this research study?
This research aims to investigate the whether disrupted sleep helps to explain memory problems in Post Traumatic Stress Disorder

5. What will be done if you take part in this research study?

In this experiment, you will be called in for 4 study sessions – 2 during the day and 2 spanning a whole night.

Before commencing the actual study, you will undergo a screening process whereby the Principal Investigator listed in # 3 of this form or her assistant, will administer a number of short psychiatric questionnaires and an IQ test. The psychiatric questionnaires will ask about your mood, your patterns of behaviour and possible symptoms you may be experiencing. One aspect of the questionnaire may ask about details relating to any traumatic events you may have experienced. These questionnaires are research instruments that allow us to identify

certain patterns of interest. During this screening the researcher will also inform you in detail about the design of the study and the research questions we hope to address with this study.

We will also take a comprehensive medical history from you where we will ask you to provide us with details of any medication you are currently on and any other things we should be aware of.

The first study session will take place during the day. You will be asked to come to UCT (PD Hahn building) at 9.00am in the morning for a study session of approximately 1.5 hours. A urine sample will be taken before the session begins. This urine sample will measure MHPG (3-Methoxy-4-Hydroxyphenylglycol) as a measure of central nervous system noradrenergic activity. MHPG is a metabolite of noradrenaline which reflects how much noradrenaline is active in your body. Noradrenaline is a neurotransmitter which is implicated in the flight or fight response as well as emotional learning. You will be asked to void into a plastic container, which will be used for scientific analysis. First you will be presented with some information that is part of a memory task. Secondly, as part of the session you will be asked to view some pictures. During this task a small device will be attached to your finger. This measures minute electrical changes on your skin. Some electrodes will also be placed on your chest to measure heart rate. This will conclude the morning session. You will be asked to return to UCT 8 hours later for a second session, which will follow exactly the same procedure.

The third session will be a sleep adaptation night at UCT's sleep laboratory. This session will be schedules 48 hours after the first session. You will be asked to come in at l.5 hours before your normal bed time. Transport will be provided if you require it. During this session you will simply get used to sleeping at the laboratory attached to all the equipment. You will be briefed in detail, on the procedure. You will be hooked to a polysomnograph (PSG) which is an EEG machine designed to monitor your sleep pattern. Electrodes will be placed on your head, chest, near your chin and temples; these are completely safe and present no danger whatsoever to your health. They are designed to transmit physiological indications of the stage of sleep you are experiencing at a given point in time, to a computer monitor. A trained researcher will be at the lab with you throughout the night for assistance at any time. In the morning all the equipment will be removed and you will be provided with a lift to Mowbray.

The fourth session will also take place at the sleep laboratory. It will be scheduled for the night after the adaptation night and will start 2.5 hours before your bedtime. During this session the testing procedure described in session 1 will be followed. That is firstly a urine sample will be taken, secondly a memory test will be administered, and thirdly some pictures will be presented alongside measures of skin conductance and heart rate. This procedure will also be followed after an 8-hour period of sleep. After testing you will again be hooked up to the polysomnograph. In the morning all the equipment will be removed and the morning testing session will begin (following the same procedure as that of the evening session).

You may also be asked to begin with the adaptation night, followed by the sleep night, followed 48 hours later by the day time testing described as the first session.

After your last session, you will be debriefed about the study. You will also have the opportunity to ask questions and thus learn more about psychological research. If you have any questions now or at any time during the study, you may contact the Principal Investigator listed in #3 of this form.

6. If you choose to participate in this study, how long will you be expected to participate in the research?

Screening and interview session: approximately 2 hours. Study sessions: 2 daytime session – one in the morning and one 8 hours later in the afternoon (each about 1.5 hours) plus 2 consecutive nights.

7. How many people are expected to participate in the research?

60

8. What are the possible discomforts and risks?

During the initial screening you may be faced with fairly specific questions regarding past traumatic events as well as your current psychological functioning. These questions may illicit painful or unpleasant memories or make you aware of various symptoms you are experiencing. Should you experience distress as a result of these memories or symptoms or wish to seek support for the symptoms experienced, the researcher will refer you to trained clinicians who will be able to provide support.

Sleeping in an environment other than your own bedroom might feel strange and uncomfortable at first. Great precautions will be taken to ensure your safety and comfort. The sleep laboratory at UCT is fully equipped with a proper bed, clean bedding, and restrooms. It is situated in a secure building with adequate security. Attempts will be made to familiarise you with the PSG and the electrodes used will be padded and lubricated so as to be as non-intrusive as possible.

Although the study sessions themselves (including the 1 daytime session and 2 nighttime sessions) will not delve into past memories and traumatic events experienced, if any difficult memories should arise during the process, you will be referred to trained clinicians for extra guidance.

9. What are the possible benefits to you?

You may or may not personally benefit from participating in this study. Participation in this study may, however, improve your understanding of some factors that affect sleep and may influence your management of your health generally.

10. What are the possible benefits to others?

The information from this study may help improve our understanding of the importance of sleep. This study aims to show that symptoms do not exist in isolation but influence each other. If it is indeed the case that difficulties in sleeping are related to difficulties in memory then we know we need to focus more on addressing sleeping patterns. In fact some research has shown that if you improve sleeping patterns other symptoms also improve and this study hopes to elaborate on this.

11. If you choose to take part in this research study, will it cost you anything?

Participating in this study will not cost you anything.

12. Will you receive compensation for taking part in this research study?

You will receive financial compensation of the amount of R150 for each of the 3 main study parts (daytime session 1 and 2, the adaptation night and the sleep study night). Thus if you participate in the research for 3 nights you will receive R450.

13a. Can you withdraw from this research study?

You are free to withdraw your consent and to stop participating in this research study at any time. If you do withdraw your consent, there will be no penalty.

If you have any questions regarding your rights as a research subject, you may phone the Psychology Department offices at 021-650-3430. You may also contact the Human Research Ethics Committee at 021-406-6626 or email: shuretta.thomas@uct.ac.za.

13b. If you withdraw, can information about you still be used and/or collected?

Information already collected may be used.

14. Once personal and performance information is collected, how will it be kept secret (confidential) in order to protect your privacy?

Information collected will be stored in locked filing cabinets or in computers with security passwords. Only certain people have the right to review these research records. These people include the researchers for this study and certain University of Cape Town officials. Your research records will not be released without your permission unless required by law or a court order.

15. What information about you may be collected, used and shared with others?

This information gathered from you will be demographic information, information on a past traumatic event and the related diagnosis of post-traumatic stress disorder and/or depression, records of your sleep architecture, performance on cognitive tests, and scores on the IQ test and psychiatric inventory. If you agree to be in this research study, it is possible that some of the information collected might be copied into a "limited data set" to be used for other research purposes. If so, the limited data set may only include information that does not directly identify you. For example, the limited data set cannot include your name, address, telephone number, ID number, or any other photographs, numbers, codes, or so forth that link you to the information in the limited data set.

16. How will the researcher(s) benefit from your being in the study?

In general, presenting research results helps the career of a scientist. Therefore, the Principal Investigator and others attached to this research project may benefit if the results of this study are presented at scientific meetings or in scientific journals. This study is being undertaken for the Principal Investigator's PhD degree.

17. Signatures

As a representative of this study, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this research study; and how the participant's performance and other data will be collected, used, and shared with others:

Signature of Person Obtaining Consent and Authorization Date

_____ _____

You have been informed about this study's purpose, procedures, possible benefits, and risks; and how your performance and other data will be collected, used and shared with others. You have received a copy of this form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask other questions at any time.

You voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your performance and other data. By signing this form, you are not waiving any of your legal rights.

Signature of Person Consenting and Authorizing Date

_____ _____

Please indicate below if you would like to be notified of future research projects conducted by our research group:
_____ (initial) Yes, I would like to be added to your research participation pool and be notified of research projects in which I might participate in the future.

Method of contact:

Phone number: _____
E-mail address: _____
Mailing address: _____
_____
_____

Appendix C

Laboratory PSQI

0=not at all 1= a little 2= quite a lot 3 = a lot

Did it take you longer than 30 minutes to fall asleep?	0	1	2	3
Did you wake up in the middle of the night or early in the morning?	0	1	2	3
Did you have to use the bathroom?	0	1	2	3
Did you have trouble breathing comfortably?	0	1	2	3
Did you snore or cough in the night?	0	1	2	3
Where you too cold?	0	1	2	3
Where you too hot?	0	1	2	3
Did you have bad dreams?	0	1	2	3
Did you have pain?	0	1	2	3
Did you have trouble sleeping because of other reasons?	0	1	2	3
Did you take medicine (prescribed or 'over-the-counter') to help you sleep?	0	1	2	3
During the day after the night in the lab, did you have trouble staying awake?	0	1	2	3
During the day after the night in the lab, did you have trouble keeping up enthusiasm to get things done?	0	1	2	3

How would you rate your sleep quality at the lab:

0 (v good) 1 (quite good) 2 (quite poor) 3 (v poor)

Did the equipment bother you?	0	1	2	3

How did you sleep in the lab in comparison with your home?

0 (better) 1 (same) 2 (little worse) 3 (worse)

Why?

How long did it take you to fall asleep?

How long did you sleep for?

How many times did you wake up during the night?

How long did you wake up for each time?

Did you dream?

Appendix D

Psychiatric diagnoses secondary to trauma experience

Participant Number	Group	Mini International Neuropsychiatric Inventory diagnosis
2	PTSD	Depression, Suicidality, Panic disorder limited symptoms, Agoraphobia
3	PTSD	Depression
5	PTSD	Depression, Panic disorder lifetime with current agoraphobia
7	PTSD	Depression
8	PTSD	Suicidality, Hypomanic episode
9	PTSD	Depression, Dysthymia, Panic attacks limited symptoms
10	PTSD	Depression, Suicidality
13	PTSD	Depression, Dysthymia, Panic disorder limited symptoms
15	PTSD	Depression, Dysthymia, Suicidality
16	PTSD	Depression, Suicidality, Past hypomanic episode, Panic disorder lifetime, Agoraphobia, Obsessive compulsive disorder
20	PTSD	Depression
24	PTSD	Panic disorder lifetime, Agoraphobia
26	PTSD	Depression, Panic disorder lifetime, Agoraphobia
27	PTSD	Depression, Dysthymia, Suicidality
48	PTSD	Depression, Suicidality, Agoraphobia
52	PTSD	Depression, Panic disorder current, Social phobia
54	PTSD	Depression, Suicidality
57	PTSD	Depression, Dysthymia, Suicidality, Agoraphobia, Mood disorder with psychotic features
58	PTSD	Depression, Dysthymia, Suicidality
60	PTSD	Depression, Dysthymia, Panic disorder limited symptoms, Agoraphobia
1	TE	Depression, Dysthymia, Suicidality
4	TE	Depression, Suicidality
6	TE	Panic disorder lifetime
12	TE	Panic disorder limited symptoms, Agoraphobia
14	TE	Depression
17	TE	Dysthymia, Suicidality
19	TE	Depression, Obsessive compulsive disorder
22	TE	Depression, Agoraphobia
44	TE	Depression, Suicidality
47	TE	Depression, Suicidality
49	TE	Suicidality
51	TE	Depression, Suicidality
53	TE	Depression, Suicidality, Agoraphobia
56	TE	Depression
59	TE	Suicidality, Panic disorder limited symptoms,

Appendix E

Participant qualitative responses regarding the difference in sleep quality between the laboratory and the home environment

Participant Number	Group	Verbatim participant response defining sleep quality difference between laboratory and home environment
2	PTSD	-
3	PTSD	-
5	PTSD	-
7	PTSD	cool and quiet
8	PTSD	felt safe
9	PTSD	-
10	PTSD	quiet; safe
13	PTSD	told herself she has to sleep
15	PTSD	not used to sleeping here
16	PTSD	I don't know, woke up many times
18	PTSD	felt the same as at home
20	PTSD	comfortable
24	PTSD	no noise - don't hear gun shots, taxi, it's just quiet
26	PTSD	-
27	PTSD	comfortable
48	PTSD	relaxed, alone in the bed - at my house I sleep with my sisters and brothers
52	PTSD	used to surroundings from the previous night and nice and quiet
54	PTSD	it's quiet
57	PTSD	I don't know, feels comfortable
58	PTSD	quiet
60	PTSD	because of environment - quiet, no disturbances
1	TE	not used to it; perhaps food poisoning on wed added to sleep difficulties
4	TE	quiet here, didn't play with the phone
6	TE	the same as usual
11	TE	always sleeps the same
12	TE	not the dream that woke me; quiet here; no distractions
14	TE	was sleepy but took a long time to fall asleep
17	TE	felt the same comfortable as home
19	TE	used to the lab now
22	TE	didn't think much; felt safe
29	TE	nice and quiet
44	TE	because its comfortable
47	TE	thinking about children
49	TE	no bad dreams - comfortable
50	TE	so comfortable and quiet
51	TE	felt like she slept in comparison to the adaptation night
53	TE	nothing new happened; slept like usually does
55	TE	quiet here, no dog chasing something

Participant Number	Group	Verbatim participant response defining sleep quality difference between laboratory and home environment
56	TE	don't know
59	TE	-
21	HC	fell asleep quick; safe; no worries
23	HC	-
25	HC	maybe because I am comfortable
28	HC	because I was so tired
30	HC	because of the comfortable bed
31	HC	-
32	HC	quiet and no TV
33	HC	whole experience, being warm, quiet, same as at home
34	HC	wake up often at home because of children
35	HC	bed is comfortable
36	HC	no one to bother, no noise
37	HC	more used to the environment
38	HC	nothing bothered me; very quiet; went straight to sleep
39	HC	used to the lab. Not used to sleeping on her own - usually sleep with baby
40	HC	comfortable
41	HC	didn't feel uncomfortable
42	HC	when not doing any projects at varsity she sleeps well
43	HC	comfortable
45	HC	my second day so getting used to it
46	HC	nothing happened and I slept as usual as at home

Appendix F

The valence and arousal properties of selected International Affective Picture System images

Night Condition - Trial 1 Evening Session								
Negative			Positive			Neutral		
IAPS number	Valence	Arousal	IAPS number	Valence	Arousal	IAPS number	Valence	Arousal
9040	1.50	6.44	1340	7.63	5.25	2101	4.49	3.57
2703	1.59	5.81	1710	8.59	5.31	2377	5.30	3.69
3191	1.68	6.26	2045	8.17	6.02	2580	5.90	2.84
6315	1.72	6.69	2150	8.31	5.29	2850	5.69	3.38
3350	1.76	5.78	2165	8.29	5.05	5531	5.07	3.80
9046	2.94	4.63	2208	7.55	6.14	7009	4.89	3.26
6263	2.06	6.72	2303	7.04	5.88	7186	4.38	3.68
6571	2.15	5.87	4505	7.20	6.46	7354	5.36	3.90
4664	2.21	6.04	4624	7.17	5.21	7493	5.56	3.39
6311	2.36	5.12	7220	7.19	5.70	7710	5.49	3.40
1205	3.22	5.94	7650	7.03	6.21	8010	4.24	4.11
1090	3.29	5.94	8200	7.86	6.37	2383	4.79	3.36
3185	2.52	5.68	8492	7.11	7.48	7255	5.13	3.41
9322	2.02	5.7	8501	7.67	6.02	7021	5.29	4.35
9342	2.53	4.56	8531	7.11	5.25	5395	5.33	4.24
1201	2.93	6.87	1463	7.81	5.11	2384	5.86	3.23
2100	3.37	5.32	2058	8.24	5.45	2493	5.10	3.54
2900	2.16	5.40	4510	7.00	6.05	2513	5.90	3.21
3015	1.34	6.11	4525	7.67	6.70	2593	5.73	3.22
3068	1.18	7.18	4623	7.49	5.37	2745.1	5.38	3.31
9265	2.42	4.48	4626	7.80	6.06	7030	4.57	3.22
9140	1.88	5.79	5629	7.15	6.52	7249	5.24	3.87
9301	1.87	5.66	5910	8.16	5.80	7300	5.70	3.33
9332	1.89	5.47	7400	7.30	5.44	7512	5.29	3.56
9584	3.29	5.15	8030	7.35	7.38	8312	5.34	3.10
3062	1.62	5.84	8496	7.94	6.38	9090	4.02	4.41
1026	3.65	5.54	8502	7.65	6.00	7247	4.85	3.92
9075	1.29	6.57	4614	7.71	5.38	7037	4.75	3.7
9430	2.3	5.57	2050	8.62	5.1	2516	4.76	3.45
2301	2.68	4.75	7430	7.35	5	7077	4.79	4.56
Mean	**2.25**	**5.76**		**7.64**	**5.85**		**5.14**	**3.60**
Standard deviation	**0.68**	**0.68**		**0.48**	**0.66**		**0.50**	**0.42**

Night Condition - Trial 2 Morning Session								
Negative			Positive			Neutral		
IAPS number	Valence	Arousal	IAPS number	Valence	Arousal	IAPS number	Valence	Arousal
6571	2.15	5.87	1340	7.63	5.25	2101	4.49	3.57
1052	2.99	6.89	1710	8.59	5.31	2377	5.30	3.69
1090	3.29	5.94	2045	8.17	6.02	2580	5.90	2.84
1205	3.22	5.94	2150	8.31	5.29	2850	5.69	3.38
2703	1.59	5.81	2165	8.29	5.05	5531	5.07	3.80
3185	2.52	5.68	2208	7.55	6.14	7009	4.89	3.26
3191	1.68	6.26	2303	7.04	5.88	7186	4.38	3.68
3225	1.66	6.32	4505	7.20	6.46	7354	5.36	3.90
3280	3.62	5.08	4624	7.17	5.21	7493	5.56	3.39
3350	1.76	5.78	7220	7.19	5.70	7710	5.49	3.40
4664	2.21	6.04	7650	7.03	6.21	8010	4.24	4.11
6212	1.81	6.53	8200	7.86	6.37	2383	4.79	3.36
6243	1.90	6.34	8492	7.11	7.48	7255	5.13	3.41
6263	2.06	6.72	8501	7.67	6.02	7021	5.29	4.35
6311	2.36	5.12	8531	7.11	5.25	5395	5.33	4.24
6315	1.72	6.69	2209	7.95	5.91	2026	4.85	3.38
6562	2.89	5.03	8163	7.38	6.53	2107	5.62	3.47
9040	1.50	6.44	5825	8.02	5.58	7001	5.51	3.38
9046	2.94	4.63	2347	8.35	5.88	2272	4.49	3.88
9322	2.02	5.7	7282	7.13	5.09	1122	4.91	4.46
9342	2.53	4.56	7508	7.03	5.06	5661	5.91	3.98
9427	2.55	5.56	1811	7.95	5.21	7248	5.19	3.78
9435	1.81	5.09	1463	7.81	5.11	2840	4.9	2.55
1201	2.93	6.87	2058	8.24	5.45	2384	5.86	3.23
1026	3.65	5.54	4510	7.00	6.05	2493	5.10	3.54
1114	3.43	6.34	4525	7.67	6.70	2513	5.90	3.21
2100	3.37	5.32	4623	7.49	5.37	2593	5.73	3.22
2301	2.68	4.75	4626	7.80	6.06	2745.1	5.38	3.31
2457	2.91	5.36	5629	7.15	6.52	7030	4.57	3.22
2900	2.16	5.40	5910	8.16	5.80	7249	5.24	3.87
3010	1.29	7.44	7400	7.30	5.44	7300	5.70	3.33
3015	1.34	6.11	8030	7.35	7.38	7512	5.29	3.56
3016	1.60	5.94	8496	7.94	6.38	8312	5.34	3.10
3062	1.62	5.84	8502	7.65	6.00	9090	4.02	4.41
3068	1.18	7.18	4614	7.71	5.38	7247	4.85	3.92
3230	1.67	5.75	2050	8.62	5.1	7037	4.75	3.7
9075	1.29	6.57	7430	7.35	5	2516	4.76	3.45
9140	1.88	5.79	8500	7.16	5.52	7077	4.79	4.56
9145	2.91	5.25	4532	7.62	5.55	2036	5.81	3.51
9265	2.42	4.48	8001	7.46	6.62	7002	5.03	3.28
9301	1.87	5.66	5460	7.30	5.76	7287	4.63	3.63
9302	1.97	6	2075	7.85	5.58	7033	5.23	4.05

Night Condition - Trial 2 Morning Session								
Negative			Positive			Neutral		
IAPS number	Valence	Arousal	IAPS number	Valence	Arousal	IAPS number	Valence	Arousal
9332	1.89	5.47	2224	7.63	5.06	7188	5.3	3.76
9430	2.3	5.57	7200	7.77	4.85	7496	5.99	4.91
9584	3.29	5.15	4610	7.79	5.04	7014	5.16	3.3
Mean	**2.28**	**5.82**		**7.63**	**5.75**		**5.17**	**3.63**
Standard deviation	**0.69**	**0.69**		**0.45**	**0.63**		**0.48**	**0.46**

Day Condition - Trial 1 Morning Session								
Negative			Positive			Neutral		
IAPS number	Valence	Arousal	IAPS number	Valence	Arousal	IAPS number	Valence	Arousal
3005.1	1.35	6.74	1630	7.74	4.45	2206	4.20	3.84
2800	1.41	5.87	2345	7.75	5.99	2435	5.96	3.87
2399	3.5	4.11	2347	8.35	5.88	2579	5.39	3.79
3530	1.51	6.80	4538	7.04	6.14	2595	4.97	3.65
9253	1.60	5.95	4575	7.61	6.12	5900	5.75	4.11
3180	1.67	6.19	4597	7.23	6.06	7110	4.59	2.59
6560	1.78	6.86	4641	7.21	5.33	7290	4.22	4.06
3195	1.79	6.42	4660	7.22	6.31	7505	5.85	4.55
6370	2.20	6.58	5270	7.32	5.72	7550	5.17	3.52
6240	3.26	5.42	7270	7.77	5.85	7820	5.18	3.95
1051	3.28	6.06	7502	8.15	6.07	8250	5.84	4.62
2278	3.34	4.70	8370	7.86	6.98	7184	4.78	3.8
9429	2.4	5.48	8380	7.88	5.47	5740	5.33	2.79
9320	2.26	5.32	8470	7.94	5.98	7130	4.75	3.2
9290	2.76	4.44	8499	7.70	5.56	7491	4.79	2.24
1033	3.25	6.29	1722	7.18	5.60	2499	5.35	2.99
2095	1.48	5.72	2216	7.85	6.29	2518	5.85	3.37
2115	3.51	5.05	4542	7.51	6.17	2749	4.97	3.81
2141	2.27	5.35	4572	7.52	6.30	7100	5.20	2.73
2205	1.65	4.65	4628	7.78	5.54	7211	4.69	4.54
2276	2.32	5.06	4640	7.64	5.94	7365	4.96	4.26
2375	1.91	5.22	7405	7.55	6.41	7500	5.23	3.08
2981	2.09	6.33	8185	7.75	7.42	7595	4.53	4.07
9280	2.69	4.05	8420	7.90	5.41	7700	4.20	3.01
3064	1.15	7.30	8490	7.44	6.97	7830	5.22	3.81
3400	2.06	7.12	2346	7.01	5.16	8121	4.72	4.29
8480	3.16	6.59	7230	7.35	5.27	8325	5.49	4.30
9042	2.10	5.86	2160	8.16	5.03	7045	4.88	3.26
9325	1.62	6.55	4603	7.58	5	7503	5.59	3.65
9902	2.05	5.81	5830	8.54	4.88	2382	5.69	3.64
Mean	**2.25**	**5.80**		**7.65**	**5.84**		**5.11**	**3.65**
Standard deviation	**0.71**	**0.88**		**0.37**	**0.65**		**0.51**	**0.61**

Day Condition - Trial 2 Afternoon Session								
Negative			Positive			Neutral		
IAPS number	Valence	Arousal	IAPS number	Valence	Arousal	IAPS number	Valence	Arousal
9290	2.76	4.44	1630	7.74	4.45	2206	4.20	3.84
2278	3.34	4.70	2345	7.75	5.99	2435	5.96	3.87
9253	1.60	5.95	2347	8.35	5.88	2579	5.39	3.79
9429	2.4	5.48	4538	7.04	6.14	2595	4.97	3.65
9320	2.26	5.32	4575	7.61	6.12	5900	5.75	4.11
3180	1.67	6.19	4597	7.23	6.06	7110	4.59	2.59
1051	3.28	6.06	4641	7.21	5.33	7290	4.22	4.06
2399	3.5	4.11	4660	7.22	6.31	7505	5.85	4.55
6240	3.26	5.42	5270	7.32	5.72	7550	5.17	3.52
3195	1.79	6.42	7270	7.77	5.85	7820	5.18	3.95
3005	1.35	6.74	7502	8.15	6.07	8250	5.84	4.62
2800	1.41	5.87	8370	7.86	6.98	7184	4.78	3.8
3530	1.51	6.80	8380	7.88	5.47	5740	5.33	2.79
6560	1.78	6.86	8470	7.94	5.98	7130	4.75	3.2
6370	2.20	6.58	8499	7.70	5.56	7491	4.79	2.24
6230	2.06	7.56	4599	7.23	5.64	2512	4.78	3.29
3181	2.01	5.16	8090	7.42	5.71	2890	5.02	2.90
6520	1.59	7.12	8034	7.19	6.38	1670	5.88	3.52
3301	1.49	5.51	5260	7.20	5.43	7090	5.44	2.92
1101	3.52	6.11	4535	7.06	5.58	7018	4.73	4
3300	2.35	4.96	7330	7.96	5.54	5120	4.15	3.24
6561	2.79	5.49	2158	7.56	5.05	2200	4.95	4.03
6836	3.05	5.78	8497	7.7	4.46	7185	5.08	2.72
1033	3.25	6.29	1722	7.18	5.60	2499	5.35	2.99
2095	1.48	5.72	2216	7.85	6.29	2518	5.85	3.37
2115	3.51	5.05	4542	7.51	6.17	2749	4.97	3.81
2141	2.27	5.35	4572	7.52	6.30	7100	5.20	2.73
2205	1.65	4.65	4628	7.78	5.54	7211	4.69	4.54
2276	2.32	5.06	4640	7.64	5.94	7365	4.96	4.26
2375	1.91	5.22	7405	7.55	6.41	7500	5.23	3.08
2981	2.09	6.33	8185	7.75	7.42	7595	4.53	4.07
9280	2.69	4.05	8420	7.90	5.41	7700	4.20	3.01
3064	1.15	7.30	8490	7.44	6.97	7830	5.22	3.81
3400	2.06	7.12	2346	7.01	5.16	8121	4.72	4.29
8480	3.16	6.59	7230	7.35	5.27	8325	5.49	4.30
9043	2.10	5.86	2160	8.16	5.03	7045	4.88	3.26
9325	1.62	6.55	4603	7.58	5	7503	5.59	3.65
9902	2.05	5.81	5830	8.54	4.88	2382	5.69	3.64
3030	1.51	7.13	8190	8.08	6.16	2305	5.14	3.05
3101	1.64	5.96	5623	7.26	5.77	5532	4.99	3.58
3213	2.61	6.79	7260	7.31	5.31	2880	5.22	3.17
9220	1.86	4.16	2071	8.21	5.33	7224	4.51	3.01

Day Condition - Trial 2 Afternoon Session								
Negative			Positive			Neutral		
IAPS number	Valence	Arousal	IAPS number	Valence	Arousal	IAPS number	Valence	Arousal
2455	2.63	4.65	2155	7.17	5.56	7183	5.53	3.75
1050	3.02	6.9	2550	8.14	5.16	7590	5.18	3.72
9186	3.03	5.14	4612	7.05	5	1675	5.1	4.36
Mean	**2.28**	**5.83**		**7.60**	**5.72**		**5.09**	**3.57**
Standard deviation	**0.69**	**0.92**		**0.39**	**0.62**		**0.48**	**0.58**

Appendix G

Valence and Arousal properties of Negative, Positive and Neutral IAPS Pictures

Difference in Valence between Negative, Positive and Neutral Pictures

	Valence				
Variable	Negative (n = 150)	Positive (n = 150)	Neutral (n = 150)	F / t	p
IAPS Valence Rating	2.27 (0.69)	7.63 (0.42)	5.13 (0.49)	3672.59	<.001
Contrast 1				-66.51	<.001
Contrast 2				47.72	<.001

Note. Means are presented with standard deviations in parentheses. IAPS = International Affective Picture System. Degrees of freedom were: (2, 447); Contrast 1 compares negative pictures to combined positive and neutral pictures; Contrast 2 compares positive to neutral pictures.

Difference in Arousal between Arousing and Non-Arousing Pictures

	Valence			
Variable	Arousing (n = 300)	Non-arousing (n = 150)	t	p
IAPS Arousal Rating	5.79 (0.72)	3.61 (0.52)	1104.61	<.001

Note. Means are presented with standard deviations in parentheses. IAPS = International Affective Picture System. Degrees of freedom were: (1, 448)

Difference in Arousal between Negative, Positive and Neutral Pictures

	Valence				
Variable	Negative (n = 150)	Positive (n = 150)	Neutral (n = 150)	F / t	p
IAPS Arousal Rating	5.81 (0.79)	5.78 (0.63)	3.61 (0.52)	551.31	<.001
Contrast 1				36.85	<.001
Contrast 2				0.34	.74

Note. Means are presented with standard deviations in parentheses. IAPS = International Affective Picture System. Degrees of freedom were: (2, 447); Contrast 1 compares neutral pictures to combined negative and positive pictures; Contrast 2 compares negative to positive pictures.

The following tables demonstrate that each category of pictures (high arousing negative, high arousing positive and low arousing neutral) had consistent arousal and valence properties irrespective of condition (*Night* vs *Day*) and trial (*Trial* 1 vs *Trial 2*).

Factorial ANOVA: Valence and Arousal Differences across Condition and Trial for High Arousing Negative Pictures

	Type III Sum of Squares	Degrees of Freedom	Mean Square	*F*	*p*
IAPS Valence Ratings					
Corrected Model	0.03	3	0.01	0.02	.99
Condition	<0.01	1	<0.01	<0.01	.99
Trial	0.03	1	0.03	0.07	.79
Condition x Trial	1.00	1	1.00	<0.01	.99
IAPS Arousal Ratings					
Corrected Model	0.09	3	0.03	0.05	.99
Condition	0.02	1	0.02	0.03	.87
Trial	0.07	1	0.07	0.11	.74
Condition x Trial	<0.01	1	<0.01	0.01	.93

Note. IAPS = International Affective Picture System.

Factorial ANOVA: Valence and Arousal Differences across Condition and Trial for High Arousing Positive Pictures

	Type III Sum of Squares	Degrees of Freedom	Mean Square	*F*	*p*
IAPS Valence Ratings					
Corrected Model	0.05	3	0.02	0.10	.96
Condition	<0.01	1	<0.01	<0.02	.88
Trial	0.03	1	0.03	0.14	.70
Condition x Trial	0.02	1	0.02	0.10	.75
IAPS Arousal Ratings					
Corrected Model	0.46	3	0.15	0.38	.77
Condition	0.01	1	0.01	0.02	.89
Trial	0.45	1	0.45	1.11	.29
Condition x Trial	0.01	1	0.01	0.01	.91

Note. IAPS = International Affective Picture System.

Factorial ANOVA: Valence and Arousal Differences across Condition and Trial for Low Arousing Neutral Pictures

	Type III Sum of Squares	Degrees of Freedom	Mean Square	*F*	*p*
IAPS Valence Ratings					
Corrected Model	0.16	3	0.05	0.23	.88
Condition	0.11	1	0.11	0.45	.50
Trial	<0.01	1	<0.01	<0.01	.95
Condition x Trial	0.03	1	0.03	0.11	.74
IAPS Arousal Ratings					
Corrected Model	0.13	3	0.04	0.16	.92
Condition	<0.01	1	<0.01	0.01	.94
Trial	0.02	1	0.02	0.07	.79
Condition x Trial	0.10	1	0.10	0.37	.55

Note. IAPS = International Affective Picture System

Appendix H

Normality across Valence and Condition for HR, PEP, LVET and SCL Related to a Comparison of Trial 1 versus Trial 2 Same Pictures

	Group					
	PTSD (n = 21)		TE (n = 16)		HC (n = 20)	
	D	*p*	*D*	*p*	*D*	*p*
HR						
Day Trial 1						
H-A Negative	0.97	.76	0.94	.33	0.94	.26
H-A Positive	0.96	.54	0.98	.99	0.94	.22
L-A Neutral	0.96	.42	0.94	.35	0.91	.06
Day Trial 2						
H-A Negative	0.92	.09	0.96	.71	0.89	.03*
H-A Positive	0.93	.11	0.97	.76	0.86	.01*
L-A Neutral	0.90	.03*	0.98	.94	0.87	.01*
Night Trial 1						
H-A Negative	0.95	.30	0.97	.87	0.94	.26
H-A Positive	0.94	.18	0.93	.28	0.87	.01*
L-A Neutral	0.93	.12	0.97	.83	0.90	.04*
Night Trial 2						
H-A Negative	0.81	<.01*	0.81	<.01*	0.96	.45
H-A Positive	0.79	<.01*	0.83	.01*	0.95	.35
L-A Neutral	0.79	<.01*	0.82	<.01*	0.92	.10
PEP						
Day Trial 1						
H-A Negative	0.94	.17	0.96	.71	0.58	<.01*
H-A Positive	0.98	.94	0.96	.58	0.54	<.01*
L-A Neutral	0.95	.32	0.91	.11	0.51	<.01*
Day Trial 2						
H-A Negative	0.96	.55	0.98	.98	0.81	<.01*
H-A Positive	0.97	.82	0.97	.87	0.79	<.01*
L-A Neutral	0.98	.86	0.98	.97	0.81	<.01*
Night Trial 1						
H-A Negative	0.75	<.01*	0.80	<.01*	0.82	<.01*
H-A Positive	0.94	.18	0.93	.28	0.87	.01*
L-A Neutral	0.71	<.01*	0.92	.16	0.80	<.01*
Night Trial 2						
H-A Negative	0.84	<.01*	0.59	<.01*	0.89	.02*
H-A Positive	0.87	.01*	0.59	<.01*	0.86	.01*
L-A Neutral	0.86	.01*	0.66	<.01*	0.85	.01*

	Group					
	PTSD (*n* = 19)		TE (*n* = 18)		HC (*n* = 20)	
	D	*p*	*D*	*p*	*D*	*p*
LVET						
Day Trial 1						
H-A Negative	0.86	.01*	0.91	.13	0.89	.03*
H-A Positive	0.86	.01*	0.90	.08	0.89	.03*
L-A Neutral	0.83	<.01**	0.90	.09	0.85	.01*
Day Trial 2						
H-A Negative	0.86	.01*	0.91	.12	0.88	.02*
H-A Positive	0.84	<.01**	0.88	.05	0.92	.08
L-A Neutral	0.85	.01*	0.89	.05	0.88	.02*
Night Trial 1						
H-A Negative	0.95	.40	0.84	.01*	0.82	<.01**
H-A Positive	0.93	.15	0.83	.01*	0.82	<.01**
L-A Neutral	0.95	.37	0.84	.01*	0.84	<.01**
Night Trial 2						
H-A Negative	0.90	.04*	0.88	.04*	0.95	.40
H-A Positive	0.91	.06	0.86	.02*	0.92	.11
L-A Neutral	0.89	.02*	0.89	.05	0.92	.12
SCL						
Day Trial 1						
H-A Negative	0.92	.08	0.97	.84	0.94	.23
H-A Positive	0.91	.06	0.97	.77	0.93	.14
L-A Neutral	0.87	.01	0.96	.71	0.95	.32
Day Trial 2						
H-A Negative	0.91	.04*	0.91	.11	0.94	.26
H-A Positive	0.92	.08	0.91	.13	0.94	.24
L-A Neutral	0.92	.10	0.91	.13	0.93	.18
Night Trial 1						
H-A Negative	0.98	.90	0.70	<.001***	0.98	.96
H-A Positive	0.98	.92	0.75	<.01*	0.99	.98
L-A Neutral	0.98	.92	0.73	<.001***	0.99	.99
Night Trial 2						
H-A Negative	0.93	0.16	0.92	.17	0.92	.11
H-A Positive	0.94	.23	0.93	.21	0.92	.11
L-A Neutral	0.94	.21	0.93	.24	0.91	.07

Note: Valence: high arousing negative, high arousing positive, low arousing neutral; Condition: Night, Day; TE = trauma-exposed non-PTSD; HC = healthy control; HR = heart rate; PEP = pre-ejection period; LVET = left ventricular ejection time; SCL = skin conductance level; H-A = high arousing; L-A = low arousing; Degrees of freedom for the PTSD, Trauma-Exposed and Healthy Control groups are 21, 16 and 20 respectively. * p < .05; ** p < .01; *** p < .001.

Appendix I

Investigation 4, Results, Testing hypothesis 2: Selecting variables of autonomic arousal for correlation analysis

I used the results from *hypothesis 1* to organise the data for correlation analysis. Each variable related to HR, PEP and LVET for the first group of analyses and PEP and LVET for the second group of analyses was reported for a specific trial, condition and arousal/valence category. However the results from *hypothesis 1* indicated that for many of the analyses there was no effect of trial, condition and arousal/valence category. Where there was no effect of these factors I collapsed the separate variables into one variable to avoid running many unnecessary correlation analyses.

For example regarding the factor of trial, because I wanted to correlate variables of emotional reactivity that were related to the sleep period, I subtracted *Trial 1* values from *Trial 2* values for HR, PEP and LVET (first group of analyses). Results from *hypothesis 1* revealed no difference between *Trial 2* original pictures and *Trial 2* new pictures for PEP and LVET (second group of analyses), so I averaged original and new pictures to form a single variable for PEP and LVET respectively.

Furthermore, the analyses from *hypothesis 1* showed no effect of arousal/valence on PEP and LVET related to the first and second groups of analyses. I therefore averaged the individual arousal/valence categories to create a single variable related to PEP and LVET for both the first and second set of analyses. This process was not completed for HR, since this variable evidenced differences between arousal/valence categories. Therefore each arousal/valence category related to HR was correlated individually with sleep variables.