Chapter 6
The Role of Sleep in Emotional Processing

Daniela Tempesta, Valentina Socci, Luigi De Gennaro, and Michele Ferrara

Abstract In this chapter, we have reviewed an extensive literature supporting the critical role of sleep for several aspects of emotional processing and regulation.

In the first part, we discussed the main behavioral and psychophysiological studies that examined how sleep influences the processes of encoding and consolidation of emotional memory. In addition, we examined how sleep modulates emotion regulation, emotional reactivity, and empathy. Further, we discussed the implication of sleep in fear conditioning memory, threat generalization, and extinction memory. In the second part, we discussed evidence specifically suggesting the implication of REM sleep in the consolidation of emotional memory and in the modulation of emotional reactivity. In particular, we will focus on the specific physiological REM features that contributed to suggest its critical involvement in emotional processing. In the third part, we overviewed the functional neuroimaging studies on the brain mechanisms that underlie the relations between sleep and emotions. Finally, we focused on the most important psychiatric disorders that express abnormalities of sleep and emotional alterations, briefly reviewing our knowledge about the relationships between sleep disturbances and mood in major depression, anxiety disorders, and post-traumatic stress disorder.

We showed that sleep helps in the formation of emotional memories at every stage of this process. On the contrary, sleep loss induces deficit in encoding of emotional information, leading to a disruptive interference with emotional memory consolidation. The reviewed literatures clearly suggest that sleep loss significantly influences emotional reactivity. Whether sleep acts to protect, potentiate, or de-potentiate emotional reactivity is, however, still debatable. Future studies will have to elucidate, at the behavioral level, the specific direction of the sleep-dependent emotional modulation. Sleep seems to be crucial also for our ability to correctly process emotional information that allows us to understand the others'

D. Tempesta · V. Socci · M. Ferrara (✉)
Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy
e-mail: michele.ferrara@univaq.it

L. De Gennaro
Department of Psychology, Sapienza University of Rome, Rome, Italy

S. K. Jha, V. M. Jha (eds.), *Sleep, Memory and Synaptic Plasticity*,
https://doi.org/10.1007/978-981-13-2814-5_6

feelings and to be empathic with them, as well as for our ability to encode and consolidate fear conditioning and extinction learning. As far as the role of REM sleep is concerned, it seems to be crucial for the consolidation of emotional memory, while its specific contribution on next-day emotional reactivity is less clear. In fact, REM sleep could act to potentiate or, conversely, de-potentiate the emotional charge associated to a memory along with its consolidation. This topic could be also relevant for its implications in clinical settings. Indeed, further explaining how sleep influences the next-day emotional brain functioning will be crucial to open a new perspective for the understanding and treatment of affective or anxiety disturbances in patients with disturbed sleep.

Keywords Emotional memory · Emotional reactivity · Empathy · Fear conditioning · REM sleep · Sleep deprivation

6.1 Introduction

In the modern Western societies, sleep is often considered a period of wasted time that might be better devoted to more productive activities. However, we spend on average about one-third of our lives asleep. Sleep is a universal need of all higher life forms including humans, the absence of which has serious cognitive and physiological consequences.

Research over the past years has shown the key function of sleep in several human abilities that mainly involve the frontal cortex, such as executive functions and working memory (Jones and Harrison 2001; Durmer and Dinges 2005), and the limbic areas, such as emotional processing (Payne and Kensinger 2011). However, even though the crucial role of sleep in the consolidation and integration memory processes is nowadays largely acknowledged, an unequivocal hypothesis about the specific role of sleep in affective and emotional processing is still lacking. Nevertheless, a number of recent evidence evaluating the effects of sleep loss on emotional reactivity (e.g., Zohar et al. 2005; Yoo et al. 2007; Tempesta et al. 2010) and emotional memory (e.g., Sterpenich et al. 2007, 2009; Tempesta et al. 2014, 2015, 2016) showed behavioral and functional alterations imposed by sleep loss.

The goal of this chapter is to provide a synthesis of these recent findings in humans, analyzing in detail the role of sleep in the different components of emotional processing. In the first section, the relations between sleep and emotions will be discussed. Particularly, we describe the main behavioral and psychophysiological studies that investigated the influence of sleep in the emotional memory encoding and consolidation processes. Thereafter, we have discussed how sleep modulates emotions. We have particularly reviewed relevant evidence regarding the role of sleep in emotional reactivity and in more complex emotional processes, such as those involved in empathy. Furthermore, we have specifically discussed the role of REM sleep in emotional memory consolidation and emotional reactivity, analyzing

the specific physiological features of REM that contributed to suggest its critical implication in emotional processing. In the third section, we have further discussed the relations between sleep and emotions by overviewing the functional neuroimaging studies on the brain mechanisms that underlie these processes. It can be observed, particularly during REM sleep, the activation of brain areas specifically involved in human emotional processing. It provides new insights into the protective role of sleep in human emotional homeostasis and emotional regulation. Finally, we turn our attention to the most important psychiatric disorders that express co-occurring sleep disorders and emotional alteration, briefly reviewing our knowledge about the relationships between sleep disturbances and mood in major depression, anxiety disorders, and post-traumatic stress disorder.

6.2 The Relations Between Sleep and Emotions: Behavioral and Psychophysiological Studies

Sleep is traditionally defined as a reversible behavioral state of perceptual disengagement from and unresponsiveness to the environment. Sleep comprises two separate states which largely differ on the basis of a constellation of physiologic parameters. These two states, rapid eye movement (REM) and non-rapid eye movement (NREM), exist in virtually all mammals, and they are as distinct from one another, as well as each one is from wakefulness.

The normal human adult enters sleep through NREM sleep. REM sleep does not usually occur until subject experience on an average 80 min or longer episodes of NREM sleep. Thereafter, NREM and REM sleep alternate through the night, with about a 90-min cycle. Both sufficient sleep continuity and sleep duration are prerequisites for recuperation and may be considered as a "restart" at many neurophysiological levels (Kahn et al. 2013).

It has been claimed that the ideal amount of sleep in healthy young adults is around 8 h per night (Ferrara and De Gennaro 2001). Deficits in daytime performance due to sleep loss are experienced universally. The first published experimental study about the effect of total sleep deprivation on cognition in humans dates back to 1896 and found that memory was significantly deteriorated after 90 h of continuous wakefulness (Patrick and Gilbert 1896). Since that time, hundreds of more detailed and systematic studies have been conducted. Most of this work has been conducted on normal, healthy individuals in the context of total sleep deprivation paradigms.

To date, it has been demonstrated that sleep deprivation significantly affects human functioning (Pilcher and Huffcutt 1996; Boonstra et al. 2007), negatively influencing levels of alertness and cognitive performance (Harrison and Horne 2000; Thomas et al. 2000; Wesensten 2006; Couyoumdjian et al. 2010; Killgore 2010).

In the last two decades sleep deprivation method has widely been used to investigate the relationship between sleep and learning/memory consolidation (see

Gais and Born 2004; Walker 2008). In such studies, participants typically learn a task prior to a good night sleep or a night of sleep deprivation. All participants are tested following one or two nights of recovery sleep to minimize any residual effects of acute sleep loss. Research in this area has been extremely fecund and has improved our understanding of how sleep loss can affect memory consolidation processes (Drummond et al. 2006; Sterpenich et al. 2009; Goulart et al. 2014). Within this framework, how sleep is beneficial for the consolidation of declarative and procedural memories has been demonstrated convincingly (Smith 2001; Walker and Stickgold 2004; Backhaus and Junghanns 2006; Marshall and Born 2007; Tucker and Fishbein 2009).

An extensive literature in the last years has provided evidence that sleep likewise supports emotional memory consolidation (Wagner et al. 2006; Hu et al. 2006; Cairney et al. 2015; Tempesta et al. 2015; Genzel et al. 2015), while sleep deprivation negatively affects it (Atienza and Cantero 2008; van der Helm et al. 2011; Morgenthaler et al. 2014; Tempesta et al. 2014, 2016). Empirical evidence suggests that the emotional strength of the material learned can modulate memory processing. In fact, emotional information is often remembered more accurately and persistently than nonemotional information (Kensinger 2004). Therefore, emotional load intensifies the subjective sense of remembering, enhancing our memory.

Here we will show that sleep supports the consolidation also of this particular type of memory. In particular, the following paragraphs propose a review of the body of research on the impact of sleep and sleep loss on emotional memory processing, emotional reactivity (e.g., Zohar et al. 2005; Tempesta et al. 2010), empathy (e.g., Guadagni et al. 2014, 2016), and fear conditioning (e.g., Milad and Quirk 2012).

6.2.1 Sleep and Emotional Memory Processing

Memory appears to develop over time into three distinct processes: memory encoding, memory consolidation, and finally memory retrieval. The "encoding" process refers to the uptake of information to be stored into a representation. The "consolidation" process refers to a post-encoding process in which the newly encoded representation, which is initially fragile and prone to decay, is transformed into a more stable and longer-lasting representation. Finally, the "recall" refers to the reactivation of the stored memory to enable the execution of an adaptive response in appropriate environmental contexts (Westermann et al. 2015).

Over the past decade, substantial evidence has been provided supporting the role of sleep in memory processing. This process is now referred to as "sleep-dependent memory processing." In the following sections, we describe how sleep is specifically implicated in all stages of the processing of emotional traces.

6.2.1.1 Emotional Memory Encoding

Most of the studies that investigated the relationship between sleep and human memory examined the influence of sleep on post-training consolidation, more than on the initial encoding stage. However, it has been likewise demonstrated that sleep deprivation negatively affects the ability to encode episodic information (Drummond et al. 2000; Walker and van der Helm 2009; Kaida et al. 2015).

As far as emotional memory is specifically concerned, the role of sleep on encoding of emotional information has only recently received attention. Only two studies till date (Kaida et al. 2015; Tempesta et al. 2016) have examined the impact of pre-training sleep or sleep loss on emotional memory formation.

Kaida and coworkers (2015) compared the effects of total sleep deprivation and of selective REM sleep deprivation on the subsequent encoding of neutral and emotional pictures. Encoding capabilities were examined, after each experimental night, by administering a picture recognition test right after encoding. A total sleep deprivation alters the ability to encode emotional pictures, but not the selective REM sleep deprivation, suggesting an essential role of NREM rather than REM sleep in encoding the emotional memory processes (see Sect. 6.3 below for a detailed evaluation of the relations between REM sleep and emotional memory). These results also suggest a proactive role of sleep deprivation in affecting emotional memory encoding.

In a recent study, we investigated the impact of sleep deprivation on emotional memory encoding of both contextual and non-contextual material (Tempesta et al. 2016). Contextual memory involves the retrieval of precise details associated with a test item, whereas non-contextual memory involves retrieval of a simple fact that an item has been encountered previously and nothing much can be recalled about its prior occurrence (Wixted et al. 2010). Subjects were sleep deprived for one night or allowed to sleep normally prior to an emotional memory encoding session in which six clips of films of emotionally negative, positive, and neutral valence were presented. In addition, after two nights of recovery sleep, all subjects performed a recall session, in which the non-contextual emotional memory was assessed by a recognition task, while the contextual emotional memory was evaluated by a temporal order task. The results suggest that sleep deprivation significantly impairs the encoding of both contextual and non-contextual aspects of memory, and it caused a significantly weak retention 2 days later. Interestingly, the sleep-deprived subjects were able to recognize the negative non-contextual events, suggesting that the encoding of negative stimuli is more "resistant" to the disruptive effects of sleep deprivation (Tempesta et al. 2016). The latter finding is in line with an established literature that demonstrates that memory processing can be modulated by the emotional strength of the material learned (see McGaugh 2004; Phelps 2004). In fact, memories with negative emotion are encoded strongly and persist longer than neutral memories.

In summary, the above reviewed studies indicate that sleep plays an essential role for the emotional memory encoding; on the other hand, lack of sleep leads to a disruptive interference with emotional memory consolidation and to the ensuing decay of instable memory traces.

6.2.1.2 Emotional Memory Consolidation

A growing body of research supports the role of sleep in memory consolidation (for a review, Born and Wilhelm 2012). An equally high number of studies suggest that sleep plays a selective and crucial role also in the consolidation of emotional memories (e.g., Holland and Lewis 2007).

The emotion may strongly modulate consolidation. The neutral memories are gradually lost over time (McGaugh 2000; Frankland and Bontempi 2005), but emotional memories are subjected to such loss to a lesser extent (LaBar and Cabeza 2006). Converging evidence indicates that sleep-based consolidation processes are crucial for the long-term maintenance of emotional information (Diekelmann et al. 2009).

In a series of behavioral studies, Wagner and colleagues have reported that the post-learning sleep has a positive influence on the retention of emotional memory contents (Wagner et al. 2001, 2006). In the first study, subjects learned neutral or emotional texts immediately before a 3-h period of wakefulness or sleep, allowed during the first or the second half of the night (Wagner et al. 2001). It was found that sleep selectively favors the retention of previously learned emotional texts relative to neutral texts. In the following study, it was demonstrated that this emotional memory enhancement persists for several years (Wagner et al. 2006). The participants were the same of the previous study (Wagner et al. 2001), recontacted after 4 years for a long-term memory assessment by means of a forced-choice recognition test. Results demonstrated that brief periods of sleep immediately following learning had led to the preservation of emotional memories over several years. However, similar memory enhancement for neutral texts was not observed. This indicates that emotional memory formation, relative to the neutral one, benefits more from the long-lasting effect of sleep after learning.

Hu and colleagues (2006) examined the impact of 12 h of sleep or wakefulness on memory for negative arousing and neutral pictures, using a recognition memory task that requires to discriminate between the original pictures and novel pictures by responding "remember," "know," or "new." In this paradigm, a list of pictures was shown to the subjects initially, and subsequently they were asked to judge test stimuli as the original or novel pictures by using the three abovementioned responses. The response "remember" indicated that the recognition of the picture was associated with retrieval of specific contextual details during encoding. The response "know" was associated with the feeling of familiarity or the definite feeling of having encoded the item, but without being able to retrieve any further specific details. The response "new" was given when the participant thought that the item had not been presented during encoding. It was observed that one night of sleep selectively improved memory accuracy for negative arousing pictures compared to

an equivalent period of daytime wakefulness, but only for "know" judgments (Hu et al. 2006). Moreover, the participants became more conservative when making "remember" judgments, especially for emotionally arousing pictures, across a night of sleep compared to a period of wakefulness. These findings suggest that the sleep selectively facilitates the consolidation of emotional memory, as indicated by the preferential overnight enhancement of both recognition accuracy and emotional bias (Hu et al. 2006).

In agreement with these results, Baran et al. (2012) performed a recognition memory task during two sessions separated either by 12 h of daytime wake or 12 h including overnight sleep and confirmed that recognition memory was better following sleep compared with a wake period of the same length. Moreover, the accuracy was higher following sleep relative to wake for both negative and neutral pictures (Baran et al. 2012).

Interestingly, Payne and colleagues observed that even a short nap in the afternoon sufficiently triggers preferential memory consolidation for emotional information associated with complex scenes (Payne et al. 2015). Along the same vein, the recent work of Cellini and colleagues indicated that a daytime nap facilitates both the consolidation and the post-sleep encoding of declarative memories, but regardless of their valence (Cellini et al. 2016).

In the last few years, some studies using the sleep deprivation paradigm have provided further evidence in support of the sleep-dependent emotional memory consolidation (Atienza and Cantero 2008; Tempesta et al. 2015). In the first of these studies, the participants were sleep deprived the night immediately following the exposure to emotional and nonemotional images, whereas the control group slept at home (Atienza and Cantero 2008). Memory was tested 1 week later with a recognition task. Sleep deprivation resulted in behavioral impairment at retrieval of both emotional and neutral images. Moreover, the subjective experience of remembering the specific details associated with test images was selectively impaired by the loss of sleep, whereas the subjective experience of just knowing that an item was previously encountered, even though nothing specific about its prior occurrence can be recalled, remained unaffected. These findings can be interpreted as a demonstration that sleep deprivation interferes with conscious contextual retrieving of old events in general, but not with non-contextual retrieving of stored information.

In a recent study from our group, sleep-deprived subjects were compared to subjects with poor sleep quality and with a normally sleeping control group, to test the hypothesis that sleep loss is associated with a lower recall of emotional stimuli (Tempesta et al. 2015). Twenty-four hours after the encoding session, all subjects were requested a yes/no memory judgment of the target pictures previously encoded ("old pictures"), intermingled with nontarget pictures ("new pictures"). We showed that individuals having poor sleep can preserve sleep-dependent consolidation of emotional information and demonstrate the same post-sleep performance accuracy as good sleepers. On the other hand, one night of sleep deprivation results in a reduced ability to recall emotional information successfully. These findings are

consistent with previous research revealing the positive effects of sleep on emotional memory consolidation (Wagner et al. 2001, 2006; Hu et al. 2006; Baran et al. 2012).

Altogether, these studies indicate that a period of (even brief) sleep is needed for the consolidation of emotional memory and that sleep quality does not significantly influence this relation. Thus, the sleeping brain seems to provide ideal conditions for emotional memory consolidation.

6.2.2 Sleep and Emotional Reactivity

Individuals differ remarkably in their emotional reactivity, that is, the quality and intensity of response to affectively evocative stimuli (Wheeler et al. 1993). Emotional reactivity can be measured along two dimensions: arousal (ranging from calm to excitement) and valence (ranging from positive to negative, with neutral often considered an intermediate value) (Lang et al. 1993; Labar and Cabeza 2006).

The International Affective Picture System (IAPS) is a validated set of visual stimuli widely used in experimental studies for evaluating emotional reactivity (Lang et al. 1998). In these studies, the subjects are typically asked to subjectively report the valence and arousal of their emotional reactions to affective pictures. These two dimensions in emotional perception have been found to correlate with facial muscle activity, skin conductance, heart rate, and startle response (Lang et al. 1998), suggesting a consistent pattern in adults' verbal, behavioral, and physiological responses to the affective pictures contained in the IAPS (Bradley et al. 1990, 2001; Lang et al. 1993, 1998).

In these studies, the subjects were asked to subjectively report the valence and arousal of their emotional reactions to affective pictures. These two dimensions in emotional perception have been found to correlate with facial muscle activity, skin conductance, heart rate, and startle response (Lang et al. 1998).

It is widely known that sleep modulates emotion regulation. In this respect, sleep loss causes mood changes and increases subjective irritability and affective volatility (Horne 1985; Rosen et al. 2006). For example, Dinges and colleagues (1997) have reported that with 5 h of sleep depriving per night, individuals develop a progressive increase in emotional disturbance across a 1-week period on the basis of subjective mood scales (Dinges et al. 1997). Accordingly, a meta-analysis of the effects of sleep deprivation has demonstrated that mood is more affected than cognitive or motor performance with sleep loss (Pilcher and Huffcutt 1996).

While the effects of sleep loss on mood are largely documented, the explicit impact of sleep deprivation on subjective reactivity to emotional stimuli has been less taken into account (Wagner et al. 2002; Zohar et al. 2005; Franzen et al. 2009; Lara-Carrasco et al. 2009; Tempesta et al. 2010; Baran et al. 2012; Groch et al. 2013; Cunningham et al. 2014). Moreover, these studies reported discordant results.

Baran et al. (2012) investigated how nocturnal sleep, compared to a period of daytime wakefulness, modulates subjective ratings of valence and arousal to negative pictures. They demonstrated an attenuation of negative ratings after 12 h of

daytime wakefulness, whereas a relative maintenance of the initial negative ratings was associated with a period of 12 h including sleep. That is, a picture that was initially deemed highly negative was rated as substantially less negative following 12 h awake, but only mildly less negative following sleep. These differential changes of emotional reactivity across periods of waking vs. sleep were interpreted as related to a habituation effect, therefore suggesting that sleep would facilitate habituation (Baran et al. 2012). Likewise, Groch et al. (2013) suggested that sleep does not modify the emotional reactivity associated with emotional stimuli. Indeed, they observed that valence and arousal ratings of emotional pictures were not affected by REM-rich or SWS-rich sleep.

Interestingly, in this study the analyses of ERPs revealed increased positivity in response to negative pictures in the frontal late positive potential (300–500 ms poststimulus onset), confirming the notion that subjective and objective parameters may not converge in experimental paradigms dealing with emotional responses (Groch et al. 2013).

At variance with the previous studies, reporting minor or no changes in emotional reactivity after a night of sleep, Wagner et al. (2002) suggested that sleep increases this reactivity. They assessed the emotional reactions by a nonverbal rating procedure along the two emotional dimensions of valence (positive vs. negative) and arousal (low vs. high). Two groups of healthy men were tested across 3-h periods of early and late nocturnal sleep or corresponding intervals filled with wakefulness. After the 3-h intervals, subjects rated new pictures mixed together with pictures already presented before. Subjective ratings of the negative valence following sleep resulted more negative for pictures viewed before sleep compared to new, unfamiliar pictures. This study, hence, demonstrates that sleep can mediate emotional reactivity and also highlights that this reactivity to an aversive event is differentially affected, depending on whether it is novel or familiar (Wagner et al. 2002). Similarly, Lara-Carrasco et al. (2009) showed that REM sleep deprivation alters emotional evaluation, in particular reducing reactivity to the negative valence of stimuli. From this, the authors argue that REM sleep enhances aversive reactivity to negative pictures. Altogether, the last two studies suggest that sleep may protect or even potentiate emotional reactivity.

In disagreement, Cunningham and colleagues (2014) have observed a general de-potentiating effect of sleep. They have shown a decrease of visceral reactivity to both negative and neutral objects following sleep. Interestingly, it has been observed that the arousal responses to negative scenes at encoding increased significantly (as measured by heart rate deceleration and skin conductance responses), which positively correlated with subsequent memory for the negative objects of scenes, but only for the subjects that had slept. This indicates that larger psychophysiological reactions to negative pictures at the time of encoding may "tag" the preferential consolidation of these images during subsequent sleep.

Other studies turned their attention to the effects of sleep loss on our responses to emotional stimuli. We all know that inadequate sleep potentiates the negative reactions to adverse experiences; at the same time it reduces the positive reactions to pleasant events. In this respect, Zohar et al. (2005) suggested that these effects on

emotional reactivity can have implication for real-word settings. In their study, they investigated the effects of sleep disruption on emotional reactivity to daytime work events in medical residents. Emotional reactivity was measured using the experience-sampling methodology. For 3 consecutive days, residents received three phone calls at random times during their working day. The residents were reminded through these calls to fill out brief questionnaires concerning change of circumstances over the previous 15 min and to rate their emotional response to these circumstances, as well as fatigue. It was found that sleep loss augmented negative emotional consequences in response to disruptive daytime events and has blunted the positive benefit underlying rewarding or goal-enhancing activities (Zohar et al. 2005).

We have also found a similar role of sleep debt as a potentiating factor of emotional reactivity (Tempesta et al. 2010). We investigated in healthy subjects the effects of one night of sleep deprivation, compared to those of one night of undisturbed sleep at home, on subjective ratings of the emotional valence and arousal of pleasant, neutral, and unpleasant pictures. Results showed that sleep-deprived subjects evaluate the neutral pictures in a more negative way compared to the subjects that slept at home. At the same time, both groups evaluate similarly the negative pictures, suggesting that sleep loss does not alter the assessment of negative stimuli. Similarly, there were no significant differences between groups in the valence ratings for pleasant pictures. Such a more negative valence rating of neutral pictures after sleep deprivation indicates that sleep subtly affects emotional evaluations. Indeed, sleep-deprived subjects did not change their judgment of explicitly positive and negative stimuli. Moreover, we found that the emotional labeling of neutral stimuli biased toward negative responses was not mediated by the increase of negative mood that typically accompanies sleep loss, indicating that sleep per se is involved in regulating emotional evaluations (Tempesta et al. 2010).

Emotional reactivity under the condition of sleep deprivation has been also measured by pupillography (Franzen et al. 2009). Although sleep deprivation did not significantly impact on subjective ratings, sleep-deprived subjects showed larger pupillary responses during the interstimulus interval following neutral trials compared to non-sleep-deprived subjects. This finding further suggests that sleep loss increases reactivity to the emotionally unloaded stimuli, in line with the results by Tempesta and coworkers (2010).

Therefore, the influence of sleep (and of its specific stages) on emotional reactivity remains not yet fully established (see below Sect. 6.3 for a detailed analysis of the studies on REM sleep), given the contradictory results of the few available studies reviewed in this section (Wagner et al. 2002; Lara-Carrasco et al. 2009; Baran et al. 2012; Groch et al. 2013; Cunningham et al. 2014). The discrepancies can be attributed to several methodological factors, including different sleep protocols. In this respect, some studies have shortened total sleep time (Wagner et al. 2002; Lara-Carrasco et al. 2009; Groch et al. 2013), while others allowed a whole night of undisturbed sleep (Baran et al. 2012; Cunningham et al. 2014). Moreover, it should be noted that the paradigm of Wagner et al. (2002) and Groch et al. (2013) relies on the differential distribution of the critical sleep stages, SWS and REM sleep, across

the early and late halves of the night. The elicitation of different emotional responses could also be because of differences in the tasks. In fact, Cunningham et al. (2014) have created different scenes containing emotional or neutral objects, whereas in all the other studies, the pictures have been taken from the International Affective Picture System. Thus, the different stimuli that can differently impact emotional reactivity, resulting in a confounding factor, cannot be ruled out. It should also be noted that many of the above results are based on subjective ratings that may be biased toward what participants think they should be feeling, more than what they actually experience (Cunningham et al. 2014). A coherence of subjective ratings and objective measures (behavioral or psychophysiological) is not guaranteed when emotional responses are taken into account (e.g., Franzen et al. 2009; Baran et al. 2012; Groch et al. 2013).

On the other hand, literature on the total sleep deprivation converges in support of the hypothesis that sleep loss significantly influences affective appraisal (Zohar et al. 2005; Franzen et al. 2009; Tempesta et al. 2010). Sleep loss indeed seems to cause a negative bias in the categorization of emotionally unloaded stimuli (i.e., neutral pictures) or in an increased emotional (subjective and autonomic) reaction to these stimuli.

Two different hypotheses have been proposed to explain the specific functions of sleep in the modulation of emotional processing. The hypothesis put forward by Walker (2009) and Walker and van der Helm (2009), currently dominating the field, suggests that when emotional memories are consolidated over sleep, the negative emotional tone is simultaneously attenuated. On the other hand, Wagner speculates that, as sleep enhances consolidation of the emotional memory, its emotional valence will also be maintained (Wagner et al. 2006). Both hypotheses will be examined in more detail in Sect. 6.3.

6.2.3 Sleep and Empathy

One of the major functions of our brain is to enable us to interact successfully in social groups. The ability to understand and share another person's mental state in terms of emotions, feelings, and thoughts has a key role for successful interactions (Shamay-Tsoory 2011). This capacity is referred to as "empathy." For example, if a person views a sad person and consequently feels sad, that subject is experiencing empathy.

It has been suggested that empathy includes two dimensions (Decety and Meyer 2008; Singer 2006): the cognitive component, also known as "theory of mind," consisting of the ability to understand and explain the mental states of others (Gallese 2007; Shamay-Tsoory 2011), and the emotional component, referring to the individuals' own experience of the others' actual or inferred emotional state (Davis et al. 1994; Dziobek et al. 2011). In addition to this bidimensional categorization of empathy, Dziobek and collaborators (2008) proposed a double dissociation

within the emotional empathy dimension: the explicit emotional empathy (rating of empathic concern) and the implicit emotional empathy (arousal ratings as a proxy for empathic concern).

Several previously revised studies provide clear evidence that sleep deprivation is detrimental to mood (Dinges et al. 1997) and emotional processing (Zohar et al. 2005; Tempesta et al. 2010; Baran et al. 2012), leading to an increase of the propensity of the individuals to assess the emotions more negatively (Tempesta et al. 2010) and to an amplification of the sympathetic responses (e.g., pupillary dilation) triggered by negative stimuli (Franzen et al. 2009). In addition, by measuring in healthy adults the intensity of facial expressiveness after one night of total sleep deprivation, Minkel et al. (2011) showed that sleep-deprived subjects resulted less emotionally expressive in response to both positive and negative emotional video clips (Minkel et al. 2012). Another study investigating the impact of sleep deprivation on the ability to recognize the intensity of human facial emotions observed that sleep deprivation selectively impairs the accurate judgment of angry and happy human facial emotions (van der Helm et al. 2010). These results are important because the recognition of facial expressions serves as an objective indicator of emotional functioning, also playing a critical role in communicating private emotional states, regulating social interactions, and even influencing subjective and physiological components of emotion (Levenson et al. 1990). Interestingly, sleep-deprived people are rated as less healthy and less attractive compared with when they are well rested, suggesting that humans are sensitive to sleep-related facial cues (Axelsson et al. 2010).

Therefore, sleep loss may have significant negative effects also on more complex emotional processes, such as those involved in empathy. To date, very few studies have investigated the relationship between sleep and empathy. Killgore and coworkers were the first to assess the effects of 55 h of sleep deprivation on perceived emotional intelligence of normal volunteers using the Emotional Quotient (EQ) inventory (Killgore et al. 2008). This self-report inventory measures self-perceived emotional intelligence and the underlying factors that contribute to emotionally intelligent behavior, which are at the basis of empathy. Relative to baseline, sleep deprivation was associated with lower total EQ scores, indicating a decreased global emotional intelligence. Analysis of the subscale scores showed that this decline in perceived emotional intelligence involved significant decreases on intrapersonal functioning (reduced self-regard, assertiveness, sense of independence, and self-actualization), interpersonal functioning (reduced empathy toward others and quality of interpersonal relationships), and stress management skills (reduced impulse control and difficulty with delay of gratification).

More recently, Guadagni and colleagues specifically evaluated the effects of sleep deprivation (Guadagni et al. 2014) and sleep quality (Guadagni et al. 2016) on empathic ability. In the first work they assessed if one night of sleep deprivation, compared to one night of sleep spent at home or a period of diurnal wakefulness, results in a reduced emotional empathic response (Guadagni et al. 2014). Emotional empathy was evaluated by a computerized test measuring direct (i.e., explicit evaluation of empathic concern) and indirect (i.e., the observer's reported

physiological arousal) emotional empathy. Sleep-deprived participants were emotionally less empathetic compared to those who had slept, as well as than those retested during the same day, without differences between direct and indirect components of emotional empathy. These results suggest for the first time that a night of sleep loss impairs the ability to share the emotional state of others (Guadagni et al. 2014). In addition, the same group investigated the potential direct relationship between naturally occurring variations in sleep quality and empathic responses of the individuals (Guadagni et al. 2016). In a group of undergraduate students, objective (actigraphy) and subjective (questionnaires and self-reports) sleep measures were collected, to characterize individuals' sleep quality. Participants were then asked to solve a computerized emotional empathy task that provides both direct and indirect emotional empathy measures. The results showed that subjective sleep quality best predicted participants' empathic sensitivity to negative images while they explicitly evaluated the emotions of others. In addition, subjective sleep quality resulted to be the best predictor of participants' arousal state in response to negative images, which is an implicit manifestation of their empathic experience. In both cases, lower subjective sleep quality was associated with lower empathic sensitivity to negative stimuli. Finally, it was found that sleep duration best predicted average empathic responses to stimuli of all valences, with shorter sleep durations associated with lower average empathic responses. Therefore, this study points to a significant relationship between the individuals' quality of sleep and their ability to share the emotions experienced by others (Guadagni et al. 2016). These results are in agreement with studies that showed that poor sleep quality is associated with the reductions in several social and emotive abilities, for instance, the optimism and sociability (Haack and Mullington 2005), and also with lesser emotional intelligence and altered constructive thinking (Killgore et al. 2008). In line with this, the recent study of Brand et al. (2016) explored, in a sample of adolescents, the association between subjective insomnia, emotional competence, and empathy. They observed that higher scores for insomnia correlated with lower scores for some aspects of emotional ability and empathy.

Although few in number, the above described studies are in strict agreement in showing that sleep loss, as well as sleep disturbances or a reduced sleep quality, has clearly negative effects on our ability to correctly process emotional information, to understand the feelings of others, and to be empathic with them.

Altogether, these results may have important clinical and operational implications. Sleep disruption has been shown to impair daytime functioning in several psychiatric disorders such as autism spectrum disorders. In keeping with the evidence that sleep plays a fundamental role in supporting social cognition skills, sleep disturbances may contribute to social cognition disability characterizing children with autism spectrum disorders. Therefore, if this relation between sleep and social behavior is confirmed, interventions to improve sleep in these children may have potential benefits on their social behaviors, with a consequent positive impact on quality of life for the entire family. The operational implications of the same results regard all the professions requiring social interactions and empathic abilities coupled with schedules that curtail sleep.

6.2.4 Sleep, Fear Conditioning, and Threat Generalization

A growing body of literature suggests that sleep plays an essential role also in the acquisition and long-term retention of negative memories such as fear. In the last years, fear conditioning paradigms provided important insights into how fears are learned and extinguished in mammals, thus becoming an important model of fear-related disorders (Milad and Quirk 2012).

In classical paradigms, fear conditioning is obtained by repeatedly pairing a neutral stimulus (e.g., a tone) with a coinciding aversive event (e.g., electric shock), resulting in a fear reaction. Initially the neutral stimulus (unconditioned stimulus, US) does not elicit any emotional reaction, but after this association is formed, the presentation of the neutral stimulus alone (now the conditioned stimulus, CS) become sufficient to evoke a conditioned fear response associated to the anticipation of impending aversive US. As measures of fear response intensity, fear condition paradigms classically include physiological (skin conductance, startle eye-blink electromyography) or behavioral (e.g., freezing) recordings. The CS-US association can also be subjected to extinction, a process that comprises the repeated presentation of the conditioned stimulus (the tone), but now in the absence of the coinciding unconditioned stimulus (the shock), leading to a gradual dissipation of the conditioned fear response (Milad et al. 2006). However, also after extinction, fear responses to the extinguished stimulus can spontaneously reappear with the passage of time (spontaneous recovery), in a new context (renewal) or can be reinstated by repeated spontaneous shock administration (reinstatement), thus suggesting the persistence of the original fear memory trace. According to this, learning that a previously dangerous stimulus no longer signals threat is not merely the erasure of the old fear association, but rather the new acquisition of a coexisting extinction memory mediated by inhibitory mechanisms (Phelps 2004). Fear responses can also be modified by unsafe (e.g., the test environment itself) or safe (e.g., a novel, safe environment) contextual cues, triggering fear reaction or promoting inhibition of the fear response. Moreover, fear learning can be subsequently generalized to other stimuli similar, but not identical to the original specific conditioned stimulus (Lissek et al. 2008).

In the animal model, the crucial role of limbic structures as the amygdala and the hippocampus in standard fear conditioning is now well established. In particular, activity in basal and lateral nuclei of the amygdala has been implicated in fear CS-IU association learning, while the central nucleus of the amygdala is involved in the expression of fear via projections to hypothalamic and brainstem nuclei, which are implicated in the expression of autonomic fear-related responses such as glucocorticoid release, heart rate, blood pressure, and respiratory alterations (Maren 2001; Sotres-Bayon et al. 2006). The hippocampus is crucially involved in detecting and processing contextual relevant information during fear learning; moreover, due to its projections to central amygdala, the hippocampus is also associated with fear expression. Amygdala-hippocampus interplay thus modulates fear response,

enhancing or weakening fear response based on the presence of safe or threatening information cues (Phelps and LeDoux 2005; Fanselow and Dong 2010).

Similarly, two different and mutually opposed networks have been proposed to regulate fear conditioning and fear extinction in humans (Graham and Milad 2011; Milad and Quirk 2012; Milad and Rauch 2012). Specifically, the association of US-CS during conditioning appears to involve basolateral amygdala, whereas extinction learning and recall are known to additionally require the contribution of vmPFC, which exerts an inhibitory modulation on the centromedial nucleus of the amygdala (Milad and Quirk 2002, 2012; Milad et al. 2007; Pitman et al. 2012). Therefore, the activation of the extinction network would inhibit the expression of fear by top-down vmPFC modulation of the amygdala. The human amygdala is involved in affective labeling of stimuli and interacts continuously with the hippocampus in processing emotional aspects of episodic memory (Phelps 2004). The hippocampus plays, in fact, a crucial role in the acquisition of an integrated representation of events and appears implicated in the processing of contextual cues associated to fear learning. In this respect, the hippocampal contribution should consist of successful context recognition for triggering top-down vmPFC inhibition of the amygdala (Pitman et al. 2012).

In the animal model, robust relations between sleep and fear memory have been reported. As an example, total sleep deprivation preceding (Ruskin et al. 2004) or following (Graves et al. 2003; Kumar and Jha 2012) fear conditioning paradigm negatively affects the consolidation of fear memory in the rat. Similarly, in humans a night of sleep has been shown to promote a strengthening of neural, physiological, and behavioral conditioned fear response, paralleled by the activation of basolateral amygdala, compared to sleep deprivation (Menz et al. 2013). In this study, participants performed a fear conditioning paradigm in which they learned to associate different visual stimuli presented in a conditioning context (a picture of a living room) to the administration of a mild electrical shock. Immediately after conditioning, one of these stimuli was presented in association of a new extinction context (a picture of a new context) without shock administration and therefore extinguished. The conditioning phase was followed by one night of regular sleep or a night of total sleep deprivation. During the retest phase, performed after a subsequent recovery night for both groups, individual responses to the administration of previously learned stimuli were tested using explicit memory test of shock expectancy, skin conductance, and functional magnetic resonance imaging (fMRI). Results showed that recall of the previously learned fear was better after the sleep condition compared to sleep deprivation, as reflected in memory performance as well as autonomous skin conductance responses and paralleled by higher activation of the basolateral amygdala. Of particular interest, the amount of time spent in REM sleep was found to be positively correlated with the magnitude of beneficial sleep-dependent consolidation, thus suggesting that sleep, and particularly REM sleep, has a key role in the consolidation of fear conditioning. The authors concluded that sleep preserved fear-related memory, resulting in a better next-day discrimination of fear-related cues (Menz et al. 2013). More recently, the same authors investigated the differential impact of early-night SWS-rich sleep and late-night REM-rich sleep on

the consolidation of conditioned fear and extinction memory (Menz et al. 2016). To this purpose, participants were assigned to four groups subjected to different sleep manipulations. Some participants performed a classical conditioning paradigm with immediate extinction in the evening before they were allowed to sleep for half a night (early sleep group) or had to stay awake until morning (early wake group). Other participants performed both conditioning and extinction after having slept in the first half of the night and were subsequently allowed to go back to sleep (late sleep group) or required to stay awake until morning (late wake group). After a recovery night for all groups, participants underwent the recall session, in which individual responses were assessed using explicit memory test, skin conductance, and fMRI. Results showed that fear memory performance (discrimination between dangerous and safety stimuli) decreased similarly in the early sleep and early wake groups, therefore irrespective of the presence of sleep. Coherently, no behavioral or physiological measures in the early SWS-rich sleep group were indicative of successful fear recall. Conversely, participants who slept in the late REM-rich part of the night showed a better discrimination of fear, at both behavioral and physiological level, in comparison to the late wake group; indeed, participants who stayed awake in the late part of the night showed decreased differentiation between dangerous and safety cues at behavioral as well as autonomic level, thus indicating worse fear memory. Moreover, participants in the REM-rich sleep manipulation showed also better extinction recall performance, while there was no behavioral and autonomic evidence of extinction memory improvements after SWS-rich early sleep. Importantly, in comparison to late REM-rich sleep, subjects who stayed awake in the second part of the night showed a return of fear at both behavioral and autonomic level (indicated by a better discrimination between the previously extinguished and neutral stimuli), paralleled by stronger activations in vmPFC and amygdala. These results indicate that fear and extinction memory performance is not affected by SWS-rich sleep, while beneficiates from REM-rich sleep; on the other hand, lack of REM sleep impairs extinction memory consolidation and promotes a return of fear after extinction. Therefore, the authors suggested that sleep, and particularly REM sleep, could be causal to successful consolidation of dangerous and safety stimuli and contributes independently to effective extinction memory consolidation (Menz et al. 2016).

In fact, sleep has already been suggested to facilitate fear extinction, which is a subsequent new learning of fear inhibition, mediated by top-down PFC inhibition of the amygdala. In the first fear conditioning/extinction study evaluating the role of sleep on extinction memory in humans, Pace-Schott and coworkers (2009) established a fear conditioning by pairing two different color stimuli to the administration of an electric shock, but, immediately after, one of these two associations was extinguished. Extinction recall was subsequently performed, for the sleep group, after a 12-h interval containing a period of nocturnal sleep or after 12 h of continuous wakefulness, for the wake group. Because skin conductance response to the previously extinguished stimulus did not significantly differ between sleep and wake group, this study failed to provide evidence in support of a beneficial role of sleep in the extinction consolidation. However, unlike the wake group, after a night of

normal sleep, participants showed reduced response to the unextinguished stimulus, thus suggesting a role of intervening sleep in the process of generalization of the extinguished memory (Pace-Schott et al. 2009). Subsequent similar protocols from the same group further confirmed a possible link between sleep, retention, and generalization of extinguished memory showing that, after a period of sleep, memory of extinction learning can generalize from an association previously extinguished to another similar but not extinguished association (Pace-Schott et al. 2013, 2014).

In this regard, increasing number of evidence indicates that, among other sleep stages, REM sleep may specifically exert a beneficial role in the processing of extinction memories. The amount of REM sleep obtained following fear extinction was shown to predict a decrease in autonomic arousal based on skin conductance measure (Spoormaker et al. 2010). Accordingly, Spoormarker et al. (2012) aimed at investigating the specific contribution of REM sleep in emotional processing. In this study, participants underwent a fear conditioning/extinction paradigm before sleeping in the laboratory and were then assigned to an experimental or a control group. Participants in the experimental group were subjected to REM sleep deprivation, while the control group received an equal amount of awakenings from NREM sleep stages. Results showed that REM sleep deprivation, in comparison to control multiple NREM awakenings, specifically impaired the consolidation of extinction memory. In addition, an intervening REM period also seems to promote optimal reengagement of ventromedial PFC (vmPFC) involvement during subsequent fear recall, thus ultimately facilitating successful fear extinction (Spoormaker et al. 2012). Spoormaker et al. (2014) have reported that REM sleep amount after fear conditioning negatively correlated with fear responses to the CS the day after. Interestingly, neuroimaging studies in humans showed that the "fear network" areas including the amygdala, vmPFC, insula, thalamus, and dorsal anterior cingulate exhibited increased activation both in fear conditioning/extinction learning and in REM sleep (see also Sect. 6.4). In summary, this evidence strongly supports a specific implication of REM sleep in emotional processing, and in particular in the mechanisms of fear consolidation and extinction, in animals as well as in humans (Dang-Vu et al. 2010). However, a beneficial role of NREM slow-wave sleep in the consolidation of emotional fear learning has been also proposed (Hauner et al. 2013; He et al. 2015).

Collectively, studies of fear learning in humans have alternatively linked sleep to the consolidation of both fear conditioning and fear extinction memory, with mixed results. However, it should be noted that, while in the animal model fear conditioning protocol is a standard, well-established procedure and rapidly induces intense fear responses, considerable methodological differences in human fear conditioning studies (e.g., the type of experimental stimuli, CS-US contingency, immediate versus delay extinction procedure, sleep versus sleep deprivation/wake) could partly underlie the conflicting results among studies.

From a phylogenetic perspective, learning both what to fear and what not to fear are equally important. Despite its fundamental self-preserving nature, the dysfunctional, abnormal persistence of fear conditioning learning could have a role in the pathogenesis and maintenance of anxiety disorders such as post-traumatic stress

disorder (PTSD) or specific phobia. Dysfunctional fear expression in anxiety disorder may indeed result from abnormally strong fear response (Orr et al. 2000; Lissek et al. 2005; Armfield 2006; Mineka and Oehlberg 2008) or alterations of the inhibitory system that normally modulates fear expression (Milad et al. 2006; Craske et al. 2008; Hofmann 2008) (see paragraph 4).

The majority of fear conditioning protocols in humans have indeed focused on the mechanism of extinction learning, due to the relevant clinical implication for exposure therapy in the behavioral treatment of anxiety disorders such as specific phobia, which largely benefit from the formation and subsequent generalization of therapeutic extinction memories (McNally 2007; Craske et al. 2008). In this context, the link between sleep and fear extinction memory has been recently explored also in clinical populations, like spider-fearing women (Pace-Schott et al. 2012; Kleim et al. 2014), showing that, compared to wakefulness, an intervening period of sleep after simulated exposure therapy improved extinction retention and generalization. These preliminary results suggest that post-theraphy sleep may have the potential to enhance the efficacy of the treatment, possibly preventing sensitization to threat and fear generalization (Pace-Schott et al. 2012).

Coherently, sleep disturbances should increase threat perception and promote threat generalization. Contrary to this assumption, Kuriyama et al. (2010) have reported that sleep loss instead resulted in less generalization of negative ratings from an aversive stimulus to a non-aversive stimulus, compared to time spent awake. More recently, Goldstein-Piekarski et al. (2015) investigated the impact of sleep and sleep deprivation on the discrimination of complex social emotion in humans, evaluating both the central and peripheral response to threatening stimuli. To this purpose, participants performed a face recognition task in the fMRI scanner in the morning, after a night of sleep and after a night of total sleep deprivation. During the face recognition task, subjects were asked to classify a set of facial stimuli from not threatening to increasingly threatening. Results showed that the sleep-deprived participants significantly categorized more stimuli as threatening, relative to the rested condition, suggesting that sleep loss could impose a negative bias on the behavioral discrimination of emotional stimuli by enhancing the subjects' tendency to judge affiliative stimuli as threatening. Furthermore, sleep deprivation was associated to alterations in both the functional central and autonomous peripheral (heart rate) activity related to emotional discrimination. Therefore, these results are suggestive of a crucial implication of sleep for an appropriate next-day discrimination of emotional stimuli; conversely, sleep loss could increase threat perception and promote threat generalization in emotional processing. Moreover, results suggest a link between central and peripheral emotional discrimination and the electrophysiology of REM sleep, specifically, the amount of EEG gamma activity during REM sleep in the rested condition (Goldstein-Piekarski et al. 2015).

On the whole, animal and human studies indicate that sleep (particularly REM sleep) is involved in the consolidation of fear memory as well as of fear extinction; yet, the specific direction of sleep-mediated modulation of fear remains to be further clarified. Nevertheless, current evidence collectively suggests an important implication of sleep in emotional memory processing and emotional homeostasis (Walker

and van der Helm 2009). Implicit to the meaning of successful memory consolidation is the crucial ability to next-day discriminate fear and safety relevant information. In this context, sleep may ultimately have the role to promote the adaptive expression of relevant emotions, mediating our ability to discriminate emotional experiences, supporting adequate recognition of salient stimuli, thus the most appropriate response to the environment.

6.3 REM Sleep and Emotions

Since its discovery by Aserinsky and Kleitman in 1953, rapid eye movement (REM) sleep has been closely linked to human emotion. The finding of this unique, paradoxical wake-like sleep stage that is typically associated to reports of emotionally intense, vivid dreams (for a review see Cipolli et al. 2016) has intuitively suggested an intimate association between REM sleep and the emotional domain. Many years of systematic sleep research have investigated the nature of this association, attempting to correlate specific REM features with emotional processing (Walker 2009). Taken as a whole, there are ample evidence now which suggest that the association between REM sleep and emotion is not a phenomenological coincidence but is probably substantial. Here we discuss the role of this unique sleep stage in the offline consolidation of emotional memory and in the modulation of emotional reactivity, with particular regard to the specific physiological REM features that lead to suggest crucial implications with emotional processing.

REM sleep typically emerge approximately 90 min after falling asleep and predominates in the second part of the night, toward the morning. REM sleep remarkably differs from other sleep stages collectively known as NREM sleep. While NREM is characterized by high-amplitude, low-frequency electroencephalographic EEG activity, reflecting a progressively higher degree of synchronization across large neuronal populations, EEG activity during REM sleep is characterized by the presence of low-voltage, mixed frequencies that resemble the activity of quiet wakefulness. Besides rapid eye movements, the hallmark of REM sleep, this stage is characterized by the presence of muscular atonia (Jouvet and Michel 1959) and high-amplitude spiky potentials which propagate from the pontine tegmentum to the lateral geniculate nuclei of the thalamus and the occipital cortex, the so-called ponto-geniculo-occipital (PGO) waves (Jeannerod et al. 1965; Nelson et al. 1983), identified also in humans (Lim et al. 2007). Interestingly, in rodents PGO waves have been linked with emotional memory consolidation (Datta et al. 2004, 2008). REM sleep is also characterized by a predominant theta rhythm, which has been implicated in the integration of information across neocortical networks (Buzsáki 2002).

The beginning of a REM period is accompanied by dramatic alterations in functional brain activity (for more details see Sect. 6.4), with brain areas implicated in memory functions during wake strongly reactivated during this state (Maquet et al. 2000). Such crucial changes are paralleled by significant alterations in brain neurochemistry. In fact, both crucial similarities and differences between the

neuromodulatory state characteristics of REM and wakefulness have been suggested as indicative of a causal role of REM sleep in emotional memory consolidation. Compared to wakefulness, acetylcholine levels in REM sleep are similar or higher. High cholinergic levels could promote synaptic consolidation by supporting plasticity-related activity (Teber et al. 2004) and long-term potentiation (Lopes Aguiar et al. 2008). Conversely, REM sleep is characterized by low noradrenaline levels. In fact, the activity of noradrenergic locus coeruleus neurons increases an animal's ability to pay attention to stimuli in the environment and is strictly related to vigilance performance (Aston-Jones et al. 1994). It has been suggested that during REM sleep, memories within the neocortex are subjected to the plasticity-related cholinergic activity but remain free from arousal-related noradrenergic interference, thus recombining and potentially integrating into existing memory networks (Walker and Stickgold 2010). As proposed, memory reactivation that occurred during REM sleep could promote the integration of recently learned representations into stored superordinate representations (Sterpenich et al. 2014).

Human amygdala and its interplay with the hippocampus has a key role in emotional regulation and in the formation of emotional memories (Strange and Dolan 2006). Stress hormones like cortisol and norepinephrine, released in response to emotional events (Sapolsky et al. 2000), in turn lead to increased activation of the amygdala. Given the strong connection between the amygdala and the hippocampus, amygdala activation by hormones is thought to increase in turn hippocampal activity, thus promoting memory consolidation, particularly for events with emotional valence (McGaugh 2004). Importantly, REM sleep is also associated to a significant increase in cortisol level (Payne and Nadel 2004). In this context, memory consolidation for emotional events may receive an additional contribution from changes in glucocorticoids balance occurring during REM sleep periods.

Converging evidence suggests a role for REM sleep in the offline consolidation of human emotional experiences. First studies on the role of REM sleep in emotional processing used a split-night paradigm (Yaroush et al. 1971). In this procedure, after a learning session, subjects are typically allowed to sleep only in the first 3-h SWS-rich part of the night, thus deprived of late nocturnal sleep, or, conversely, only in the second 3-h part of the night, in which REM predominates, thus deprived of early sleep. In this way, this paradigm is assumed to allow a dissociation of the effects of SWS and REM sleep. In the first split-night study on the role of REM sleep in emotional memory (Wagner et al. 2001), retention of emotional and neutral text was compared over periods of wake, early and late sleep. It has been shown a memory improvement for arousing negative stimuli compared to neutral ones after a late-night REM-rich sleep. Conversely, such beneficial effect on emotional memory retention was not observed after a corresponding wake retention interval or after early-night SWS-rich sleep; the authors therefore concluded that REM sleep can selectively facilitate the consolidation of emotional stimuli (Wagner et al. 2001). Similarly, Groch et al. (2013) investigated the role of early and late sleep on emotional memory retention of emotional or neutral pictures. They reported that compared to early SWS-rich sleep, late-night REM-rich sleep enhanced the retention of negative arousing pictures relative to neutral pictures. More recently, the same

authors confirmed that only late REM-rich sleep enhances the retention of negative relative to neutral stimuli (Groch et al. 2015). However, it was also found that early SWS-rich sleep enhances the retention of the contextual details of the neutral pictures, thus suggesting a differential role of SWS and REM sleep in the consolidation of emotional and neutral stimuli.

Split-night paradigms have demonstrated a better recall of emotional stimuli, compared to neutral stimuli, when the recall session was explicitly performed after a post-learning period containing REM-rich nocturnal sleep. It should, however, be considered that the split-night paradigm, although thought to be less disruptive for the normal sleep architecture in comparison to the selective REM deprivation procedure – which, to a higher extent than SWS deprivation, may include stressful awakenings – is not free from limitations. As an example, testing sessions are typically performed at different time of the day, leading to circadian confounds. Moreover, in the first or second half of the night, a relative predominance of a certain sleep stage on others does not implicate the exclusive presence of this stage, so that, in principle, the split-night design does not allow to selectively refer a specific sleep stage to the observed effect.

The relations between emotional memory and sleep structure have been assessed also by using the napping paradigm. In one of these studies, Nishida et al. (2009) aimed at evaluating the influence of a short nap and a corresponding control wake interval on emotional memory retention. Compared to wake, a nap augmented the consolidation of emotional, but not neutral stimuli. Moreover, it was observed a positive correlation between emotional memory retention and the amount of post-learning REM sleep during the nap. Further, a recent nap study (Gilson et al. 2016) showed that REM density positively correlated with recall performance of sad material in comparison to neutral material. Coherently, Payne et al. (2012) showed a correlation between REM sleep quantity during a nocturnal sleep episode and correct recognition of previously learned emotional stimuli but not with the neutral stimuli. Given the lack of similar correlations for any other sleep stage, results are suggestive of a selective implication of REM sleep in memory processing of emotional stimuli (see also par. 1.4 for a discussion on the contribution of REM sleep to fear memory consolidation and extinction).

In the same direction, a selective sleep stage deprivation paradigm has recently been used to examine the role of SWS and REM sleep in the consolidation and affective evaluation of emotional memories (Wiesner et al. 2015). Here, participants evaluated and learned a set of neutral and negative pictures during the encoding session. Recall session was then performed after a 9-h interval in which participants were subjected to selective SWS or REM sleep deprivation, also including a control wake group who performed the recall after 9 h of wakefulness. Result revealed improvements in the consolidation of the emotional stimuli compared to the neutral ones only in the group that underwent SWS deprivation and conversely had a normal amount of REM sleep.

In accordance with the above results, REM sleep has been proposed as necessary for emotional memory processing. Given the REM sleep-mediated emotional memory enhancement, some authors argued that also the associated emotional charge will

be consolidated along with the memory (Wagner et al. 2002). On the contrary, REM sleep deprivation should inhibit sleep-dependent neural reactivation, which is considered to be essential for memory consolidation processes, thus impairing the long-term retention of a memory and of its emotional tone (Wagner et al. 2006). As per such assumption, and considering the facilitatory role of sleep in emotional memory consolidation, the use of sleep deprivation as a potential therapeutic tool to prevent long-term retention of traumatic events has been also suggested (Wagner et al. 2006).

Although results suggest that during REM sleep an active consolidation process of emotional experiences takes place, nevertheless the direction and specificity of the effects of REM sleep in emotional memory processing is still debatable. In fact, alternative to the previous hypothesis, the "sleep to remember, sleep to forget" model (Walker and van der Helm 2009) argues that the unique neurobiological state of REM sleep could act to de-potentiate, rather than strengthen, the emotional charge of a memory. In particular, the reprocessing of emotional memories would be supported by the reactivation during REM sleep of specific brain areas implicated in memory function in wake, such as the amygdala and the hippocampus (see Sect. 6.3 of this chapter). Further suggestive of a causal role of sleep in memory processing, theta oscillations, which dominates REM stage, are supposed to be implicated in the consolidation and integration of different aspects of memory representations (Buzsáki 2002). In this respect, recall of dreaming experience is associated to higher theta oscillations only upon awakening from REM sleep (Marzano et al. 2011; Scarpelli et al. 2015). Crucially, unlike emotional memory formation during wakefulness, these memory-relevant processes occur in a brain state characterized by dramatically reduced aminergic, particularly noradrenergic, neurochemical concentration. Thus, within this unique *scenario*, the activation of the amygdala-hippocampal network is proposed to facilitate the long-term retention of the informational, salient elements of an emotional experience ("sleep to remember"). Contextually, the suppressed adrenergic activity during REM sleep, which in wake is associated to arousal, is supposed to separate from the emotional memory the visceral, autonomic charge originally associated to emotional experiences and gradually dissipate it ("sleep to forget"). In this way, according to the authors, REM sleep could be viewed as an "overnight therapy" which adaptively protects the salient aspects of a memory, obliterating at the same time the associated emotional tone (Goldstein and Walker 2014).

In this respect, although a negative correlation between REM sleep and subsequent attenuation of negative emotional response to affective stimuli has been reported (Baran et al. 2012), there are also evidence suggesting a sleep-dependent decrease in both subjective emotional arousal and autonomic response to negative stimuli compared to a comparable wake interval in humans. Therefore, these results support the "sleep to forget" part of the hypothesis. In this direction, van der Helm et al. investigated the role of sleep, with particular regard to REM sleep, on emotional processing (van der Helm et al. 2011). Participants performed 2 repeated fMRI tests in which they were asked to view 150 affective pictures and rate the subjective emotional intensity associated to each picture. The second fMRI session was performed after a 12-h interval of wake or after an equal interval containing a

night of sleep. Results indicated an overnight decrease in amygdala responsiveness at retest paralleled by a corresponding behavioral decrease in emotional reactivity to the emotional stimuli. Emotional intense ratings indeed significantly decreased in the sleep group, with a progressive increase in neutral subjective ratings. Interestingly, this study also provided insight into a link between REM sleep physiology and emotional processing, showing a relation between decreased reactivity at both cerebral and behavioral level and the extent of reduced EEG gamma activity during REM sleep, which is considered a marker of reduced central adrenergic activity (Maloney et al. 1997; Cape and Jones 1998).

Moreover, according to this theory and opposite to the Wagner and colleagues' hypothesis (Wagner et al. 2006), sleep deprivation should block the beneficial overnight emotional depotentiation. Neuroimaging (see the next section) and behavioral studies seem to support to this prediction. In fact, sleep loss is associated to a reduced functional connectivity between the amygdala and the vmPFC and therefore a lack of top-down limbic control by the PFC, resulting in an amplified limbic activity in response to negative emotional stimuli (Yoo et al. 2007). The hyperlimbic activation observed after sleep deprivation could also affect the assessment of emotional stimuli, leading to an increased negative evaluation of these stimuli (Yoo et al. 2007) or even to an increased tendency to judge neutral stimuli as more negative (Tempesta et al. 2010). Moreover, such amplified reactivity of the amygdala after sleep loss in response to negative pictures could also explain the specific resistance of unpleasant stimuli to the detrimental effect of sleep loss on memory, as assessed by a recognition memory task (Tempesta et al. 2016). Thus, according to the implications of the theory, REM sleep may represent a preventive therapeutic measure for emotional brain homeostasis, preparing the organism for next-day emotional functioning, priming brain areas to appropriately react to emotional experiences, and thus ultimately promoting an adaptively accurate discrimination of the emotional stimuli (Goldstein and Walker 2014).

However, it should be noted that the available findings on the specific involvement of REM sleep in offline emotional memory consolidation or emotional reactivity are in part contradictory. In fact, in other selective REM deprivation paradigms, a specific beneficial role of REM sleep in emotional memory processing was not observed (Morgenthaler et al. 2014; Kaida et al. 2015). Furthermore, in a recent daytime nap study, it has been shown that a brief sleep period improves memory consolidation of both emotional and neutral material, regardless of the presence of REM sleep (Cellini et al. 2016). As far as emotional reactivity is concerned, the above reported study by Baran and colleagues (2012) showed that a longer time in REM sleep is related to a protection – more than a depotentiation – of emotional reactivity. As suggested by the authors, although the reduction of emotional reactivity to new stimuli would positively contribute to mental health, in an evolutionary perspective, the preservation of salience might have been of great advantage to survival. Indeed, by maintaining the negative tone together with the strengthened memory trace, the individual will not only remember the emotional event but also the degree of threat associated with it (Baran et al. 2012). Further, in the study of Groch and coworkers (2013), the improvement of emotional memory

dependent on REM sleep was not accompanied by a next-day significant decrease in subjective emotional ratings indicative of a beneficial role of REM on emotional reactivity. Therefore, the lack of significant decreases in emotional evaluation after both early SWS-rich and late REM-rich sleep suggests a protective role of sleep per se also on the affective tone associated to emotional memories, which is obtained along with their sleep-dependent processing and consolidation. Moreover, as a further contribution to the assumption that REM sleep may strengthen the emotional charge of a memory, Lara-Carrasco and colleagues (2009) observed after partial REM sleep deprivation, an increased emotional adaptation to negative stimuli with a corresponding decrease in subjective arousal ratings for those stimuli, in comparison to subjects that underwent undisturbed nocturnal sleep and therefore had more REM sleep. Therefore, as suggested in this study, REM sleep could even enhance emotional reactivity to negative stimuli.

In conclusion, the large overlapping between the neuroanatomophysiology of REM sleep and emotional processing continues to appear not coincidental to many researchers. On the whole, increasing results observed with different experimental paradigms suggest a critical implication of REM sleep in overnight emotional modulation, although the direction of this effect is not established. Indeed, there are now two opposite theories regarding the specific modulation by REM sleep of the salience associated to memory traces, something that ultimately makes our episodic memories, emotional memories. According to these different assumptions, REM sleep could therefore facilitate the retention of the emotional memory charge (Wagner et al. 2006) or, conversely, de-potentiate the visceral tone associated to a memory (Walker and van der Helm 2009) with some evidence existing in support or against both models, showing enhanced (Wagner et al. 2002; Lara-Carrasco et al. 2009; Baran et al. 2012) or diminished (van der Helm et al. 2011) REM-related emotional reactivity, as well as no effect specifically associated to REM sleep (Groch et al. 2013; Wiesner et al. 2015). When trying to account for such discrepancies, it should be considered that the remarkable variety of the experimental paradigms, each one with specific limitations, often makes difficult a direct comparison of the results, so that such methodological differences may have a substantial role in the interpretation of the contrasting results. Further, a potential limitation in studies on sleep and emotions lies in the experimental task used, which typically involve the administration of stimuli (such as emotional pictures) that may be not sufficient to elicit strong emotional reactions. This could be even more relevant considering the clinical implications of both models for the processing of traumatic experiences, which are – at least quantitatively – different from standardized negative emotional stimuli and far from being elicited by the experimental administration of emotionally arousing pictures. Further studies are required in order to better elucidate the sleep and emotions relationship, including more ecological experimental tasks and limiting other possible multiple confounding factors.

6.4 Sleep and Emotions: Insights into the Brain Mechanisms by Neuroimaging Studies

The introduction of neuroimaging techniques, particularly positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), marked the beginning of a new era in the neurosciences. Such techniques, by detecting increases in regional cerebral blood flow or blood-oxygen level-dependent (BOLD) signal as markers of neuronal activity, allowed to explore functional brain processes in the intact human brain and shed light into the functional neuroanatomy of a variety of processes, including human emotion. Examining emotion-related activity in human brain, neuroimaging allows to identify brain areas specifically associated to emotional states, obtaining therefore a direct measure of emotions at their source. Importantly, neuroimaging insights into the neural correlates of emotional processing have corroborated and substantiated behavioral results as well prior investigations based on animal and brain lesion model.

Functional neuroimaging techniques have contributed to identify several brain areas involved in human emotional processing. Essential, in this human emotional network, is the hippocampal-amygdala-medial prefrontal cortex network. Amygdala has a key role in emotional processing. The influence of emotional arousal on memory specifically involves the activation of the amygdala. Indeed, during emotional arousing events, the crucial interaction between stress hormones and amygdala represents an endogenous memory-modulating system which regulates memory storage processes in other emotional relevant brain regions. The amygdala has been implicated in emotional responsiveness to aversive stimuli also in humans (for a review, Cahill and McGaugh 1998). The activation of this structure is indeed closely linked to emotional intensity of the stimulus and has been shown to correlate with subjective emotional arousal (Phan et al. 2003) and autonomic arousal skin conductance response (Williams et al. 2001). Importantly, amygdala activation also results in behavioral changes, as both PET and fMRI studies showed that amygdala activity induced by emotional stimuli at encoding highly correlates with memory at subsequent recall, suggesting a clear implication of the amygdala in modulating hippocampal memory consolidation (for a review, Phelps 2004). Indeed, converging evidence support the idea that amygdala activation has a crucial role also in promoting subsequent memory consolidation processes, modulating striatal, prefrontal, and particularly hippocampal activity, which is critically implicated in memory storage (for a review, McGaugh 2004). In this emotional network, the medial prefrontal cortex (mPFC) has been shown to have a crucial role in emotional processing; importantly, mPFC, via strong inhibitory top-down projections, is proposed to exert a modulatory impact on amygdala activation, thus resulting in contextually appropriated emotional responses (Davidson 2002; Sotres-Bayon et al. 2004).

In recent years, the introduction of neuroimaging techniques in sleep research is progressively providing important insights into a possible implication of human sleep in memory processing and emotional reactivity. PET studies showed a whole-brain metabolism decline from waking to NREM sleep, while global brain metabolism levels are comparable between REM sleep and wakefulness (Maquet et al. 2000; Nofzinger et al. 2002). Importantly, neuroimaging studies revealed that brain areas involved in emotional memory processing during wakefulness are strongly reactivated during sleep (Nir and Tononi 2010). In fact, the earlier PET studies showed specific neuronal network activity throughout REM sleep within the amygdala, entorhinal cortex, and anterior cingulate (Hong et al. 1995; Maquet et al. 1996; Braun et al. 1997, 1998; Nofzinger et al. 1997; Buchsbaum et al. 2001; Peigneux et al. 2001). The higher activation during REM sleep of emotion-related cerebral areas has been confirmed by the few available fMRI studies (Miyauchi et al. 2009; Dang-Vu et al. 2010). Moreover, transient co-activation of the amygdala, hippocampus, and cingulate has been reported by an EEG-fMRI co-registration study (Wehrle et al. 2007), suggesting that REM sleep could have a fundamental implication in emotional memory reprocessing.

Importantly, Yoo and coworkers (2007), using fMRI, aimed at investigating the impact of sleep and sleep loss on the emotional memory network. In this study, participants were subjected to a night of normal sleep or total sleep deprivation prior to an fMRI scanning session in which emotional pictures ranging from neutral to increasingly negative were administered. In response to increasingly negative emotional stimuli, participants that were sleep-deprived exhibited a significantly greater amygdala activation compared to the sleep group. Moreover, sleep-deprived subjects also showed an increase in the volumetric extent of the amygdala activation in response to negative stimuli. Interestingly, an altered pattern of functional connectivity was also reported. Specifically, sleep deprivation was associated to a loss of functional connectivity between amygdala and mPFC, along with an increased connectivity between amygdala and autonomic-activating brainstem areas. Conversely, after a night of sleep, a significant stronger amygdala-mPFC functional connectivity was observed (Yoo et al. 2007). Therefore, these results indicate that a night of sleep deprivation is associated to an amplified limbic response to negative stimuli. This activity pattern suggests a failure of top-down prefrontal control over emotional areas.

Moreover, the effects of sleep restriction on emotional reactivity to emotional faces showing happy, fearful, and neutral expression have also been investigated (Motomura et al. 2013). In this study, participants underwent a sleep restriction paradigm in which time in bed was limited to 4 h a day for a period of 5 days, or conversely they were allowed to regularly sleep at home. Sleep restriction was associated to a greater amygdala activation for negative stimuli, along with a reduced amygdala-anterior cingulate cortex connectivity. This result again suggests a detrimental role of sleep loss on emotional regulation. However, sleep loss could not be exclusively associated with enhanced reactivity to negative stimuli (Yoo et al. 2007; Franzen et al. 2009), but rather to a more generic lability in emotional regulation. Indeed, Gujar and coworkers observed, after a night of total sleep deprivation, higher

activity in mesolimbic regions in response to pleasure-evoking stimuli with a reduced connectivity in medial- and orbitofrontal areas (Gujar et al. 2011).

Therefore, sleep deprivation could promote a generalized affective imbalance leading to an amplified reactivity across different affective valence, including negative as well pleasant experiences. In summary, these evidences confirm the importance of sleep for brain emotional homeostasis, in order to preserve an effective functional PFC-limbic connectivity and thus to restore an appropriate next-day emotional reactivity (Yoo et al. 2007; Walker 2009).

In order to assess a specific implication of REM sleep in emotional processing, Rosales-Lagarde and colleagues (2012) evaluated the effect of selective REM sleep deprivation on emotional responses to threat-related visual stimuli. To this purpose, subjects underwent fMRI scan twice, after a baseline night and after one night of either selective REM sleep deprivation or a control night in which participants were subjected to an equal amount of NREM sleep interruptions. During the emotional reactivity task, participants viewed threating or not threating pictures, and they were asked to imagine themselves as a part of the scene and rapidly react to the situation by choosing to defending themselves or not. Emotional reactivity, behaviorally assessed as the number of defensive choices against threatening scenes, resulted enhanced after selective REM deprivation but not after comparable NREM interruptions, relative to the baseline night. Moreover, at the neural level, results showed an overall decrease of activation in areas involved in emotional processing, particularly occipital and temporal areas and ventrolateral prefrontal cortex in the control NREM group, while the activity in these areas was similar or higher compared to baseline in the REM deprivation group. This result seems to indicate that lack of REM sleep leads to enhanced emotional next-day reactivity to threats, supporting, therefore, the role of this sleep stage in emotional homeostasis (Walker and van der Helm 2009). Indeed, fMRI studies indicated that sleep affects emotional memory network, leading to post-sleep increased activity in amygdala and ventromedial PFC (vmPFC) and to strengthened connectivity between the amygdala and both vmPFC and hippocampus during successful retrieval of negative objects (Payne and Kensinger 2011). This result could be relevant not only for adequate emotional reactivity but also for emotional memories encoding and consolidation processes.

In fact, converging evidence suggest that sleep could also have a direct implication in all stages of emotional memory formation. In this regard, the impact of sleep loss on the neural dynamics associated with emotional memory encoding and consolidation can be successfully elucidated using sleep deprivation paradigms that include event-related fMRI acquisition in conjunction with behavioral measures. In a behavioral-fMRI study, Sterpenich et al. (2007) examined the impact of sleep and sleep deprivation on emotional memory consolidation. Participants were subjected to a first fMRI scanning session in which they encoded a set of neutral or emotional pictorial stimuli. In the first post-encoding night, subjects were allowed to regularly sleep at home, or, conversely, they were sleep deprived. A second fMRI scanning session was performed 3 days later for both groups, during the recall session. During recall, participants made recognition memory judgments about previously learned pictures and new pictures. Behavioral results here showed that

recollection of neutral or positive stimuli, but not negative stimuli, was significantly deteriorated after sleep deprivation. At the neural level, compared to neutral items, recollection of emotional stimuli was associated with increased responses in the hippocampus and several cortical areas, including the mPFC, in subjects that were allowed to sleep the first night post-encoding session, relative to sleep-deprived participants. Furthermore, regarding the recollection of negative stimuli, while the sleep group elicited a consistent hippocampo-neocortical activity pattern, an alternate amygdalo-neocortical network was recruited after sleep deprivation, compared to the sleep group. The authors suggest that such activity pattern in sleep-deprived subjects could represent an adaptive strategy to keep track of salient, potentially dangerous environmental features, despite the detrimental effects of sleep deprivation on cognition (Sterpenich et al. 2007). In a subsequent fMRI study, the same authors (Sterpenich et al. 2009) assessed the impact of sleep in the first post-encoding night on the recall of remote emotional memory. Participants were therefore scanned during a delayed second retest session, performed 6 months later, in which they were asked to make a recognition memory judgment about formerly learned pictures mixed with additional new ones. At the behavioral level, results showed that recollection rate decreases over time, but the emotional items remained still better remembered than the neutral ones, 3 days as well 6 months later. Although no significant behavioral differences in the recall session between the two groups were observed, after 6 months the recollection elicited significantly higher responses in subjects that were allowed to sleep, compared to the sleep-deprived ones, in the vmPFC and precuneus, as in the amygdala and occipital cortex. A stronger connectivity was also found between the vmPFC and precuneus, amygdala and occipital cortex, as well as amygdala and vmPFC (Sterpenich et al. 2009). Thus, sleep during the first post-encoding night can exert a significant impact on the long-term consolidation of memories at the system level. These evidences suggest that the offline processing of emotional memory during the first night is linked to a progressive consolidation process, resulting in strengthening of connections among those areas that are subsequently recruited during memory recall.

Nevertheless, the fact that the same brain areas involved in fear learning and emotional processing during wake are selectively reactivated during REM sleep (e.g., Nir and Tononi 2010) encourages to explore more directly the functional implications of this neuro-anatomo-physiological overlapping. In a recent study, Sterpenich et al. (2014) aimed at investigating the role of specific memory reactivation during REM sleep on subsequent memory performance and brain activations. In this study, participants underwent fMRI scanning both at encoding session, in which they rated emotional negative and neutral face stimuli, and at recall session, when they underwent a recognition task. During the encoding, two distinct auditory cues were associated to the administration of emotional or neutral faces. During the subsequent post-encoding night, the same auditory cues previously associated to the stimuli were again delivered during periods of phasic REM or during stage 2 NREM, while some participants were administered two new sounds, during phasic REM sleep, or slept undisturbed. Results indicated that the administration of auditory cues during REM periods in post-encoding night is capable of

inducing significant changes in brain activations and next-day memory performance. Specifically, the association between visual and auditory features of a memory was effectively strengthened by subsequent memory reactivations experimentally induced by the presentation of cues during REM sleep, as suggested by enhanced activity in the areas recruited during encoding. Notably, at the behavioral level, the administration of auditory cues during REM sleep, in comparison to cues delivered during NREM and unstimulated sleep, resulted in both correct and incorrect recollection enhancement, at memory retest. In other words, cues delivered during REM sleep selectively enhanced subsequent correct face recognition, but also false recognition, when participants were asked to make recognition judgments at retrieval. As argued by Sterpenich and coworkers, therefore, memory reactivation during REM could enhance brain responses at retrieval, indicating a process of integration of new memories within cortical circuits. Moreover, behavioral evidence indicates that REM sleep promotes a process of feature extraction of a memory and the subsequent association with other semantically related representations, leading to an identification bias of new faces as previously learned. Therefore, REM sleep could have an important role for the progressive integration of new episodic memories into existing representation stored in cortical networks (Sterpenich et al. 2014).

In conclusion, although at an initial stage, the introduction of functional neuroimaging techniques in the study of the relations between sleep and emotions is progressively contributing to disclose a protective role of sleep on human emotional homeostasis and emotional regulation. Further, sleep seems to be critically involved also in the ability to form and retain emotional episodic memory. Finally, some evidence suggests that particularly REM sleep, a period characterized by a high activity in brain regions involved in emotional memory processing, could be implicated in the processing of emotional information.

6.5 Sleep and Emotions in Psychiatric Disorders

The importance of understanding the links between sleep and emotion is apparent in light of the robust scientific evidence demonstrating associations between sleep and affective or anxiety disorders (Dahl and Harvey 2007; Baglioni et al. 2010; Gregory and Sadeh 2012). It's not a coincidence if, in the Diagnostic and Statistical Manual of Mental Disorders-V (DSM-V) and in the International Classification of Diseases (ICD-10), disturbed sleep is a key symptom of many psychiatric disorders. For example, poor sleep is a pervasive problem for patients suffering from depression or post-traumatic stress disorder (PTSD). Epidemiological studies demonstrated that sleep disturbances such as insomnia are found in up to 80% of the individuals with major depressive disorder (Selvi et al. 2010), and the rate rises to nearly 90% when an anxiety disorder is present concomitantly (Ohayon et al. 2000).

Insomnia is one of the most prevalent sleep disorders and has a significant impact on individual's health. This disorder is characterized by difficulties initiating or maintaining sleep or non-restorative sleep, accompanied by significant daytime

impairments (Feige et al. 2013). Several studies found a relationship between poor sleep quality in insomnia and emotional functioning. For example, it has been recently shown that insomnia affects the subjective ratings of emotional stimuli (Kyle et al. 2014). Moreover, functional neuroimaging studies reported that subjects with insomnia show an increased amygdala activation to insomnia-related stimuli compared to healthy subjects (Baglioni et al. 2014). In line with these data, it has been also observed in participants reporting poor sleep a significant association between amygdala reactivity and levels of depression and perceived stress (Prather et al. 2013).

These data suggest that sleep quality is an important behavioral modulator of the neural correlates of mood and emotional processing, underscoring the bidirectional relationship between poor sleep quality and affective or anxiety disorders. Therefore, as much mood and anxiety disturbances may be attributable to the emotional instability due to sleep loss, as poor sleep quality may be attributable to the mood and anxiety disturbances.

6.5.1 Major Depressive Disorder (MMD)

Major depressive disorder (MDD) is the most prevalent mood disorder, characterized by a prolonged dysphoric mood state usually accompanied by debilitating emotional, behavioral, cognitive, and physical symptoms. One of the most consistent symptoms associated with major depressive disorder is sleep disturbance (Peeters et al. 2006; Peterson and Benca 2008; Baglioni et al. 2011). Whereas about 80% of the patients complains of insomnia, 15–35% suffers from hypersomnia (Hawkins et al. 1985; Armitage 2000).

Typical symptoms of patients with MDD are difficulty getting to sleep, frequent awakenings during the night, early morning awakening, or nonrestorative sleep. Polysomnographic studies in adult depression confirm a clear pattern of altered sleep, characterized by a shortened REM latency, a prolongation of the first REM period, an increased number of eye movements (REM density) during REM sleep, and an attenuation of slow-wave sleep, particularly early in the night (Pillai et al. 2011; Baglioni et al. 2016). These data clearly indicate that sleep and depression are closely intertwined.

Such a strict relation is also supported by a bulk of data on the effects of sleep loss on mood. The negative consequences of lower quantities of sleep on mood have been repeatedly observed (Pilcher and Huffcutt 1996; De Valck and Cluydts 2001; Dahl and Lewin 2002; Oginska and Pokorski 2006). For example, De Valck and Cluydts (2001), comparing in young adults the depressed mood the day after 4.5 h or 7.5 h of sleep, observed that the subjects who slept less reported higher depressed mood compared with the group who slept longer. Accordingly, a meta-analysis indicated that partial and total sleep deprivation exert their largest effects on

mood, more than on performance (Pilcher and Huffcutt 1996). These findings demonstrate that a poor night's sleep have profoundly negative effects on depressed mood.

Several studies have identified alterations in functional brain activity during sleep in subjects with mood disorders in comorbidity with sleep disturbances (Germain et al. 2004; Nofzinger et al. 2004). During NREM sleep, the typical decrease of metabolic activity in the frontal, temporal, and parietal cortex compared with waking levels is smaller in depressed compared to healthy subjects (Ho et al. 1996; Peterson and Benca 2008; Nofzinger et al. 2004). Instead, during REM sleep an activation in the anterior paralimbic structures relative to waking was observed both in healthy and in depressed subjects, even if the spatial extent of this activation was greater in depressed patients (Nofzinger et al. 2004). In addition, during REM sleep patients showed a greater activation in prefrontal areas. These evidence suggest that the accentuated activation of paralimbic and prefrontal circuits during REM sleep could reflect the emotional dysregulation typical of depression disorder (Davidson et al. 2002; Tsuno et al. 2005). In these subjects an analogous dysregulation in the activation of the amygdala has been shown to affect the assessment of emotional, especially negative, visual stimuli (Jaworska et al. 2015). Moreover, in MDD patients a non-specific amygdala reactivity has been shown that does not discriminate between negative, neutral, and positive images (Ritchey et al. 2011).

Similarly, in patients with insomnia disorder compared to healthy good sleepers, heightened amygdala responses to insomnia-related pictures eliciting negative emotions have been observed (Baglioni et al. 2014). Such amygdala hyper-activation in response to negative emotional stimuli resulted to negatively correlate with total sleep time, sleep efficiency, slow-wave sleep, and REM sleep, further supporting a key role of sleep for emotional balance (Baglioni et al. 2014).

While the association between sleep disturbances and depression seems well clarified, the debate about the cause and effect relationship is still open. Even though insomnia can be an independent diagnostic entity, it has been pointed out that often this disturbance precedes the onset of mental disturbances such as major depression (Livingston et al. 1993; Weissman et al. 1997; Breslau et al. 1997; Chang et al. 1997; Riemann and Voderholzer 2003; Baglioni et al. 2010, 2011). In fact, several longitudinal studies have shown that sleep disturbances act as risk factors for depression (e.g., Eaton et al. 1995; Cole and Dendukuri 2003; Taylor et al. 2003; Buysse et al. 2008). Non-depressed people with insomnia have a twofold risk to develop depression, compared to people with no sleep difficulties (Baglioni et al. 2011). Coherently, it has been found that from 17% to 50% of subjects with insomnia, symptoms lasting 2 weeks or longer showed the development of a major depressive episode in a later interview (Buysse et al. 2008).

Whether sleep disorders trigger depression symptoms, their treatment could be important because it might influence the onset of depression. However, insomnia does not always precede depression. Other longitudinal studies have indeed found evidence for depression as a risk factor for developing insomnia (e.g., Jansson and Linton 2006; Morphy et al. 2007).

In conclusion, even if there is ample evidence about the reciprocal relationships between sleep disturbances and depression, the direction of this relation is still a matter of debate. However, the fact that emotion regulation is altered in insomnia subjects could explain why insomnia leads to depression (Koffel and Watson 2009; Baglioni et al. 2010). An altered pattern of brain activation during sleep (such as the increased activation of paralimbic and prefrontal circuits during REM sleep) may lead to alterations in emotional reactivity and then to greater likelihood of developing depression.

6.5.2 Anxiety Disorders

Anxiety disorders constitute the most frequent mental disorder in the general population yet often go undiagnosed. The overall lifetime prevalence of anxiety disorders is 24.9% (Bruce et al. 2005). Most anxiety disorders have a strong relationship with sleep problems (Ramsawh et al. 2009). Among anxiety disorders, the generalized anxiety disorder and social phobia had the strongest relationships with global sleep quality. Similarly, in a study on the prevalence of sleep-related problems in youth with anxiety disorders, one or more sleep-related problem was reported in 88% of the participants (Alfano et al. 2007).

Subjective complaints of difficulty falling asleep and frequent night-time awakening are the most common complaints in people with anxiety disorders. Objective polysomnographic data demonstrated a disrupted sleep continuity with significant reduction of total sleep time and sleep efficiency. In addition, sleep latency was prolonged, while NREM sleep amount was reduced (Benca et al. 1992; Papadimitriou and Linkowski 2005).

The clinical picture for sleep changes in anxiety disorders is similarly to that described for depression. Insomnia, frequently associated with the anxiety disorders, may precede or follow the onset of a comorbid anxiety disorder (Ohayon and Roth 2003; Johnson et al. 2006; Jansson-Frojmark and Lindblom 2008).

While there is less evidence compared to depression for the relationship between sleep disturbance and anxiety, some studies have found that chronic insomnia predict the first onset of anxiety disorders (Jansson-Frojmark and Lindblom 2008; Jackson et al. 2014). Ohayon and Roth (2003) showed that anxiety disorder appears before insomnia in 43% of cases, but in 18% of cases insomnia appears before the anxiety disorder.

Anxiety may also be a risk factor for future insomnia (e.g., Ohayon and Roth 2003; Jansson and Linton 2006; Morphy et al. 2007). In fact, it has been observed that high anxiety increased the risk of developing insomnia by more than three times (Jansson and Linton 2006).

Anxious individuals seem to show emotional hyper-reactivity, manifested as relatively intense and frequent negative emotional responses to perceived threat. Consequently, since anxious individuals provide exaggerated negative emotional

response to threatening scenes, they experience frequent and intense negative emotions (Carthy et al. 2010).

Emotion dysregulation is thought to be a core feature of anxiety disorders (e.g., Mennin et al. 2007). In fact these patients have an exaggerated negative emotional reactivity (Goldin et al. 2009; Mennin et al. 2005), an impaired facial emotion recognition (Melfsen and Florin 2002), and react with a higher increase of heart rate to threatening stimuli or situations, compared with non-anxious controls (e.g., Beidel et al. 1985).

Additionally, trait anxiety is associated with reduced prefrontal-amygdala connectivity involved in emotional modulation (see Greening and Mitchell 2015). Interestingly, this lack of prefrontal-amygdala functional connectivity has been found also after sleep loss (Yoo et al. 2007). This evidence, emphasizing the importance of the interactions between these brain structures in modulating anxiety, may also suggest an additional role of sleep in emotional modulation. However, to date no studies have investigated the presence of prefrontal-amygdala connectivity also in anxiety disorders with sleep disturbances. This could represent an important direction for further research.

6.5.3 Post-traumatic Stress Disorder (PTSD)

PTSD is another major psychiatric disorder with poor sleep being one of its principal symptoms (see Germain 2013). In fact, in the 5th edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-V; APA 2013), sleep disorders are included among the criteria for PTSD. These include re-experiences of traumatic symptoms (nightmares, criteria B) as well as alterations in arousal and reactivity (sleep disturbance, criteria E).

We have recently found that the exposure to a traumatic disaster was related to a significant deterioration of sleep quality and an increased occurrence of disturbing nocturnal behaviors, even 2 years after the event (Tempesta et al. 2013). Indeed, sleep disturbances were the prevalent symptoms among persons who survived the 1995 Hanshin earthquake in Japan (Kato et al. 1996) and among survivors of the Holocaust (Kuch and Cox 1992).

The most commonly reported complaints of PTSD patients are difficulties in falling asleep, regular awakenings (with difficulties in falling back to sleep), reduced sleep duration, restless sleep, fatigue, and, above all, anguished nightmares and anxiety dreams. The 44–90% of combat veterans with PTSD reported some sleep disturbances (Mellman et al. 1995; Neylan et al. 1998), and 52–87% reported having persistent nightmares (Inman et al. 1990). The nightmares are the most constant evidence in the majority of studies that have investigated sleep in PTSD patients (Lichstein and Morin 2000; Ohayon and Shapiro 2000), so that they are considered a core symptom of PTSD (Spoormaker and Montgomery 2008).

Meta-analytic review (Kobayashi et al. 2007) of 20 polysomnographic studies comparing sleep in people with and without PTSD showed that PTSD patients had

more stage 1 sleep, less slow-wave sleep, and greater REM density compared to people without PTSD. Conversely, reduction or fragmentation of REM sleep has been observed in the acute aftermath of trauma exposure and in symptomatic populations within several years of the onset of PTSD (Mellman et al. 2002; Redline et al. 2004; Habukawa et al. 2007).

According to the Walker and van der Helm model (2009), REM sleep could play an important role in PTSD development. In fact, REM sleep would be important not only for the persistence, in memory, of the emotional experience, but also for the depotentiation of the affective tone associated with the experience (Walker and van der Helm 2009). Therefore, when during the night after the traumatic event, sleep is disrupted, the process of separating the affective tone from the emotional experience cannot be accomplished; consequently, the subjects continue to display hyperarousal reactions to associated trauma cues (Harvey et al. 2003; Pole 2007) (for a more detailed explanation of the model, see Sect. 6.4).

Conversely, on the basis of the evidence that REM sleep following learning supports emotional memory consolidation (Wagner et al. 2001), Wagner and colleagues (2006; for more details, see Sect. 6.4) argue that after traumatic events, REM sleep may contribute to the development of haunting emotional memories, which can resist forgetting over long time periods and, in extreme cases, eventually manifest themselves in PTSD. From this perspective, these authors suggest the use of sleep deprivation in the immediate aftermath of traumatic events as a possible therapeutic measure to prevent a long-term persistence of these events in memory or at least to partly counteract the development of PTSD (Wagner et al. 2006).

In summary, REM sleep has been suggested to be crucial for the traumatic memory retention; however, regarding the affective tone associated to a traumatic memory, according to different views, REM sleep could promote its strengthening (Wagner et al. 2006) or, conversely, could dissipate (Walker and van der Helm 2009) its emotional charge.

Over the past several years, structural neuroimaging studies provided evidence that PTSD patients exhibit structural abnormalities in brain regions that are involved in stress regulation and fear responses, such as the amygdala, anterior cingulate cortex, and ventromedial prefrontal cortex (Shin et al. 2004; Driessen et al. 2004). Functional neuroimaging studies have also reported an increased activation of limbic structures, such as the insula and amygdala, during emotional tasks in PTSD individuals compared to healthy subjects (e.g., Mazza et al. 2013). Other studies have also demonstrated that patients with PTSD show reduced neural activity in the medial prefrontal cortex (mPFC) and increased activity in the amygdala during exposure to negative stimuli (Liberzon et al. 1999; Shin et al. 2004; Ganzel et al. 2008). In a study investigating the effective connectivity between the specific brain areas activated during emotional processing of negative stimuli, we observed that the higher reactivity to negative emotional stimuli in limbic brain regions is paralleled by a modification of the fronto-limbic functional connectivity in PTSD subjects (Mazza et al. 2013). Such dysfunction, which leads to a reduced cortical control of limbic areas that, in turn, result hyperactivated, may be the substrate of the peculiar

emotional symptoms of PTSD. Among these symptoms, individuals with PTSD experience feelings of detachment from others, disinterest in once pleasurable activities, and a restricted range of emotions, a class of problems referred to as emotional numbing. This may lead to a reduction of emotional ability and affective inclination for others and, generally, to a decrease of social interactions (Litz and Gray 2002).

Moreover, there is evidence that PTSD patients have difficulty to experience intimacy and tenderness and feel at times emotional disconnected from other people (Porto et al. 2009). We have reported that PTSD is characterized by impairments in emotional empathy, accompanied by a reduced neural activity in the left insula and the left inferior frontal gyrus (Mazza et al. 2015). Interestingly, the functional connectivity of the cortical areas involved in empathic behavior is also altered in PTSD. In these patients, increased activity in limbic regions such as the insula and the amygdala modulates activity in the frontal cortex while performing an emotional empathy task, suggesting a lack of cortical top-down control of the frontal cortex on the limbic system (Pino et al. 2016).

Both the behavioral results and the altered functional patterns of activation in empathy-related brain structures may be associated with the reduced sleep quality in PTSD patients. In fact, sleep loss and sleep disturbances may alter the functional connectivity of the neural networks that are critical for emotional empathy, explaining the emotional and social difficulties experienced by individuals suffering from PTSD. Future neuroimaging studies in larger samples of PTSD subjects should shed light on this important issue.

Therefore, taken together, these evidence support the notion that sleep disturbances play a significant role in emotional processing in PTSD, suggesting the importance of preventive strategies to improve sleep quality in the aftermath of a stressful/traumatic event. Along this line of reasoning, treating sleep disturbances with a specific cognitive-behavioral therapy immediately after the trauma exposure may reduce the development of PTSD.

6.6 Conclusions

In the last two decades, a growing number of experimental investigations have focused on the relationship between sleep and emotional processing. In the present chapter, we have reviewed several studies supporting the notion that sleep is critical for several aspects of emotional regulation. It has been demonstrated that sleep affects the formation of emotional memories throughout all the stages of this process. In fact, as sleep loss deteriorates the encoding of emotional information, it leads to a disruptive interference with emotional memory consolidation.

The relationship between sleep and emotional memory processing is less clear in people with poor sleep quality. Indeed, we showed a preserved sleep-dependent consolidation of emotional information in poor sleepers, but a more negative

affective tone to memories. In this regard, converging evidence indicates that sleep loss significantly affects emotional reactivity. However, whether sleep acts to protect, potentiate, or de-potentiate emotional reactivity is still a matter of debate. Future studies will have to clarify, at the behavioral level, the specific direction of the sleep-dependent emotional modulation.

Moreover, sleep has been shown to have a key role both in complex emotional processes, such as those involved in empathy, and in more basic emotions such as fear. In this respect, sleep seems to be crucial for our ability to correctly process emotional information that allows us to understand the others' feelings and to be empathic with them, as well as for our ability to form and retain fear conditioning and extinction learning.

Notably, several studies have found REM sleep as the specific sleep stage responsible for an optimal emotional processing. In fact, the functional and neurochemical changes that characterize this sleep stage show a strong convergence with the brain mechanisms and substratum of emotional memory formation as well as appraisal during wakefulness. Although there is a general consensus on the role of REM sleep in the consolidation of emotional memory, to date the specific contribution of REM sleep on next-day emotional reactivity is less clear. In fact, REM sleep could act to potentiate or, conversely, de-potentiate the emotional charge associated to a memory along with its consolidation. This topic could be also relevant for its implications in clinical settings. Indeed, further expanding our knowledge on the relation between sleep and next-day emotional brain functioning will be crucial to open a new perspective for the understanding and treatment of affective or anxiety disturbances.

References

Alfano CA, Ginsburg GS, Kingery JN (2007) Sleep-related problems among children and adolescents with anxiety disorders. J Am Acad Child Adolesc Psychiatry 46:224–232

American Psychiatric Association (2013) Diagnostic and statistical manual of mental disorders: DSM-V, 5th edn. American Psychiatric Publishing, Arlington

Armfield JM (2006) Cognitive vulnerability: a model of the etiology of fear. Clin Psychol Rev 26:746–768

Armitage R (2000) Microarchitectural findings in sleep EEG in depression: diagnostic implications. Biol Psychiatry 47:338–350

Aserinsky E, Kleitman N (1953) Regularly occurring periods of eye motility, and concomitant 1515 phenomena, during sleep. Science 118:273–274

Aston-Jones G, Rajkowski J, Kubiak P, Alexinsky T (1994) Locus coeruleus neurons in monkey are selectively activated by attended cues in a vigilance task. J Neurosci 14:4467–4480

Atienza M, Cantero JL (2008) Modulatory effects of emotion and sleep on recollection and familiarity. J Sleep Res 17:285–294

Axelsson J, Sundelin T, Ingre M et al (2010) Beauty sleep: experimental study on the perceived health and attractiveness of sleep deprived people. BMJ 341:c6614

Backhaus J, Junghanns K (2006) Daytime naps improve procedural motor memory. Sleep Med 7:508–512
Baglioni C, Lombardo C, Bux E et al (2010) Psychophysiological reactivity to sleep-related emotional stimuli in primary insomnia. Behav Res Ther 48:467e75
Baglioni C, Battagliese G, Feige B et al (2011) Insomnia as a predictor of depression: a meta-analytic evaluation of longitudinal epidemiological studies. J Affect Disord 135:10–19
Baglioni C, Regen W, Teghen A et al (2014) Sleep changes in the disorder of insomnia: a meta-analysis of polysomnographic studies. Sleep Med Rev 18:195–213
Baglioni C, Nanovska S, Regen W et al (2016) Sleep and mental disorders: a meta-analysis of polysomnographic research. Psychol Bull 142:969–990
Baran B, Pace-Schott EF, Ericson C, Spencer RM (2012) Processing of emotional reactivity and emotional memory over sleep. J Neurosci 32:1035–1042
Beidel DC, Turner SM, Dancu CV (1985) Physiological, cognitive and behavioral aspects of social anxiety. Behav Res Ther 23:109–117
Benca RM, Obermeyer WH, Thisted RA, Gillin JC (1992) Sleep and psychiatric disorders: a meta-analysis. Arch Gen Psychiatry 49:651–668
Boonstra TW, Stins JF, Daffertshofer A, Beek PJ (2007) Effects of sleep deprivation on neural functioning: an integrative review. Cell Mol Life Sci 64:934–946
Born J, Wilhelm I (2012) System consolidation of memory during sleep. Psychol Res 76:192–203
Bradley MM, Cuthbert BN, Lang PJ (1990) Startle reflex modification: emotion or attention? Psychophysiology 27:13–523
Bradley MM, Codispoti M, Sabatinelli D, Lang PJ (2001) Emotion and motivation II: sex differences in picture processing. Emotion 1:300–319
Brand S, Kirov R, Kalak N et al (2016) Poor sleep is related to lower emotional competence among adolescents. Behav Sleep Med 14:602–614
Braun AR, Balkin TJ, Wesenten NJ et al (1997) Regional cerebral blood flow throughout the sleep-wake cycle. An H2(15)O PET study. Brain 120:1173–1197
Braun AR, Balkin TJ, Wesensten NJ et al (1998) Dissociated pattern of activity in visual cortices and their projections during human rapid eye movement sleep. Science 279:91–95
Breslau N, Roth T, Rosenthal L, Andreski P (1997) Daytime sleepiness: 20. An epidemiological study of young adults. Am J Public Health 87:1649–1653
Bruce SE, Yonkers KA, Otto MW et al (2005) Influence of psychiatric comorbidity on recovery and recurrence in generalized anxiety disorder, social phobia, and panic disorder: a 12-year prospective study. Am J Psychiatry 162:1179–1187
Buchsbaum MS, Hazlett EA, Wu J, Bunney WE Jr (2001) Positron emission tomography with deoxyglucose-F18 imaging of sleep. Neuropsychopharmacology 25:S50–S56
Buysse DJ, Angst J, Gamma A et al (2008) Prevalence, course, and comorbidity of insomnia and depression in young adults. Sleep 31:473–480
Buzsáki G (2002) Theta oscillations in the hippocampus. Neuron 33:325–340
Cahill L, McGaugh JL (1998) Mechanisms of emotional arousal and lasting declarative memory. Trends Neurosci 21:294–299
Cairney SA, Durrant SJ, Power R, Lewis PA (2015) Complementary roles of slow-wave sleep and rapid eye movement sleep in emotional memory consolidation. Cereb Cortex 25:1565–1575
Cape EG, Jones BE (1998) Differential modulation of high-frequency γ-electroencephalogram activity and sleep–wake state by noradrenaline and serotonin microinjections into the region of cholinergic basalis neurons. J Neurosci 18(7):2653–2666
Carthy T, Horesh N, Apter A et al (2010) Emotional reactivity and cognitive regulation in anxious children. Behav Res Ther 48:384–393
Cellini N, Torre J, Stegagno L, Sarlo M (2016) Sleep before and after learning promotes the consolidation of both neutral and emotional information regardless of REM presence. Neurobiol Learn Mem 133:136–144

Chang PP, Ford DE, Mead LA et al (1997) Insomnia in young men and subsequent depression. The Johns Hopkins precursors study. Am J Epidemiol 146:105–114
Cipolli C, Ferrara M, De Gennaro L, Plazzi G (2016) Beyond the neuropsychology of dreaming: insights into the neural basis of dreaming with new techniques of sleep recording and analysis. Sleep Med Rev pii: S1087-0792(16)30067–3
Cole MG, Dendukuri N (2003) Risk factors for depression among elderly community subjects: a systematic review and meta-analysis. Am J Psychiatry 160:1147–1156
Couyoumdjian A, Sdoia S, Tempesta D et al (2010) The effects of sleep and sleep deprivation on task-switching performance. J Sleep Res 19:64–70
Craske MG, Kircanski K, Zelikowsky M et al (2008) Optimizing inhibitory learning during exposure therapy. Behav Res Ther 46:5–27
Cunningham TJ, Crowell CR, Alger SE et al (2014) Psychophysiological arousal at encoding leads to reduced reactivity but enhanced emotional memory following sleep. Neurobiol Learn Mem 114:155–164
Dahl RE, Harvey AG (2007) Sleep in children and adolescents with behavioral and emotional disorders. Sleep Med Clin 2:501–511
Dahl RE, Lewin DF (2002) Pathways to adolescent health sleep regulation and behavior. J Adolesc Health 31:175–184
Dang-Vu TT, Schabus M, Desseilles M et al (2010) Functional neuroimaging insights into the physiology of human sleep. Sleep 33:1589–1603
Datta S, Mavanji V, Ulloor J, Patterson EH (2004) Activation of phasic pontine-wave generator prevents rapid eye movement sleep deprivation-induced learning impairment in the rat: a mechanism for sleep-dependent plasticity. J Neurosci 24:1416–1427
Datta S, Li G, Auerbach S (2008) Activation of phasic pontine-wave generator in the rat: a mechanism for expression of plasticity-related genes and proteins in the dorsal hippocampus and amygdala. Eur J Neurosci 27:1876–1892
Davidson RJ (2002) Anxiety and affective style: role of prefrontal cortex and amygdala. Biol Psychiatry 51:68–80
Davidson RJ, Pizzagalli D, Nitschke JB et al (2002) Depression: perspectives from affective neuroscience. Annu Rev Psychol 53:545–574
Davis MH, Luce C, Kraus SJ (1994) The heritability of characteristics associated with dispositional empathy. J Pers 62:369–379
De Valck E, Cluydts R (2001) Slow-release caffeine as a countermeasure to driver sleepiness induced by partial sleep deprivation. J Sleep Res 10:203–209
Decety J, Meyer M (2008) From emotion resonance to empathic understanding: a social developmental neuroscience account. Dev Psychopathol 20:1053–1080
Diekelmann S, Wilhelm I, Born J (2009) The whats and whens of sleep-dependent memory consolidation. Sleep Med Rev 13:309–321
Dinges DF, Pack G, Williams K et al (1997) Cumulative sleepiness, mood disturbance, and psychomotor vigilance performance decrements during a week of sleep restricted to 4–5 hours per night. Sleep 20:267–277
Driessen M, Beblo T, Mertens M et al (2004) Posttraumatic stress disorder and fMRI activation patterns of traumatic memory in patients with borderline personality disorder. Biol Psychiatry 55:603–611
Drummond SP, Brown GG, Gillin JC et al (2000) Altered brain response to verbal learning following sleep deprivation. Nature 403:655–657
Drummond SP, Paulus MP, Tapert SF (2006) Effects of two nights sleep deprivation and two nights recovery sleep on response inhibition. J Sleep Res 15:261–265
Durmer JS, Dinges DF (2005) Neurocognitive consequences of sleep deprivation. Semin Neurol 25:117–129
Dziobek I, Rogers K, Fleck S et al (2008) Dissociation of cognitive and emotional empathy in adults with Asperger syndrome using the Multifaceted Empathy Test (MET). J Autism Dev Disord 38:464–473

Dziobek I, Preissler S, Grozdanovic Z et al (2011) Neuronal correlates of altered empathy and social cognition in borderline personality disorder. Neuroimage 57:539–548
Eaton WW, Badawi M, Melton B (1995) Prodromes and precursors: epidemiologic data for primary prevention of disorders with slow onset. Am J Psychiatry 152:967–972
Fanselow MS, Dong HW (2010) Are the dorsal and ventral hippocampus functionally distinct structures? Neuron 65:7–19
Feige B, Baglioni C, Spiegelhalder K et al (2013) The microstructure of sleep in primary insomnia: an overview and extension. Int J Psychophysiol 89:171–180
Ferrara M, De Gennaro L (2001) How much sleep do we need? Sleep Med Rev 5:155–179
Frankland PW, Bontempi B (2005) The organization of recent and remote memories. Nat Rev Neurosci 6:119–130
Franzen PL, Buysse DJ, Dahl RE et al (2009) Sleep deprivation alters pupillary reactivity to emotional stimuli in healthy young adults. Biol Psychol 80:300–305
Gais S, Born J (2004) Declarative memory consolidation: mechanisms acting during human sleep. Learn Mem 11:679–685
Gallese V (2007) Before and below 'theory of mind': embodied simulation and the neural correlates of social cognition. Philos Trans R Soc Lond Ser B Biol Sci 362:659–669
Ganzel BL, Kim P, Glover GH, Temple E (2008) Resilience after 9/11: multimodal neuroimaging evidence for stress-related change in the healthy adult brain. Neuroimage 40:88–795
Genzel L, Spoormaker VI, Konrad BN, Dresler M (2015) The role of rapid eye movement sleep for amygdala-related memory processing. Neurobiol Learn Mem 122:110–121
Germain A (2013) Sleep disturbances as the hallmark of PTSD: where are we now? Am J Psychiatry 170:372–382
Germain A, Nofzinger EA, Kupfer DJ et al (2004) Neurobiology of non-REM sleep in depression: further evidence for hypofrontality and thalamic dysregulation. Am J Psychiatry 161:1856–1863
Gilson M, Deliens G, Leproult R et al (2016) REM-enriched naps are associated with memory consolidation for sad stories and enhance mood-related reactivity. Brain Sci 6(1):1
Goldin PR, Manber T, Hakimi S et al (2009) Neural bases of social anxiety disorder: emotional reactivity and cognitive regulation during social and physical threat. Arch Gen Psychiatry 66:170–180
Goldstein AN, Walker MP (2014) The role of sleep in emotional brain function. Annu Rev Clin Psychol 10:679–708
Goldstein-Piekarski AN, Greer SM, Saletin JM, Walker MP (2015) Sleep deprivation impairs the human central and peripheral nervous system discrimination of social threat. J Neurosci 35:10135–10145
Goulart LI, Pinto LR Jr, Perlis ML (2014) Effects of different sleep deprivation protocols on sleep perception in healthy volunteers. Sleep Med 15:1219–1224
Graham BM, Milad MR (2011) The study of fear extinction: implications for anxiety disorders. Am J Psychiatry 168:1255–1265
Graves LA, Heller EA, Pack AI, Abel T (2003) Sleep deprivation selectively impairs memory consolidation for contextual fear conditioning. Learn Mem 10:168–176
Greening SG, Mitchell DG (2015) A network of amygdala connections predict individual differences in trait anxiety. Hum Brain Mapp 36:4819–4830
Gregory AM, Sadeh A (2012) Sleep, emotional and behavioral difficulties in children and adolescents. Sleep Med Rev 16:129–136
Groch S, Wilhelm I, Diekelmann S, Born J (2013) The role of REM sleep in the processing of emotional memories: evidence from behavior and event-related potentials. Neurobiol Learn Mem 99:1–9
Groch S, Zinke K, Wilhelm I, Born J (2015) Dissociating the contributions of slow-wave sleep and rapid eye movement sleep to emotional item and source memory. Neurobiol Learn Mem 122:122–130

Guadagni V, Burles F, Ferrara M, Iaria G (2014) The effects of sleep deprivation on emotional empathy. J Sleep Res 3:657–663
Guadagni V, Burles F, Valera S et al (2016) The relationship between quality of sleep and emotional empathy. J Psychophysiol. https://doi.org/10.1027/0269-8803/a000177
Gujar N, Yoo SS, Hu P, Walker MP (2011) Sleep deprivation amplifies reactivity of brain reward networks, biasing the appraisal of positive emotional experiences. J Neurosci 31:4466–4474
Haack M, Mullington JM (2005) Sustained sleep restriction reduces emotional and physical well-being. Pain 119:56–64
Habukawa M, Uchimura N, Maeda M et al (2007) Sleep findings in young adult patients with posttraumatic stress disorder. Biol Psychiatry 62:1179–1182
Harrison Y, Horne JA (2000) Sleep loss and temporal memory. Q J Exp Psychol 53:271–279
Harvey AG, Jones C, Schmidt DA (2003) Sleep and posttraumatic stress disorder: a review. Clin Psychol Rev 23:377–407
Hauner KK, Howard JD, Zelano C, Gottfried JA (2013) Stimulus-specific enhancement of fear extinction during slow wave sleep. Nat Neurosci 16:1553–1555
Hawkins DR, Taub JM, Van de Castle RL (1985) Extended sleep (hypersomnia) in young depressed patients. Am J Psychiatry 142:905–910
He J, Sun HQ, Li SX et al (2015) Effect of conditioned stimulus exposure during slow wave sleep on fear memory extinction in humans. Sleep 38:423–431
Ho AP, Gillin JC, Buchsbaum MS et al (1996) Brain glucose metabolism during non-rapid eye movement sleep in major depression: a positron emission tomography study. Arch Gen Psychiatry 53:645–652
Hofmann SG (2008) Cognitive processes during fear acquisition and extinction in animals and humans: implications for exposure therapy of anxiety disorders. Clin Psychol Rev 28:199–210
Holland P, Lewis PA (2007) Emotional memory: selective enhancement by sleep. Curr Biol 17: R179–R181
Hong CCH, Gillin JC, Dow BM et al (1995) Localized and lateralized cerebral glucose metabolism associated with eye movements during REM sleep and wakefulness: a positron emission tomography (PET) study. Sleep 18:570–580
Horne JA (1985) Sleep function, with particular reference to sleep deprivation. Ann Clin Res 17:199–208
Hu P, Stylos-Allan M, Walker MP (2006) Sleep facilitates consolidation of emotionally arousing declarative memory. Psychol Sci 10:891–898
Inman DJ, Silver SM, Doghramji K (1990) Sleep disturbance in posttraumatic stress disorder: a comparison with non-PTSD insomnia. J Trauma Stress 3:429–437
Jackson ML, Sztendur EM, Diamond NT et al (2014) Sleep difficulties and the development of depression and anxiety: a longitudinal study of young Australian women. Arch Womens Ment Health 17:189–198
Jansson M, Linton SJ (2006) The role of anxiety and depression in the development of insomnia: cross-sectional and prospective analyses. Psychol Health 21:383–397
Jansson-Frojmark M, Lindblom K (2008) A bidirectional relationship between anxiety and depression, and insomnia? A prospective study in the general population. J Psychosom Res 64:443–449
Jaworska N, Yang XR, Knott V, MacQueen G (2015) A review of fMRI studies during visual emotive processing in major depressive disorder. World J Biol Psychiatry 16:448–471
Jeannerod M, Mouret J, Jouvet M (1965) Étude de la motricité oculaire au cours de la phase paradoxale du sommeil chez le chat. Electroencephalogr Clin Neurophysiol 18:554–566
Johnson EO, Roth T, Breslau N (2006) The association of insomnia with anxiety disorders and depression: exploration of the direction of risk. J Psychiatr Res 40:700–708
Jones K, Harrison Y (2001) Frontal lobe function, sleep loss and fragmented sleep. Sleep Med Rev 5:463–475
Jouvet M, Michel F (1959) Corrélations électromyographique du sommeil chez le chat décortiqué et mesencéphalique chronique. C R Seances Soc Biol Fil 153:422–425

Kahn M, Sheppes G, Sadeh A (2013) Sleep and emotions: bidirectional links and underlying mechanisms. Int J Psychophysiol 89:218–228
Kaida K, Niki K, Born J (2015) Role of sleep for encoding of emotional memory. Neurobiol Learn Mem 121:72–79
Kato H, Asukai N, Miyake Y et al (1996) Posttraumatic symptoms among younger and elderly exacuees in the early stages following the 1995 Hanshin-Awaji earthquake in Japan. Acta Psychiatr Scand 93:477–481
Kensinger EA (2004) Remembering emotional experiences: the contribution of valence and arousal. Rev Neurosci 15:241–251
Killgore WD (2010) Effects of sleep deprivation on cognition. Prog Brain Res 185:105–129
Killgore WDS, Kahn-Greene ET, Lipizzi EL et al (2008) Sleep deprivation reduces perceived emotional intelligence and constructive thinking skills. Sleep Med 9:517–526
Kleim B, Wilhelm FH, Temp L et al (2014) Sleep enhances exposure therapy. Psychol Med 44:1511–1519
Kobayashi I, Boarts JM, Delahanty DL (2007) Polysomnographically measured sleep abnormalities in PTSD: a meta-analytic review. Psychophysiology 44:660–669
Koffel E, Watson D (2009) The two-factor structure of sleep complaints and its relation to depression and anxiety. J Abnorm Psychol 118:183–194
Kuch K, Cox B (1992) Symptoms of PTSD in 124 survivors of the Holocaust. Am J Psychiatry 149:337–340
Kumar T, Jha SK (2012) Sleep deprivation impairs consolidation of cued fear memory in rats. PLoS One 7:e47042.10.137
Kuriyama K, Soshi T, Kim Y (2010) Sleep deprivation facilitates extinction of implicit fear generalization and physiological response to fear. Biol Psychiatry 68:991–998
Kyle SD, Beattie L, Spiegelhalder K et al (2014) Altered emotion perception in insomnia disorder. Sleep 37:775e83
LaBar KS, Cabeza R (2006) Cognitive neuroscience of emotional memory. Nat Rev Neurosci 7:54–64
Lang PJ, Greenwald MK, Bradley MM, Hamm AO (1993) Looking at pictures: affective, facial, visceral, and behavioral reactions. Psychophysiology 30:261–273
Lang PJ, Bradley MM, Cuthbert BN (1998) Emotion, motivation, and anxiety: brain mechanisms and psychophysiology. Biol Psychiatry 44:1248–1263
Lara-Carrasco J, Nielsen TA, Solomonova E et al (2009) Overnight emotional adaptation to negative stimuli is altered by REM sleep deprivation and is correlated with intervening dream emotions. J Sleep Res 18:178–187
Levenson RW, Ekman P, Friesen WV (1990) Voluntary facial action generates emotion specific autonomic nervous system activity. Psychophysiology 27:363–384
Liberzon I, Taylor SF, Amdur R et al (1999) Brain activation in PTSD in response to trauma-related stimuli. Biol Psychiatry 45:817–826
Lichstein KL, Morin CM (2000) Treatment of late-life insomnia. Sage, Thousand Oaks
Lim AS, Lozano AM, Moro E et al (2007) Characterization of REM–sleep associated ponto-geniculo-occipital waves in the human pons. Sleep 30:823–827
Lissek S, Powers AS, McClure EB et al (2005) Classical fear conditioning in the anxiety disorders: a meta-analysis. Behav Res Ther 43:1391–1424
Lissek S, Biggs AL, Rabin SJ et al (2008) Generalization of conditioned fear-potentiated startle in humans: experimental validation and clinical relevance. Behav Res Ther 46:678–687
Litz BT, Gray MJ (2002) Emotional numbing in posttraumatic stress disorder: current and future research directions. Aust N Z J Psychiatry 36:198–204
Livingston G, Blizard B, Mann A (1993) Does sleep disturbance predict 19. Depression in elderly people? A study in inner London. Br J Gen Pract 43:445–448
Lopes Aguiar C, Romcy-Pereira RN, Escorsim Szawka R et al (2008) Muscarinic acetylcholine neurotransmission enhances the late-phase of long-term potentiation in the hippocampal-

prefrontal cortex pathway of rats in vivo: a possible involvement of monoaminergic systems. Neuroscience 153:1309–1319
Maloney KJ, Cape EG, Gotman J, Jones BE (1997) High-frequency gamma electroencephalogram activity in association with sleep-wake states and spontaneous behaviors in the rat. Neuroscience 76:541–555
Maquet P, Peters J, Aerts J et al (1996) Functional neuroanatomy of human rapid-eye-movement sleep and dreaming. Nature 383:163–166
Maquet P, Laureys S, Peigneux P et al (2000) Experience-dependent changes in cerebral activation during human REM sleep. Nat Neurosci 3:831–836
Maren S (2001) Neurobiology of Pavlovian fear conditioning. Annu Rev Neurosci 24:897–931
Marshall L, Born J (2007) The contribution of sleep to hippocampus-dependent memory consolidation. Trends Cogn Sci 11:442–450
Marzano C, Ferrara M, Mauro F et al (2011) Recalling and forgetting dreams: theta and alpha oscillations during sleep predict subsequent dream recall. J Neurosci 31:6674–6683
Mazza M, Tempesta D, Pino MC et al (2013) Regional cerebral changes and functional connectivity during the observation of negative emotional stimuli in subjects with post-traumatic stress disorder. Eur Arch Psychiatry Clin Neurosci 26:575–583
Mazza M, Tempesta D, Pino MC et al (2015) Neural activity related to cognitive and emotional empathy in post-traumatic stress disorder. Behav Brain Res 282:37–45
McGaugh JL (2000) Memory—a century of consolidation. Science 287:248–251
McGaugh JL (2004) The amygdala modulates the consolidation of memories of emotionally arousing experiences. Annu Rev Neurosci 27:1–28
McNally RJ (2007) Mechanisms of exposure therapy: how neuroscience can improve psychological treatments for anxiety disorders. Clin Psychol Rev 27:750–759
Melfsen S, Florin I (2002) Do socially anxious children show deficits in classifying facial expressions of emotions? J Nonverbal Behav 26:109e26
Mellman TA, David D, Kulick-Bell R et al (1995) Sleep events among veterans with combat related posttraumatic stress disorder. Am J Psychiatry 152:110–115
Mellman TA, Bustamante V, Fins AI et al (2002) REM sleep and the early development of posttraumatic stress disorder. Am J Psychiatr 159:1696–1701
Mennin DS, Heimberg RG, Turk CL, Fresco DM (2005) Preliminary evidence for an emotion dysregulation model of generalized anxiety disorder. Behav Res Ther 43:1281–1310
Mennin SD, Holaway RM, Fresco DM et al (2007) Delineating components of emotion and its dysregulation in anxiety and mood psychopathology. Behav Ther 38:284–302
Menz MM, Rihm JS, Salari N et al (2013) The role of sleep and sleep deprivation in consolidating fear memories. Neuroimage 75:87–96
Menz MM, Rihm JS, Buchel C (2016) REM sleep is causal to successful consolidation of dangerous and safety stimuli and reduces return of fear after extinction. J Neurosci 36:2148–2160
Milad MR, Quirk GJ (2002) Neurons in medial prefrontal cortex signal memory for fear extinction. Nature 420:70–74
Milad MR, Quirk GJ (2012) Fear extinction as a model for translational neuroscience: ten years of progress. Annu Rev Psychol 63:129–151
Milad MR, Rauch SL (2012) Obsessive-compulsive disorder: beyond segregated cortico-striatal pathways. Trends Cogn Sci 16:43–51
Milad MR, Rauch SL, Pitman RK, Quirk GJ (2006) Fear extinction in rats: implications for human brain imaging and anxiety disorders. Biol Psychol 73:61–71
Milad MR, Wright CI, Orr SP et al (2007) Recall of fear extinction in humans activates the ventromedial prefrontal cortex and hippocampus in concert. Biol Psychiatry 62:446–454
Mineka S, Oehlberg K (2008) The relevance of recent developments in classical conditioning to understanding the etiology and maintenance of anxiety disorders. Acta Psychol 127:567–580
Minkel J, Htaik O, Banjs S, Dinges D (2011) Emotional expressiveness in sleep-deprived healthy adults. Behav Sleep Med 9:5–14

Minkel JD, Banks S, Htaik O, Moreta MC, Jones CW, McGlinchey EL, Simpson NS, Dinges DF (2012) Sleep deprivation and stressors: evidence for elevated negative affect in response to mild stressors when sleep deprived. Emotion 12(5):1015–1020

Miyauchi S, Misaki M, Kan S et al (2009) Human brain activity time-locked to rapid eye movements during REM sleep. Exp Brain Res 192:657–667

Morgenthaler J, Wiesner CD, Hinze K (2014) Selective REM-sleep deprivation does not diminish emotional memory consolidation in young healthy subjects. PLoS One 9:e89849

Morphy H, Dunn KM, Lewis M, Boardman HF, Croft PR (2007 Mar) Epidemiology of insomnia: a longitudinal study in a UK population. Sleep 30(3):274–280

Motomura Y, Kitamura S, Oba K et al (2013) Sleep debt elicits negative emotional reaction through diminished amygdala-anterior cingulate functional connectivity. PLoS One 8:e56578

Nelson JP, McCarley RW, Hobson JA (1983) REM sleep burst neurons, PGO waves, and eye movement information. J Neurophysiol 50:784–797

Neylan TC, Mannar CR, Metzler TJ et al (1998) Sleep disturbances in the Vietnam generation: findings from a nationally representative sample of male Vietnam veterans. Am J Psychiatry 155:929–933

Nir Y, Tononi G (2010) Dreaming and the brain: from phenomenology to neurophysiology. Trends Cogn Sci 14:88–100

Nishida M, Pearsall J, Buckner RL, Walker MP (2009) REM sleep, prefrontal theta, and the consolidation of human emotional memory. Cereb Cortex 19:1158–1166

Nofzinger EA, Mintun MA, Wiseman M et al (1997) Forebrain activation in REM sleep: an FDG PET study. Brain Res 770:192–201

Nofzinger EA, Buysse DJ, Miewald JM et al (2002) Human regional cerebral glucose metabolism during non-rapid eye movement sleep in relation to waking. Brain 125:1105–1115

Nofzinger EA, Buysse DJ, Germain A et al (2004) Functional neuroimaging evidence for hyperarousal in insomnia. Am J Psychiatry 161:2126–2128

Oginska H, Pokorski J (2006) Fatigue and mood correlates of sleep length in three agesocial groups: school children, students, and employees. Chronobiol Int 23:1317–1328

Ohayon MM, Roth T (2003) Place of chronic insomnia in the course of depressive and anxiety disorders. J Psychiatr Res 37:9–15

Ohayon MM, Shapiro CM (2000) Sleep disturbances and psychiatric disorders associated with posttraumatic stress disorder in the general population. Compr Psychiatry 41:469–478

Ohayon MM, Shapiro CM, Kennedy SH (2000) Differentiating DSM-IV anxiety and depressive disorders in the general population: comorbidity and treatment consequences. Can J Psychiatr 45:166–172

Orr SP, Metzger LJ, Lasko NB et al (2000) De novo conditioning in trauma-exposed individuals with and without posttraumatic stress disorder. J Abnorm Psychol 109:290–298

Pace-Schott EF, Milad MR, Orr SP et al (2009) Sleep promotes generalization of extinction of conditioned fear. Sleep 32:19–26

Pace-Schott EF, Verga PW, Bennett TS, Spencer RM (2012) Sleep promotes consolidation and generalization of extinction learning in simulated exposure therapy for spider fear. J Psychiatr Res 46:1036–1044

Pace-Schott EF, Spencer RMC, Vijayakumar S et al (2013) Extinction of conditioned fear is better learned and recalled in the morning than in the evening. J Psychiatr Res 47:1776–1784

Pace-Schott EF, Tracy LE, Rubin Z et al (2014) Interactions of time of day and sleep with between-session habituation and extinction memory in young adult males. Exp Brain Res 232:1443–1458

Papadimitriou GN, Linkowski P (2005) Sleep disturbance in anxiety disorders. Int Rev Psychiatry 17:229–236

Patrick G, Gilbert J (1896) Studies from the psychological laboratory of the University of Iowa: on the effects of loss of sleep. Psychol Rev 3:469–483

Payne JD, Kensinger EA (2011) Sleep leads to changes in the emotional memory trace: evidence from fMRI. J Cogn Neurosci 23:1285–1297

Payne JD, Nadel L (2004) Sleep, dreams, and memory consolidation: the role of the stress hormone cortisol. Learn Mem 11:671–678
Payne JD, Chambers AM, Kensinger EA (2012) Sleep promotes lasting changes in selective memory for emotional scenes. Front Integr Neurosci 6:1–11
Payne JD, Kensinger EA, Wamsley EJ et al (2015) Napping and the selective consolidation of negative aspects of scenes. Emotion 15:176–186
Peeters F, Berkhof J, Delespaul P et al (2006) Diurnal mood variation in major depressive disorder. Emotion 6:383–391
Peigneux P, Laureys S, Fuchs S et al (2001) Generation of rapid eye movements during paradoxical sleep in humans. Neuroimage 14:701–708
Peterson MJ, Benca RM (2008) Sleep in mood disorders. Sleep Med Clin 3:231–249
Phan KL, Taylor SF, Welsh RC et al (2003) Activation of the medial prefrontal cortex and extended amygdala by individual ratings of emotional arousal: a fMRI study. Biol Psychiatry 53:211–215
Phelps EA (2004) Human emotion and memory: interactions of the amygdala and hippocampal complex. Curr Opin Neurobiol 14:198–202
Phelps EA, LeDoux JE (2005) Contributions of the amygdala to emotion processing: from animal models to human behavior. Neuron 48:175–187
Pilcher JJ, Huffcutt AI (1996) Effects of sleep deprivation on performance: a meta-analysis. Sleep 19:318–326
Pillai V, Kalmbach DA, Ciesla JA (2011) A meta-analysis of electroencephalographic sleep in depression: evidence for genetic biomarkers. Biol Psychiatry 70:912–919
Pino MC, Tempesta D, Catalucci A et al (2016) Altered cortico-limbic functional connectivity during an empathy task in subjects with post-traumatic stress disorder. J Psychopathol Behav Assess. https://doi.org/10.1007/s10862-016-9538-x
Pitman RK, Rasmusson AM, Koenen KC et al (2012) Biological studies of post-traumatic stress disorder. Nat Rev Neurosci 13:769–787
Pole N (2007) The psychophysiology of posttraumatic stress disorder: a meta-analysis. Psychol Bull 133:725–746
Porto PR, Oliveira L, Mari J et al (2009) Does cognitive behavioral therapy change the brain? A systematic review of neuroimaging in anxiety disorders. J Neuropsychiatry Clin Neurosci 21:114–125
Prather AA, Bogdan R, Hariri AR (2013) Impact of sleep quality on amygdala reactivity, negative affect, and perceived stress. Psychosom Med 75:350e8
Ramsawh HJ, Stein MB, Belik SL et al (2009) Relationship of anxiety disorders, sleep quality, and functional impairment in a community sample. J Psychiatr Res 43:926–933
Redline S, Kirchner HL, Quan SF et al (2004) The effects of age, sex, ethnicity, and sleep disordered breathing on sleep architecture. Arch Int Med 164:406–418
Riemann D, Voderholzer U (2003) Primary insomnia: a risk factor to develop depression? J Affect Disord 76:255–259
Ritchey M, Dolcos F, Eddington KM et al (2011) Neural correlates of emotional processing in depression: changes with cognitive behavioral therapy and predictors of treatment response. J Psychiatr Res 45:577–587
Rosales-Lagarde A, Armony JL, Del Río-Portilla Y et al (2012) Enhanced emotional reactivity after selective REM sleep deprivation in humans: an fMRI study. Front Behav Neurosci 18:6–25
Rosen IM, Gimotty PA, Shea JA, Bellini LM (2006) Evolution of sleep quantity, sleep deprivation, mood disturbances, empathy, and burnout among interns. Acad Med 81:82–85
Ruskin DN, Liu C, Dunn KE et al (2004) Sleep deprivation impairs hippocampus mediated contextual learning but not amygdala-mediated cued learning in rats. Eur J Neurosci 19:3121–3312
Sapolsky RM, Romero LM, Munck AU (2000) How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. Endocr Rev 21:55–89

Scarpelli S, Marzano C, D'Atri A et al (2015) State- or trait-like individual differences in dream recall: preliminary findings from a within-subjects study of multiple nap REM sleep awakenings. Front Psychol 6:928

Selvi Y, Aydin A, Boysan M et al (2010) Associations between chronotype, sleep quality, suicidality, and depressive symptoms in patients with major depression and healthy controls. Chronobiol Int 27:1813–1828

Shamay-Tsoory SG (2011) The neural bases for empathy. Neuroscientist 17:18–24

Shin LM, Orr SP, Carson MA et al (2004) Regional cerebral blood flow in the amygdala and medial prefrontal cortex during traumatic imagery in male and female Vietnam veterans with PTSD. Arch Gen Psychiatry 61:168–176

Singer T (2006) The neuronal basis and ontogeny of empathy and mind reading: review of literature and implications for future research. Neurosci Biobehav Rev 30:855–863

Smith C (2001) Sleep states and memory processes in humans: procedural versus declarative memory systems. Sleep Med Rev 5:491–506

Sotres-Bayon F, Bush DE, LeDoux JE (2004) Emotional perseveration: an update on prefrontal-amygdala interactions in fear extinction. Learn Mem 11:525–535

Sotres-Bayon F, Cain CK, LeDoux JE (2006) Brain mechanisms of fear extinction: historical perspectives on the contribution of prefrontal cortex. Biol Psychiatry 60:329–336

Spoormaker VI, Montgomery P (2008) Disturbed sleep in post-traumatic stress disorder: secondary symptom or core feature? Sleep Med Rev 12:169–184

Spoormaker VI, Sturm A, Andrade KC et al (2010) The neural correlates and temporal relationship between shock exposure, disturbed sleep and impaired consolidation of fear extinction. J Psychiatr Res 44:1121–1128

Spoormaker VI, Schroter MS, Andrade KC et al (2012) Effects of rapid eye movement sleep deprivation on fear extinction recall and prediction error signaling. Hum Brain Mapp 33:2362–2376

Spoormaker VI, Gvozdanovic GA, Samann PG, Czisch M (2014) Ventromedial prefrontal cortex activity and rapid eye movement sleep are associated with subsequent fear expression in human subjects. Exp Brain Res 232:1547–1554

Sterpenich V, Albouy G, Boly M et al (2007) Sleep-related hippocampo-cortical interplay during emotional memory recollection. PLoS Biol 5:e282

Sterpenich V, Albouy G, Darsaud A et al (2009) Sleep promotes the neural reorganization of remote emotional memory. J Neurosci 29:5143–5152

Sterpenich V, Schmidt C, Albouy G (2014) Memory reactivation during rapid eye movement sleep promotes its generalization and integration in cortical stores. Sleep 37:1061–1075

Strange BA, Dolan RJ (2006) Anterior medial temporal lobe in human cognition: memory for fear and the unexpected. Cogn Neuropsychiatry 11:198–218

Taylor DJ, Lichstein KL, Durrence HH (2003) Insomnia as a health risk factor. Behav Sleep Med 1:227–247

Teber I, Köhling R, Speckmann EJ et al (2004) Muscarinic acetylcholine receptor stimulation induces expression of the activity-regulated cytoskeleton-associated gene (ARC). Brain Res Mol Brain Res 121:131–136

Tempesta D, Couyoumdjian A, Curcio G et al (2010) Lack of sleep affects the evaluation of emotional stimuli. Brain Res Bull 82:104–108

Tempesta D, Curcio G, De Gennaro L, Ferrara M (2013) Long-term impact of earthquakes on sleep quality. PLoS One 8:e55936

Tempesta D, De Gennaro L, Presaghi F, Ferrara M (2014) Emotional working memory during sustained wakefulness. J Sleep Res 23:646–656

Tempesta D, De Gennaro L, Natale V, Ferrara M (2015) Emotional memory processing is influenced by sleep quality. Sleep Med 16:862–870

Tempesta D, Socci V, Coppo M et al (2016) The effect of sleep deprivation on the encoding of contextual and non-contextual aspects of emotional memory. Neurobiol Learn Mem 131:9–17

Thomas M, Sing H, Belenky G et al (2000) Neural basis of alertness and cognitive performance impairments during sleepiness. I. Effects of 24 h of sleep deprivation on waking human regional brain activity. J Sleep Res 9:335–352
Tsuno N, Besset A, Ritchie K (2005) Sleep and depression. J Clin Psychiatry 66:1254–1269
Tucker MA, Fishbein W (2009) The impact of sleep duration and subject intelligence on declarative and motor memory performance: how much is enough? J Sleep Res 18:304–312
Van der Helm E, Gujar N, Walker MP (2010) Sleep deprivation impairs the accurate recognition of human emotions. Sleep 33:335–342
Van der Helm E, Yao J, Dutt S et al (2011) REM sleep depotentiates amygdala activity to previous emotional experiences. Curr Biol 21:2029–2032
Wagner U, Gais S, Born J (2001) Emotional memory formation is enhanced across sleep intervals with high amounts of rapid eye movement sleep. Learn Mem 8:112–119
Wagner U, Fischer S, Born J (2002) Changes in emotional responses to aversive pictures across periods rich in slow-wave sleep versus rapid eye movement sleep. Psychosom Med 64:627–634
Wagner U, Hallschmid M, Rasch B, Born J (2006) Brief sleep after learning keeps emotional memories alive for years. Biol Psychiatry 60:788–790
Walker MP (2008) Cognitive consequences of sleep and sleep loss. Sleep Med 9:S29–S34
Walker MP (2009) The role of sleep in cognition and emotion. Ann N Y Acad Sci 1156:168–197
Walker MP, Stickgold R (2004) Sleep-dependent learning and memory consolidation. Neuron 44:121–133
Walker MP, Stickgold R (2010) Overnight alchemy: sleep-dependent memory evolution. Nat Rev Neurosci 11:218–220
Walker MP, Van der Helm E (2009) Overnight therapy? The role of sleep in emotional brain processing. Psychol Bull 135:731–748
Wehrle R, Kaufmann C, Wetter TC et al (2007) Functional microstates within human REM sleep: first evidence from fMRI of a thalamocortical network specific for phasic REM periods. Eur J Neurosci 25:863–871
Weissman MM, Greenwald S, Nino-Murcia G, Dement WC (1997) The morbidity of insomnia uncomplicated by psychiatric disorders. Gen Hosp Psychiatry 19:245–250
Wesensten NJ (2006) Effects of modafinil on cognitive performance and alertness during sleep deprivation. Curr Pharm Des 12:2457–2471
Westermann J, Lange T, Textor J, Born J (2015) System consolidation during sleep – a common principle underlying psychological and immunological memory formation. Trends Neurosci 38:585–597
Wheeler RE, Davidson RJ, Tomarken AJ (1993) Frontal brain asymmetry and emotional reactivity: a biological substrate of affective style. Psychophysiology 30:82–89
Wiesner CD, Pulst L, Krause F et al (2015) The effect of selective REM-sleep deprivation on the consolidation and affective evaluation of emotional memories. Neurobiol Learn Mem 122:131–141
Williams LM, Phillips ML, Brammer MJ et al (2001) Arousal dissociates amygdala and hippocampal fear responses: evidence from simultaneous fMRI and skin conductance recording. Neuroimage 14:1070–1079
Wixted JT, Mickes L, Squire LR (2010) Measuring recollection and familiarity in the medial temporal lobe. Hippocampus 20:1195–1205
Yaroush R, Sullivan MJ, Ekstrand BR (1971) Effect of sleep on memory. II. Differential effect of the first and second half of the night. J Exp Psychol 88:361–366
Yoo SS, Gujar N, Hu P et al (2007) The human emotional brain without sleep – a prefrontal amygdala disconnect. Curr Biol 17:877–878
Zohar D, Tzischinsky DO, Epstein R, Lavie P (2005) The effects of sleep loss on medical residents' emotional reactions to work events: a cognitive-energy model. Sleep 28:47–54