The emotional brain and sleep: An intimate relationship

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\textbf{S U M M A R Y}

Research findings confirm our own experiences in life where daytime events and especially emotionally stressful events have an impact on sleep quality and well-being. Obviously, daytime emotional stress may have a differentiated effect on sleep by influencing sleep physiology and dream patterns, dream content and the emotion within a dream, although its exact role is still unclear. Other effects that have been found are the exaggerated startle response, decreased dream recall and elevated awakening thresholds from rapid eye movement (REM)-sleep, increased or decreased latency to REM-sleep, increased REM-density, REM-sleep duration and the occurrence of arousals in sleep as a marker of sleep disruption. However, not only do daytime events affect sleep, also the quality and amount of sleep influences the way we react to these events and may be an important determinant in general well-being. Sleep seems restorative in daily functioning, whereas deprivation of sleep makes us more sensitive to emotional and stressful stimuli and events in particular. The way sleep impacts next day mood/emotion is thought to be affected particularly via REM-sleep, where we observe a hyperlimbic and hypoactive dorsolateral prefrontal functioning in combination with a normal functioning of the medial prefrontal cortex, probably adaptive in coping with the continuous stream of emotional events we experience.

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\textbf{Introduction}

Even though the relationship between pre-sleep emotional experiences and quality of sleep, as well as the reason why we sleep, seems intuitively evident, until recently this topic has gotten increased attention. The scarce amount of research is surprising given the importance of sleep in emotional well-being and the occurrence of disturbed sleep in many psychological and psychiatric disorders. In this review, the scope will concentrate on the relationship between emotion and sleep, particularly rapid eye movement (REM)-sleep and its emotion modulatory and even emotion regulatory functions in especially healthy individuals.

In the first part, we review how to understand how emotional situations affect sleep and how sleep affects emotional processing of affective information. In the second part, the discussed findings are evaluated in light of neurophysiological insights.

Research findings appear to confirm our own life-experience where daytime events, especially emotionally stressful events, have an impact on the quality of our sleep and well-being. Daytime emotional stress may have a twofold effect on sleep: first by influencing sleep physiology and second by influencing dream patterns, dream content and the emotion within a dream, although its exact role still is unclear. Even social phenomena such as reduced social support and increased patterns of avoidance in a person’s emotion regulation, appear to result in psychological distress and sleep complaints.\textsuperscript{1} Furthermore, the association between cortical and emotional arousal and disrupted sleep in individuals with insomnia suggests a strong relationship between daytime events and disrupted sleep. As a matter of evidence, it is clear that the individual’s response and coping with the emotional stress associated with daytime events involves the capacity to de-arouse or disengage from active wake processing interfering with the normal initiation of sleep processes. Sleep latency, especially REM-sleep alterations or abnormalities, have been related to variables associated with the affective state of individuals during the day.\textsuperscript{2} Watching aversive films before sleep for instance, has been reported to influence emotional experiences in the first REM-periods of the night.\textsuperscript{3} Reported effects of emotion and of pre-sleep mood and stress on sleep include: decreased dream recall and elevated awakening thresholds from REM-sleep,\textsuperscript{4} increased or decreased latency to REM-sleep, increased REM-density, REM-sleep duration,\textsuperscript{5} occurrence of arousals in sleep as a marker of sleep disruption\textsuperscript{6} as well as disturbances in sleep continuity.
Acute stress

In some studies, investigating the effects of especially acute stress exposure on sleep in healthy persons found that REM-sleep alterations are more frequent than nonREM-alterations. For instance, in a study of Germain and others,7 they found that acute stress exposure where subjects had been told that they had to give a speech in the morning and that their performance would be evaluated, resulted in an increase in REM-density across REM-periods, a decrease in late-night average REM-count and a slower rate of increase across successive REM-periods immediately after the stress exposure. The result that the average REM-density increased is in line with some previous studies on the effects of acute stress exposure.8,9 However, in other studies, acute stress exposure has been associated inconsistently with increased percentage of REM-density and REM-sleep duration10,11 or alterations within REM- or nonREM-sleep. Hall and coworkers12 correctly claim that the pathways in which stress affects sleep and produces frequent awakenings from sleep, lightens nonREM-sleep, or affects the quantitative and qualitative components of REM-sleep are not as well defined. In the case of clinical disorders subsequent to the experience of a traumatic life event, such as posttraumatic stress disorder, also only a few studies investigated posttraumatic stress disorder directly after the traumatic life event. In one such study investigating three patients hospitalized for acute combat fatigue, sleep was fragmented, of short duration and characterized by high motoric reactivity. REM-sleep had been found to be rare and short.13

Transient or chronic stress

REM-sleep alterations also have been found in people undergoing transient or chronic life events with and without comorbid depression.14 With depression, a prolonged duration of the first REM-period, an increased density of eye movements, REM-percentage, and total sleep time have been reported.13,14 Also, in suicide-attempters, an increase in REM-activity and REM-sleep duration over the entire night and in the first REM-sleep period have been found.15 These abnormalities in patients with depression in the first nonREM/REM-sleep cycle16 have been related to the dysfunctions in the emotional and cognitive processing in clinical disorders such as depression.17 Also, a reduced REM-sleep latency has been identified as an objective indicator of depressive disorder and suicide.18 Furthermore, increased risk for relapse in depressed persons and in alcoholics has been found to be related to increased REM-density.8,19 Furthermore, at pre- and post-treatment psychotherapy, affect intensity in depressed men has been correlated significantly and positively with phasic REM-sleep measures, characterized by REM-bursts.17,20 A decrease in REM-density, on the other hand, has been correlated with remission with therapy and reductions in negative affect intensity in depression.5,17,21 Phasic REM-sleep decreases over the course of psychotherapeutic treatment in depressed patients, in comparison with more tonic aspects of REM-sleep involving REM-sleep latency, wherein change may be a marker of manifestations of depression.21 In correspondence, failure to remit with psychotherapy in depressed persons has been correlated with increased REM-density.18

In summary, abundant evidence confirms a relationship between the emotional experiences we have during the day and changes in sleep physiology, in particular modified, enhanced or decreased REM-sleep.

Sleep and its impact on emotional well-being

Not only do daytime events affect sleep, the quality and amount of sleep also influences the way we react to these events and may be an important determinant in general well-being. A good night of rest seems to help us to feel good and to be able to cope with the emotional challenges of the next day, especially with emotionally painful events. Sleep seems restorative in daily functioning, whereas deprivation of sleep makes us particularly more sensitive to emotional and stressful stimuli and events. Even more, sleep seems to buffer the relationship between stress and negative affect. Probably, it plays a facilitating role in the processing and the regulation of emotional stress. As we discussed previously, REM-sleep in particular is affected by emotional events in daily life; the way sleep impacts next day mood/emotion is thought to be particularly affected via REM-sleep. REM-sleep appears to modulate our daily mood as well as to facilitate the integration of affective life events into long-term memory.18,22 As a consequence, sleep deprivation, and especially REM-sleep deprivation, has a strong impact on the way we process, consolidate and buffer our daily experiences. Globally, the effects of sleep deprivation have been described on different levels of functioning, especially on the cognitive (attention, memory), psychomotor or sensorimotor (balance) level of functioning and on the level of mood (irritability, dysphoria, maleaise).23,24 Focusing on the emotional effects, they also might be more obvious in daily life than the cognitive or motor effects. Of chronic sleep restriction and acute sleep deprivation in healthy individuals and animals. After a sleepless night or several sleepiness nights, the experiences of feeling drowsiness, awkwardness, getting irritated quickly and feeling down are a common phenomenon. As both phenomena negatively influence each other, a vicious dysfunctional, even psychopathological, circle might develop. Sleep disturbances not only restrict our daily happiness, but even may have a prognostic meaning in predicting mental well-being, emotional reactivity, adaptation to negative affect and the evolution of affective disorders. Without enough healthy sleep, negative emotional reactivity seems to be enhanced significantly and positive reactions to positive events often are subdued.25 Adaptation to stress induced by an emotionally arousing film not only influences sleep but has, as described before, also been found to be reduced after REM-deprived sleep compared with non-REM deprived or normal sleep.26 Enhanced signs of anxiety to stressful stimuli after deprivation of REM-sleep in comparison with non-REM-deprivation have been reported in healthy subjects after reviewing the film. The REM-deprived group was significantly more anxious after the second viewing of the film (autopsy) than the non-REM-deprived group. These findings were confirmed by Zohar et al.,25 who investigated the relationship between sleep loss and emotional reactivity in medical residents who were monitored for 5–7 days every 6 months over a two-year period. The results show that sleep loss not only intensified negative emotions, but even diminished positive emotions following a goal thwarting or goal enhancing event. Also, in animal studies, suppression of REM-sleep during the second and third week of postnatal development in rats using an antidepressant drug such as clomipramine or a hypertensive like clonidine, showed enhanced anxiety, decreased sexual activity and disturbed sleep among the neonatally REM-sleep deprived animals.27 As a consequence, the neonatal treated rats showed reductions in the cerebral cortex and brainstem in adulthood. Another study in which REM-sleep in rats was suppressed in a similar way as in the preceding study, the rats showed depressive symptoms like despair behaviour, reduced pleasure seeking and increased alcohol preference.28

Also, in studies with children and adolescents it has been shown that sleep deprivation increases depression, confusion, and anger,29 subjective feelings of frustration and irritability/agression.30 Even after two nights of sleep deprivation, a significant increase in psychopathology scores in particular have been found for somatic complaints, anxiety, depression and paranoia.31

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For depressive complaints, sleep deprivation was even associated with a mild increase in depressive thinking by including feelings of powerlessness, failure, worthlessness, inadequacy, lack of self-esteem and decreased life satisfaction. In line with these findings, social interpersonal functioning as investigated by Killgore and colleagues has been found affected. They found a significant decline in perceived emotional intelligence affecting three major areas of functioning, including intrapersonal awareness, interpersonal skills and stress management. In another study of this research group, sleep deprivation was associated with an increase of extrapunitive responses that reflected the tendency to direct blame or hostility towards people or objects in the environment. In other words, a decrease to accept blame for a frustrating circumstance was found.

However, while summarizing these effects of sleep on emotional functioning, a few opposing findings have been reported, too. Surprisingly, in a study of Wagner and coworkers, emotional reactivity was enhanced on (familiar) affective pictures following sleep during the late, REM-sleep rich part of the night in comparison with the effects of early sleep and wake periods. Wagner and coworkers suggested that the increased negative valence ratings of old pictures after late sleep suggest that REM-sleep enhances aversive reactivity towards these stimuli. After a total night of 7 h of sleep, the effect of increased emotional reactivity was even more enhanced, suggesting a cumulative effect of REM-sleep periods during early sleep and the longer REM-sleep periods during late sleep. They concluded that some findings confirm the relieving or cathartic effect of REM-sleep. Replication of these results, given most opposing results and thus confounding effects, is necessary. However, in line with these former research findings, are the effects of sleep deprivation on depression. Total or partial sleep deprivation, or selective restriction of REM-sleep in depression, showed that these acute sleep manipulations often lead to a temporary improvement in energy and mood with a regression towards depression after any subsequent sleep. The improvement of mood has been found even stronger in ‘evening types’ assessed by the Hamilton Depression Rating (HDR) Scale. In line with the discussed findings, it also has been found that sleep deprivation is followed by nights of increased REM-sleep and SWS (Slow Wave Sleep). This rebound effect suggests that a certain amount of these sleep stages is needed. Although the reason why it is necessary is still unclear, these findings nearly consistently let us assume that REM-sleep may have an adaptive emotion modulatory function, whereas in accordance with this function, deprivation of REM-sleep reduces this adaptive functioning.

**REM-dreaming as emotion modulatory function?**

Characteristic to emotional stress is that it may influence dreaming and dream content as has been shown after watching a stressful film shortly before sleep. Dream content includes a series of images, thoughts, affects, emotions and sensations. The emotional character of dream content leads to the question of whether it plays a role in the regulation or adaptation of emotion. Or, can we suggest that the dream is just another series of brain processes among others combining memories and experienced emotions? Several studies suggest an enhanced role of REM-sleep in more emotional processing tasks in comparison with non-REM-sleep. In a review, Payne & Nadel conclude that dream content varies as a function of sleep stage or time of night. Dreams seem to be more vivid and emotionally loaded during REM-sleep in comparison with dreaming in other sleep stages like NREM-dreaming where they have been found to be more of a thought-like cognitive nature. In REM-sleep, mentation has been found to be more expressive of motives and emotions, emotional vividness, intensity or complexity, which leads us to suggest a qualitative difference between REM and NREM mentation and processing, where REM-sleep has a more clear emotional dream-like character in comparison with NREM-dreaming. InQ research of Cartwright and coworkers, the role of daytime emotion in sleep and in REM-dream functioning has been investigated several times. For instance, they investigated people who divorced recently from a marital partner. Subjects were awakened in the sleep lab several minutes after REM-sleep onset for dream collection. Each participant was assessed for depression at baseline and at 1-year follow-up. Sleep was monitored for three nights at each assessment point. Dream characteristics appear to respond adaptively during life events, but delayed when subjects are depressed. One year later, 72% of the 39 participants classified as suffering from depression could be classified correctly as remitted or not remitted based on the presence of negative/unpleasant dreams during awakenings from REM-sleep at baseline. Subjects who were not depressed at the time of divorce or later on had few negative dreams throughout the night and subjects who were depressed at the time of divorce but were not one year later, had a higher percentage of negative dreams early in the night and less late at night. The direction of the relationship was that the more expression of negative affect in dream reports arising from REM-awakenings during the first half of the night, the less likely the person suffered from depression one year later.

In another study, Cartwright and coworkers did similar research on a non-depressed group of ‘normal’ students. Before and after each night of sleep, they filled out a mood scale. The second night they were awakened after several minutes of each REM-period and asked to report what they had been experiencing. The students who were more depressed showed better moods after dreaming. Even the content of dreaming was influenced by the presence of a negative mood before sleep. The dreams contained more negative affect and less positive affect early in the night, with the negative ones decreasing and the positive ones increasing. This effect could not be found when there was no negative mood before sleep. Cartwright and coworkers concluded that a depressive mood correlates with negative dream content and that the modulatory function of REM-sleep dreaming appears when a negative mood is moderate.

Similarly, in a study of Foulkes, he found that when subjects reported in a spontaneous way about their dreams there was a bias towards the recall of emotionally unpleasant, more dramatic, especially anxious loaded contents. On the other hand, in a study of Fosse et al., emotion in sleep was investigated by the use of instrumental awakenings. Subjects themselves had to score segments of their reports for the presence of emotions. Combining first-person ratings with instrumental awakenings from REM, they found more positive emotions (joy/elation) reported compared to negative emotions. The authors warned that this might reflect characteristics of the group. In contrast, other studies using this method of instrumental awakening reported more negative emotions such as anger and fear. Even when we take into account that dream reports are always given in a waking state and therefore are constrained by the actual state of the person as well as the cognitive and linguistic abilities of the individual, we notice in most studies a clear tendency towards reporting of negative emotions.

**Sleep and emotion on the neurophysiological level**

**Limbic system**

Emotion modulatory functions of sleep involves the limbic and extended limbic system. Sleep neuroimaging studies in humans have shown that neuronal activity in amygdala and anterior
paralimbic cortices, including the medial prefrontal cortex, varies across the sleep–wake cycle. Of particular relevance to the anatomy of REM-sleep are the forebrain structures that are essential to motivation and emotion-lateral hypothalamic- and limbic areas including the amygdaloid complex.\(^{45-47}\) In REM-sleep, enhanced activations have been found in the pontine tegmentum,thalamic nuclei, primary visual cortex, both amygdaloid complexes, hippocampal formation, anterior cingulate cortex and parietal operculum.\(^{46,48,49}\) Also, Payne and Nadef\(^{20}\) found activations in the amygdala and parahippocampal gyrus that may be related to dream generation during REM-sleep but did not find hippocampal activation, as Maquet and coworkers did. On the other hand, Braun et al.\(^{45}\) confirmed the findings of Maquet and coworkers of REM-related brainstem, limbic and paralimbic activations. In REM-sleep compared to delta NREM-sleep and to pre- and post-sleep waking, they showed relative activation of the pons, midbrain, anterior hypothalamus, the hippocampus, the caudate, the anterior cingu late, and medial prefrontal, caudal orbital, parahippocampal and inferior temporal cortices. Also, posterior cortices in temporoparietal areas are activated related to the visual character of dreaming. Hippocampal and parahippocampal areas, together with the occipital area, have been found to be more active during the processing of visual stimuli and the recall of images.\(^{50}\) Structures such as the medial temporal lobe especially the hippocampus, are involved in the formation of a temporally ordered retrieval storage for neocortically stored information. Integration of semantic explicit memory content as well as masked or unmasked more episodic autobiographical recollection in dream content may be mediated by a distributed fronto–temporo–parietal system.\(^{51}\) The right parietal operculum, which is activated during REM-sleep, can be related to spatial imagery active in the processing of situations and memories in dreaming.\(^{46}\) Hippocampus-independent declarative memories of lower emotional valence seem to rely on early nocturnal sleep when slow-wave sleep (SWS) prevails and cortisol release is minimal.\(^{52}\) Nonconscious nondeclarative memory such as procedural memory (i.e., knowing “how”), as well as implicit affective processing and learning within dreaming, seems to be less dependent on medial temporal lobe structures and more on sensorimotor and limbic regions such as the amygdala. The amygdala and the hippocampus are among the most active brain structures during REM-sleep, a condition which is likely to favor amygdala–hippocampal interactions compared to NREM-sleep. More amygdala-dependent emotional memory is supported by late sleep, when REM-sleep predominates. Emotion processing, emotion regulation and integration into memory not only involve the processing of emotional information during wakefulness, but especially reprocessing during the night. The mediotemporal and limbic system is known to influence these emotion processes night and day.

**Amygdala**

REM-related brain activation is rich in afferentation from the amygdala and those areas that are deactivated in REM-sleep are poor in afferentation.\(^{53}\) Activation of the amygdala varies across the sleep–wake cycle, with higher neuronal firing rates during wakefulness and REM-sleep compared to NREM-sleep.\(^{46}\) More specifically, in a recent fMRI-study\(^ {53}\) during phasic REM-periods, the thalamocortical network including limbic and para-hippocampal areas, is particularly active. The amygdala, deep inside the antero-inferior region of the temporal lobe, connects with the hippocampus, the septal nuclei, the prefrontal area and the medial dorsal nucleus of the thalamus. These connections make it possible for the amygdala, together with these other brain structures, to play an important role in assigning affective meaning and significance to experiential stimuli initiating emotional arousal and affective learning. Affective meaning initiates the handling and coping of demanding situations such as the cognitive control of stress and major affective processes. Although the amygdala clearly tends to respond to stimuli that predict threats or to threatening stimuli such as fearful or angry faces, a more general role is to modulate the organism’s overall state of vigilance, wakefulness and, in the face of ambiguous stimuli, to potentiate higher order cortical structures for subsequent information processing.\(^ {54}\) Due to this overall anatomical connectivity, the amygdala also is in a particularly good position to influence key regions involved in cardiovascular regulation like the hypothalamus and the parabrachial complex in the brainstem. More specifically, the central nucleus of the amygdala with afferent and efferent connections with the parabrachial area and dorsal raphe nuclei appears to be associated with activation of the area involved not only in emotional processing but also in the regulation of sleep and wakefulness. In particular, as discussed before, phasic REM-sleep has been considered as the EEG-variable influenced by day-to-day limbic changes in emotional state.\(^{2}\) Phasic REM-sleep ‘measured by REM-activity and REM-density’ is refined by the presence of phenomena correlated with ponto-geniculo-occipital spike activity. The REM-related activation of the primary visual cortex and the visual input from the retina provides neural evidence for the ponto-geniculo-occipital waves (PGO-waves) and a link between REM-sleep and dreaming. PGO-waves are related to sensory-motor integration, dreaming, learning and development of the visual system.\(^{55}\) Electrical stimulation of the central nucleus of the amygdala during REM-sleep has been found to increase PGO-wave amplitude, whereas stimulation during non-REM-sleep decreases PGO-wave frequency. The results indicate that the amygdala not only has a central role in emotion processing but also is involved in the modulating brainstem neural mechanisms underlying alertness during sleep and wakefulness.

**Cingulate cortex**

Among these limbic areas with their extensive connections with the amygdala, the anterior cingulate cortex active during REM-sleep generally functions as a mediator between acts of attention and emotion and affective consciousness. The anterior cingulate activity accompanies the representation and affective awareness of almost all stimuli. It contributes to the affective character and motivational salience of dreaming, expressed in the fictive actions during dreaming. Premotor areas of the anterior cingulate cortex might even integrate dream movement and emotion.\(^ {56}\) More specifically, the precuneus and midline cingulate regions appear to be connected functionally with all types of awareness of stimuli and reflective self-aware processing or self-related information processing across all sensory modalities. Related to this function, the hypoactivation of the precuneus, next to and traditionally considered as a totality with the posterior cingulate cortex adjacent to the medial parietal cortex, helps partly to explain why there is little access of episodic memories.\(^ {57}\) Together with the deactivation of the dorsolateral cortex, activation of the hippocampus, the right inferior parietal lobe—a brain region involved in spatial imagery construction and the processing of emotionally influenced memories in REM-sleep, we can speculate that the underactivation of the precuneus also explains the rather non-self-reflective character of dreaming, with only fragmented self-related episodic/autobiographical memory retrieval activation during sleep due to a global lack of directed self-reflective processes. Self-reflective processes and propositional representations of the experiences of the self in awareness or self-awareness not only require the posterior cingulate cortex but also higher executive processes.
requiring dorsolateral prefrontal involvement in particular, which is deactivated in REM-dreaming.

**Inferior parietal lobe**

Maquet et al. reported activation of the right parietal operculum during REM-sleep, despite general deactivation in much of the parietal cortex. The inferior parietal lobe may be involved in the visualization of a fictive situational dream space in the total experience of dreaming. It may have a role in various aspects of mental and spatial imagery like mental moving through a spatial contextual environment. Within dreaming, the individual falls together with his own actions while there is little or no space left for mental perspective taking. The deactivation of the temporoparietal junction may reflect diminished functioning of social perspective taking, in identifying the goals or intentions behind behaviors in particular as well as the switch between first and third person perspective and theory of mind (e.g.,). During REM-sleep, the low activation of the right temporoparietal junction may be related to a loosening of the distinction between first and third level perspectives. It is only in a retrograde dream report that the self can participate in the dream action both in a first-person (i.e., the self sees and acts) and in a third-person (i.e., the dreamer sees the self acting in the dream) perspective. Especially perspective-taking relevant social emotions such as jealousy, pride, embarrassment, infatuation, sexual love, shame, guilt and pride often are reported in dreaming.

**The (dorsolateral) prefrontal cortex**

The prefrontal lobes commonly are deemed to be the seat of the highest mental function, playing a prominent role in engendering higher levels of awareness. Interacting closely with other brain areas such as the amygdala, the parietal and cingulate cortex, the prefrontal cortex, especially medial regions, play a central role in the representations of the self, the processes of being aware of oneself and one’s perspectives in the world. The frontal lobes allow us self-regulation in function of our self-referential anticipation of future possibilities in the context of personal attributions, goals and aspirations. In REM-sleep, reflective thought and self-reflection anticipating future goals and situations seem to be absent or rather minimal. The reflective self permits us to be aware of oneself, opposed to the rather unknowing non-reflective experience of oneself during sleep and during dream activity. Also, in the selection of information entering consciousness and self-reflection, the organization of information awareness and memory and the searching after specific memories, as well as the initiation and the maintenance of higher intentional behaviors, the executive capacities of the prefrontal cortex and the dorsolateral prefrontal cortex in particular are of major importance. During REM-sleep, activity in the dorsolateral prefrontal cortex and locus coeruleus drops to the lowest levels of the day, as a consequence, the feedback these areas normally give is disenabled. The dorsolateral frontal cortex receives input from the motor cortex as well as from the multimodal sensory convergence areas of the parietal and temporal lobes. Within sleep and dreaming, it seems as if there is no clear selective information process entering in awareness that might be served by the dorsolateral prefrontal cortex, whereas the caudal dorsal cortex is more involved in visual control and the ventral and rostral prefrontal cortex in episodic control (e.g., the selection of information according to events that occurred in the past). In a state of being awake, the dorsolateral cortex can evaluate and regulate information from the affective-somatic sensory system to the motor cortex to increase a response, whereas during sleep due to its inactivity, there is a relative lack of intentional and coherent movement. In particular, in REM-sleep, the deactivation of the anterior prefrontal areas and of the dorsolateral prefrontal cortex may explain the little notion of directed and relevant goal-oriented behavior or self-regulation and the loss of working memory and logic reasoning. During dreaming, the sequence of dream events cannot be controlled. Sleep especially is characterized by the lack of own intentional instrumental behavior or retrieval of clear or intact episodic memories. The retrieval of episodic information, for instance, is dependent on a proper functioning of the (dorsolateral) prefrontal cortex and several other related brain structures like the medial temporal area. As a consequence, some fragments or aspects of memories as residues are noticeable in dreaming through the activation of the medial temporal lobes, but do not result in an exact realistic unfolding of an autobiographical event with an episodic character in time and context. Due to its important general control functioning, deactivation of the prefrontal cortex also explains the destructive effects of sleep deprivation. Prefrontal cortex activation is reduced significantly even after 24 h of continuous wakefulness. Accompanied by decreased prefrontal activation is the decrease in prefrontal related functions. As we discussed before, sleep deprivation results in dysfunctional prefrontal top–down processing and control. A night of sleep deprivation decreases performance on neuropsychological tasks subserved by the prefrontal cortex. However, other studies did not confirm these deficits in executive function following one night’s sleep deprivation, which may be due to their adaptation on a normal sleep deprived state of living. As illustrated previously, lack of sleep inappropriately modulates the human emotional brain response to negative aversive stimuli. Prefrontal regions usually are held to comprise central components of the highest order control and modulatory system for emotion. They contribute to reality monitoring and top-down levels of control, which explains the loss of reality and onological character of dreams. We hypothesize that the diminished prefrontal control may enable the sleeping brain to increase significantly the adaptive and necessary processing of emotions related to ongoing or unfinished negative life experiences. We suggest that the relatively “non-disturbed” affective “working through” of emotional information, not only during daytime but also during the night, might be possibly more adaptive in facilitating especially painful emotional processing and stress regulation (cf. Vandekerckhove, Houthuys, Weiss, De Valck, Cluydts et al. in preparation).

Furthermore, during REM-sleep we notice reactivation in other important emotion regulation areas such as the caudal orbital and medial prefrontal area. With the onset of REM-sleep, accompanied with continued deactivation of anterior and lateral portions of the prefrontal cortex, posterior prefrontal areas and parts of the ventromedial, limbic-related prefrontal cortex and closely associated the medial subcortex and cortex, have been found reactivated sometimes to levels that exceed those of waking.

**Ventromedial prefrontal cortex**

There have been only a few studies that focused on the relationship between the human ventromedial prefrontal cortex and natural sleep, especially REM-sleep. The ventromedial prefrontal cortex consists primarily of the orbitofrontal cortex and the anterior cingulate cortex, and also is known as the ‘limbic’ cortex important in decision making and social judgment. In particular, the orbitofrontal cortex enables the more complex “higher order” abstract processing of the neocortex to be integrated with the “lower order” somatic and emotional functions of the deeper structures, integrating input from the limbic area and the cortex. This area receives input from different sensory modalities whereby pathways between the amygdala and the orbitofrontal cortex may
serve to place sensory and affective stimuli in the appropriate context for action. The orbitofrontal cortex controls the sympathetic and parasympathetic branches of the autonomic nervous system and thus cardiac and respiratory responses in emotional and stressful situations in dream-sleep. In correspondence and in daily life, especially with the assistance of other prefrontal- as well as limbic functions, it has an important function in social knowl-
edge on how to behave, the selection of appropriate behavior and emotional, social and interpersonal self-regulation. During sleep, especially REM-sleep rather than NREM-sleep, together with the amygdala and the anterior cingulate cortex, the orbitofrontal cortex is active in emotional and social processing in particular, which may explain the adaptive functioning of these areas in a more “free and unlimited” processing of especially social and emotional events that happened during the day characterized by the overwhelming emotional character of many dreams.

Speechless limbic functioning during REM-sleep adaptive in the coping with the continuous stream of emotional life-events?

Alterations in daily life events and also in emotional and cognitive processing during wakefulness, such as the experience of an emotional event or depressive functioning, becomes expressed in sleep, especially in REM-sleep. In correspondence, deactivation of the prefrontal cortex not only has been found in REM-sleep, but also has been found consistently in psychopathological states such as depression and posttraumatic stress disorder. In the extreme case, without specific prefrontal feedback regarding the level of threat, the organism is locked in an amygdala-driven response state longer than necessary and may activate overwhelming stressful emotional responses associated with enhanced levels of stress hormones. Overwhelming emotions or apparently uncontrollable situations within dreaming, immersed with driving feelings as fear and anxiety are satisfied by idiosyncratic dreaming plots, may be the result. What happens during dreaming can thus be compared to some extent with a posttraumatic stress disorder where a negative correlation between amygdala and prefrontal activation in responses to fearful versus happy faces has been found. In other words, in anxiety disorders such as posttraumatic stress disorder depression, similarly as in sleep, we also notice an enhanced emotional processing and thus an increased activation of the amygdala with a low activation of the prefrontal area involved in the modulation and inhibition of the amygdala. The amygdala and prefrontal cortex are neurological correlates of emotional disorders influencing the regulation and expression of REM- and NREM-sleep. A hyperactive limbic activation in combination with a hypo-
activation of the prefrontal area may cause or sustain increased affective processing. Diminished capacity of the regulatory function of the dorsolateral cortex may result in irrational behavior, like disinhibition of affect and behavior. During dreaming, similarly to the processes during posttraumatic stress disorder in wakefulness, the processed information may be organized and follow some still unknown logic, where the brain combines certain aspects of life by inhibiting some and selecting others, resulting in an under- or overrepresentation of certain themes and emotions.

However, activated patterns of brain area in affect-related disorders such as PTSD, are only partly similar to the patterns of active brain area in REM-sleep. In REM-sleep we see at the onset of REM-sleep, for instance, a reactivation of the medial prefrontal area which is deactivated in PTSD or anxiety disorders. This reactivation in REM-sleep is probably functional in the regulatory and modula-

atory function of REM-sleep. Generally speaking, the engagement of the amygdala and the cingulate cortex in the emotion regulation of painful information during the day or during sleep becomes especially modulated and regulated by the medial prefrontal cortex while it exerts a top-down regulatory function of amygdala functioning. The activation of the amygdala, the anterior cingulate cortex, the superior parietal cortex, the superior and medial prefrontal cortex have, as we suggest, an adaptive and healthy role in emotion modulatory and regulatory functions, processing and integrating traumatic and other distressing emotions and memo-
ries in REM-sleep.

During REM-sleep relative to emotional disorders in waking time, there is a diminished functioning of the working memory and executive function circuit combined with an enhanced adaptive functioning of networks subserving emotional and memory consolidation processes necessary to cope with the events we meet during daily life. In line with these findings, dreaming may be functional to process averse experiences such as traumatic expe-
iences, presented under strange images and fragmented episodes of related or similar stories. REM-sleep and dreaming functions are a crucial phase of the masked or unmasked reactivation and reprocessing of emotions and emotional occurrences during the day.

Even more, REM-sleep has been assumed to have a role in integrating traumatic and other disturbing memories into memory. Overnight improvement of memory is specifically sleep and time dependent and correlates positively with the amount of both early-night SWS- and late-night REM-sleep. Vividness and emotionality also are strong determinants within the integra-
tion of memories into long-term memory and subsequent recall.

Not only emotional and other kinds of information become consolidated in memory during sleep but, as we discussed in the beginning, sleep also becomes changed by events that happened before sleeping. This might lead to an increase in REM-sleep, sleep spindle density, etc. As we discussed previously, not only the representation of emotional events becomes changed but also the architecture of subsequent sleep stages. It promotes the reactivation of neural ensembles during subsequent sleep. Changes in motivation and emotion are prominent aspects in mood disorders related with alterations in limbic processing not only in daytime, but also during REM-sleep. Every reprocessing in dreaming, such as the reconsoli-
dation of negative stressful events visually appearing in conversions or transformations of what has happened in the day, may be func-
tional to integrate negative experiences into long-term memory and may help us to be prepared for future negative experiences.

Even when we consider some opposing findings (e.g., Wagner and colleagues), it appears that the dream-production especially in REM-sleep that contains vivid simulations of painful and threat-
ening events within real life, facilitates the processing of distressing emotions. Earlier REM-sleep onset and higher dream activity in the initial REM-period even has been found to predict a greater reduction of depressive symptoms after a distressing life event. It aids the processing of negative information, making averse events bearable. In particular, intensification of phasic REM-sleep appears to be a marker of dysfunctional or too little emotion regulation during the day, indicating the need for further emotion processing and emotion regulation during sleep. REM-sleep after stress may function as a regulatory mechanism of waking emotional arousal. Also, increased phasic REM-sleep in persons suffering from stress possibly may reflect an incapacity to down-regulate experienced emotional arousal during sleep or during the day.

As a consequence, the adaptive influence of REM-sleep on the regulation of emotion appears to be reduced after REM-sleep deprivation in comparison with non-REM-deprived or undisturbed sleep. Sleep deprivation interferes with the processing and inte-
gation of negative information such as painful life events into memory, affecting psychological well-being and health. It changes the metabolic activity within several crucial affect-regulating areas of the brain like the medial prefrontal cortex. Without enough
healthy sleep, negative emotional reactivity seems to be enhanced significantly and positive reactions to positive events often are subdued. The discussed studies of Killgore and coworkers even suggest that sleep deprivation diminishes moral behavior, responsible behavior, interpersonal skills and inventiveness. As we discussed before, sleep disturbances not only restrict our daily well-being and social functioning, but even may have a prognostic meaning in the evolution of affective disorders like depression.

In longer periods of sleep deprivation, the brain has more difficulties processing emotionally stressful and complex social events in an adaptive way. As sleep or REM-sleep serve the modulation of emotional and motivational drives, making the individual more adaptively flexible during wakefulness, REM-deprivation may lead to increased excitation in many brain structures, resulting in enhanced emotional and drive-motivated behavior. For instance, morning mood improves when REM-sleep is intact but worsens after a night of sleep deprivation. After deprivation of sleep, the normal regulation of the amygdala fails. Increased activation of the amygdala and a loss of functional connectivity with the medial prefrontal cortex occur. Sleep deprivation is characterized by an increased attention and reactivity towards aversive emotional information. Together with the decrease in prefrontal activation, emotion regulatory functions become dysfunctional. A night of sleep may therefore repair adaptive processing and functional brain activity and the integrity of the medial prefrontal cortex-amygdala connections. Although we notice the negative effects of sleep deprivation in healthy subjects, positive effects of REM-deprivation on depression questions the therapeutic function of REM-sleep. In line with Cartwright et al., there might be a floor and a ceiling effect. As a consequence of the positive effect of REM-sleep deprivation on depression, REM-sleep should be functional on specific and relatively normal grades of negative affect. The more direct positive regulating effect of REM-sleep occurs in normal levels of negative mood and not when higher levels of negative emotion should be regulated. In major depression, a higher amount of REM-sleep, poor sleep efficiency, and reduced amounts of delta sleep have been reported. Also, dream affect is more negative. Cartwright et al. suggest that the loss of these unpleasant dreams and the reduction of eventual ‘dysfunctional’ REM-sleep might account for the positive effect of REM-deprivation, whereas a longer deprivation of REM-sleep followed by a night of sleep intensifies REM-sleep and dream affect. This effect of ‘rebound’ may reflect the adaptive function of REM-sleep as ‘processing through,’ which may explain this mood improvement in depression. Another possible explanation is that REM-sleep-deprivation alleviates clinical depression because it mimics selective reuptake inhibitors (SSRI) that should be linked with increased brain derived neurotrophic factors (BDNF) in major depression.

In summary, these data suggest an amplified, hyperlimbic response by limbic area to negative emotional information under conditions of REM-sleep as well as in sleep or REM-deprivation. Furthermore, this increased magnitude of limbic activity is associated with a loss of functional connectivity with the dorsolateral prefrontal cortex and ventromedial prefrontal cortex during the day, suggesting a failure of top-down, prefrontal control which, in the case of REM-sleep deprivation, becomes repaired after a night of normal sleep. During sleep, the ventromedial prefrontal area becomes reactivated, which in combination with enhanced limbic functioning, explains the influence of REM-sleep, especially in emotion modulatory functions and on the integration of emotional events in sleep. Considering the discussed findings, we noticed an enhanced effective emotional adjustment and amelioration of mood and well-being after intact sleep, especially REM-sleep.

In other words, good sleep may work as a biobehavioral regulatory and restorative process regulating daily emotional experiences and allostatic loads of emotional stress.

### Practice points

Research findings confirm our own experiences in life where daytime events and especially emotionally stressful events have an impact on sleep quality and well-being:

1. Daytime emotional stress has an effect on sleep physiology by elevated awakening thresholds from REM-sleep, increased or decreased latency to REM-sleep, increased REM-density, REM-sleep duration and the occurrence of arousals in sleep as a marker of sleep disruption.
2. Daytime emotional stress affects dream patterns, dream content and the emotion within a dream as well as decreased dream recall, although its exact role still is unclear.
3. Not only do daytime events affect sleep, the quality and amount of sleep also influences the way we react to these events and may be an important determinant in general well-being.
4. Sleep seems restorative in daily functioning, whereas deprivation of sleep in opposition makes us particularly more sensitive to emotional and stressful stimuli and events.
5. The impact of sleep on next day mood/emotion is thought to be particularly affected via REM-sleep.
6. In REM-sleep, a hyperlimbic and hypoactive dorsolateral prefrontal functioning and a normal functioning of the medial prefrontal cortex may explain its adaptive role in the coping with the continuous stream of emotional events we experience.

### Research agenda

Experimental research is needed to explore the exact role of sleep and its different stages in emotional processing, emotional learning and emotion regulation.

Neurophysiological research is needed on the role of the amygdala, the anterior cingulate cortex and orbitofrontal cortex in sleep in the processing of emotion and painful life events.

### References


* The most important references are denoted by an asterisk.


