Physiological Basics of Healthy and Disturbed Sleep

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In contrast to wakefulness, sleep is characterized by very low motor activity and responsiveness. Body functions and hormone secretion are modulated during sleep. Core body temperature and cortisol secretion are markers of the endogenous rhythm that is synchronized by the suprachiasmatic nucleus with the 24-h-day rhythm. The change of sleep and wakefulness is controlled by a homeostatic and a circadian process (approximately 24 h) and the change between REM and non-REM sleep by an ultradian process (<24 h). The importance of sleep for physical and mental recuperation, thermoregulation, the immune system, memory consolidation, and ontogenesis is discussed. In healthy sleepers, non-REM sleep (N1, N2, N3), REM sleep (R), and wakefulness (W) are distinguished based on EEG, EOG, and submental EMG. In the third version of the *International Classification of Sleep Disorders* (ICSD-3, 2014), seven main groups are differentiated.

1.1 History of Sleep Medicine

Since humans have started thinking about themselves and their lives, they have also reflected upon sleep and dreaming. For a long time, sleep was considered to be a passive and inactive condition. In Greek mythology, this idea was personified by Hypnos, the god of sleep, who had a close relationship to his twin brother Thanatos, the god of death. Passiveness and inactivity were also included in the Proto-Germanic origin of the word "sleep" (or "schlafen" in German), which originally had the meaning of becoming relaxed ("schlaff/schlapp werden").

In ancient times, Aristotle, and later Galen, assumed that sleep was caused by changes in the brain, such as thickening of the blood. They interpreted the role of sleep as restoration of the brain and for regeneration of mental perceptiveness as well as internal heat. In later times, medical research on the context of sleep was based only on ancient manuscripts and their interpretation.

Only in the second half of the nineteenth century was sleep investigated with an experimental approach. In 1863, Kohlschütter was the first who tried to assess the waking level at different phases of sleep by applying acoustic stimuli of various volumes. In this way, he wished to determine the depth of sleep. The experiments performed by Jouvet and by Moruzzi and Magoun in the first half of the twentieth century showed sleep to be a highly active process of the human brain.

In 1929, the psychiatrist Hans Berger published his invention of electroencephalography (EEG), which allowed measuring brain electrical activity at the intact skin in the waking state as well as during sleep. A first classification of sleep in different stages was performed by Loomis in 1937 based on EEG. With the detection of rapid eye movements (REM) in 1953 by Aserinsky and Kleitman, it was possible for the first time to describe REM sleep.

Based on EEG, electrooculography (EOG), and electromyography (EMG), a group of experts with Rechtschaffen and Kales published criteria for the evaluation of sleep stages in humans. However, these criteria were based exclusively on the examinations of healthy individuals and could not always be suitably applied into the sleep disorders that were increasingly described in the following years. This situation only changed with the publication of the new standards of the American Academy of Sleep Medicine (AASM) in 2007, which were revised several times in some aspects until today.

1.2 Classification of Sleep Disorders

The possibility to register many biosignals during sleep completed the merely subjective description of the symptoms of sleep disorders by the patient or an observer. Sleep disorders could be characterized, defined, and differentiated more precisely. In the past decades, this was the basis of developing different classifications of sleep disorders.

In a first classification, in 1979 sleep disorders were differentiated only based on the predominant symptoms into these:

- Disorders of initiating and maintaining sleep (insomnias)
- Disorders with excessive sleepiness (hypersomnias)
- Disorders of the sleep–wake rhythm
- Disorders in relationship with sleep, sleep stages, or partial awakening (parasomnias)

In 1990, a classification based on the etiopathogenesis of sleep disorders was published

(*International Classification of Sleep Disorders*, ICSD), which differentiated:

- Disorders regarding the quantity, quality, or the time of sleep (dyssomnias)
- Parasomnias
- Disorders related to physical or psychiatric diseases
- Proposed sleep disorders

Dyssomnias were classified into these categories:

- Intrinsic sleep disorders (e.g., narcolepsy; see ▶ Chap. 5)
- Extrinsic sleep disorders (e.g., environment-related sleep disorders; see ▶ Chap. 9)
- Circadian rhythm sleep disorders (e.g., advanced sleep phase syndrome; see ▶ Chap. 6)

In most cases, the diagnosis required polysomnography (PSG) (see ▶ Sect. 2.6), which made it impossible to assign a complained sleep disorder to one of the four main groups based only on the symptoms.

In 2005, the American Academy of Sleep Medicine (AASM) published the second version of the *International Classification of Sleep Disorders* (ICSD-2), which was revised in 2014 (ICSD-3). ICSD-2 and ICSD-3 not only included new findings about sleep disorders and thus specified the diagnoses, but in some aspects returned to a phenomenological classification, as is elucidated in the following overview of ICSD-3.

Main Groups of Sleep Disorders According to the American Academy of Sleep Medicine (AASM) from 2014

- Insomnias
- Sleep-related breathing disorders
- Hypersomnias of central origin
- Circadian rhythm sleep–wake disorders
- Parasomnias
- Sleep-related movement disorders
- Other sleep disorders

Sleep-related organic and neurological disorders are listed in an appendix.

The outline of the present manual and the mentioned diagnostic criteria of sleep disorders follow the ICSD-3.

Practical Tip

The current classification of sleep disorders (ICSD-3) consists of seven main groups. The disorders were classified according to etiological and also phenomenological aspects as far as possible. The main groups were completed by explicitly sleep-related organic and neurological disorders. Sleep disorders observed in the context of organic or psychiatric diseases are not described separately.

1.3 Phenomenology of Sleep

According to the criteria of the AASM of 2020, four different stages of sleep and wakefulness (◘ Fig. 1.1) can be defined as of the age of 2 to 6 months (see also ▶ Chap. 11, Sleep disorders in children). Their properties with regard to EEG, EOG, and EMG are partly different in children and adults (◘ Table 1.1). Sleep is divided into epochs of 30 s that are assigned to the stages based on the following criteria:

- *Sleep stage N1* (◘ Fig. 1.2) describes the transition from wakefulness to sleep, that is, a kind of dozing.
- *Sleep stage N2* (◘ Fig. 1.3) describes stable sleep.
- *Sleep stage N3* (◘ Fig. 1.4) is deep sleep.
- *Sleep stage R* (◘ Fig. 1.5), REM sleep, is often called—even if it is not really correct—the dream sleep phase or also paradoxical sleep. In this stage, the most intensive dreams take place (see ▶ Sect. 1.8); when awakened in this phase, people often remember the contents of their dreams. Furthermore, despite high EEG activity, which is similar to stage N1 or W, the arousal threshold is paradoxically highest.

The percentage of the sleep stages N1 and N2 in the entirety of the sleep of an adult healthy sleeper, about 30 years old, amounts to about 55–60%. The deep, or also slow-wave, sleep is described by sleep stage N3; its percentage is about 15–25%. REM sleep generally encompasses 20–25% of the total sleep time. The percentage of wakefulness is typically less than 5% of the sleep period.

The sequence of the single sleep stages results in a profile, the so-called *hypnogram*. The

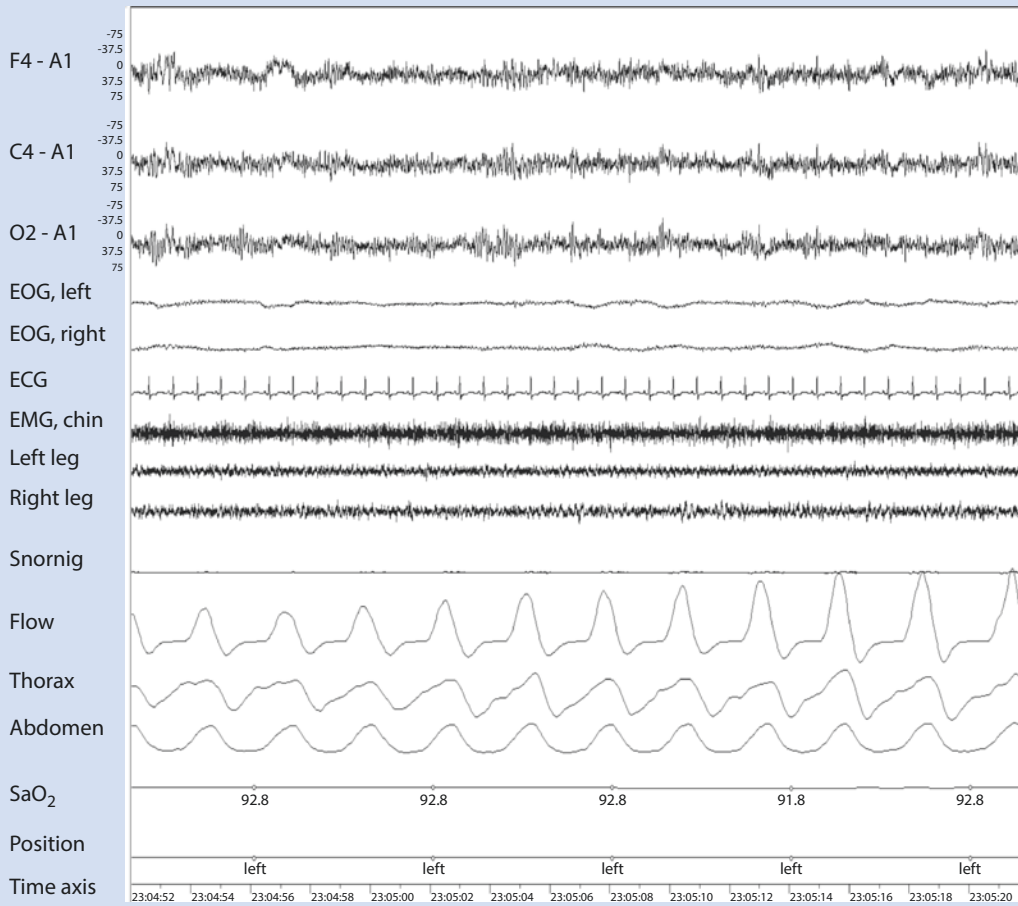

Fig. 1.1 Typical stage of wakefulness within a 30-s epoch of polysomnography in a 40-year-old male individual. In the EEG, an alpha rhythm is found with a frequency of 8–12 Hz. In the second half of the epoch, the EOG reveals low-amplitude, slow eye movements

sequence of sleep stages reveals a characteristic pattern over the sleep period. The first sleep cycle starts with superficial sleep (N1) after falling asleep, followed by stable sleep (N2) and deep sleep (N3). Finally, REM sleep can be observed, which completes every sleep cycle. Each sleep cycle has a duration of about 90 to 110 min. Depending on the duration of sleep and interindividual variance four to seven sleep cycles can be observed in healthy sleepers. The amount of deep sleep decreases with the number of sleep cycles within a sleep period, and the percentage of REM sleep increases continuously (Fig. 1.6).

The duration of the nighttime sleep period is intraindividually rather stable; however, in the interindividual context, the durations may vary greatly and are influenced by several factors.

Newborns (see ▶ Sect. 11.1) sleep for about 16 h, distributed over four or five sleep phases; about half the sleep time is REM sleep (so-called polyphasic sleep pattern).

In prepubertal schoolchildren, generally day sleep or a power nap is no longer observed, and the night sleep amounts to approximately 10 to 11 h (so-called monophasic sleep pattern). REM sleep is now reduced to less than 35% of the total (see ▶ Chap. 11).

In later ages, again increasingly polyphasic sleep patterns are found, although the total sleep time over 24 h neither increases nor decreases. Besides the increase of organic and psychic diseases (see ▶ Chap. 10), in particular the loss of social factors determining a rhythm (e.g., work, children) and the reduction of the endogenous rhythm (see ▶ Sect. 1.5) are responsible. Generally,

Table 1.1 Characteristics of the sleep stages in adults according to the American Academy of Sleep Medicine (AASM) scoring manual (V2.6 2020)

Stage	EEG	EOG	EMG
W	Dominating alpha and beta activity	Eyeblinks, rapid eye movements, sometimes even slow, partly rolling eye movements at the transition to N1	High tone, movement artifacts
N1	Theta activity (vertex spikes)	Slow, partly rolling eye movements	Reduction of muscle tone (<W)
N2	Theta activity, K complexes, sleep spindles	No eye movements, EEG artifacts, sometimes even slow, partly rolling eye movements at the transition from N1	Reduction of muscle tone (<N1)
N3	Delta waves <2 Hz (slow waves): >20%	No eye movements, EEG artifacts	Reduction of muscle tone (<N2)
R	Theta (also slow alpha) activity, sawtooth waves	Conjugated, rapid eye movements (REM)	Lowest muscle tone (≤N3), partly phasic activation

W wake, *R* REM (rapid eye movements)
Only stage W and N1 are differently defined in children (► Chap. 11)

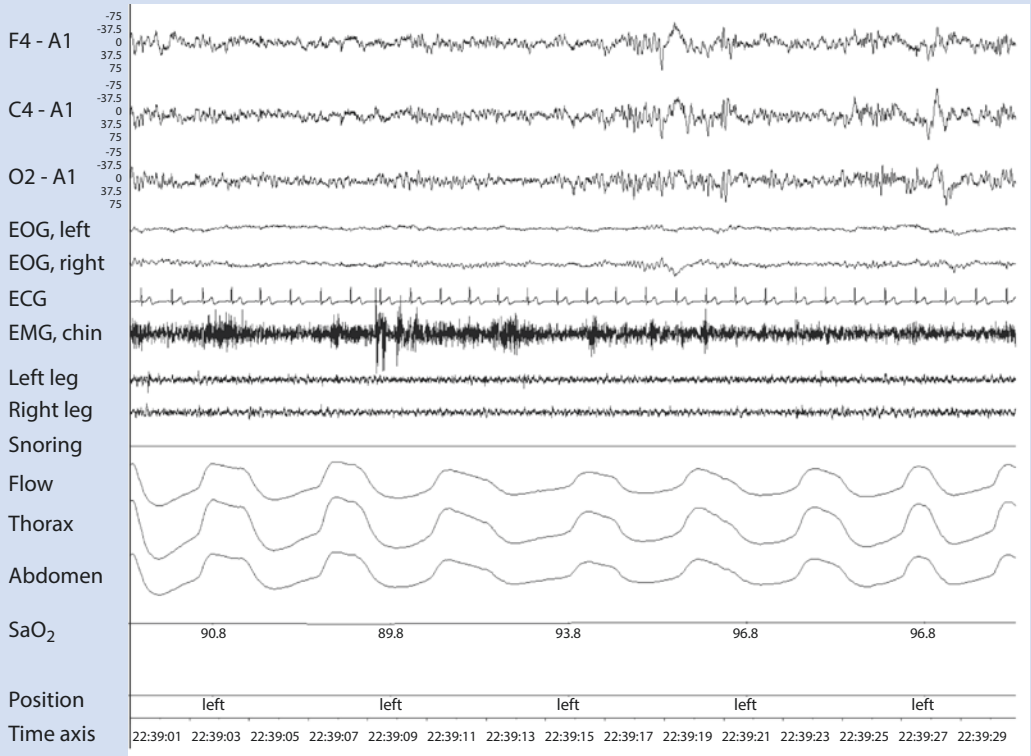

Fig. 1.2 Typical stage N1 within a 30-s epoch of polysomnography in a 40-year-old man. In the EEG, predominantly a theta rhythm (low amplitude, mixed frequency) is found with a frequency between 3 and 7 Hz. In the second half of the epoch, an abortive sleep spindle is seen that does not lead to the assignment of N2 because of its phenomenology, but in particular because of its occurrence in the second half of the epoch

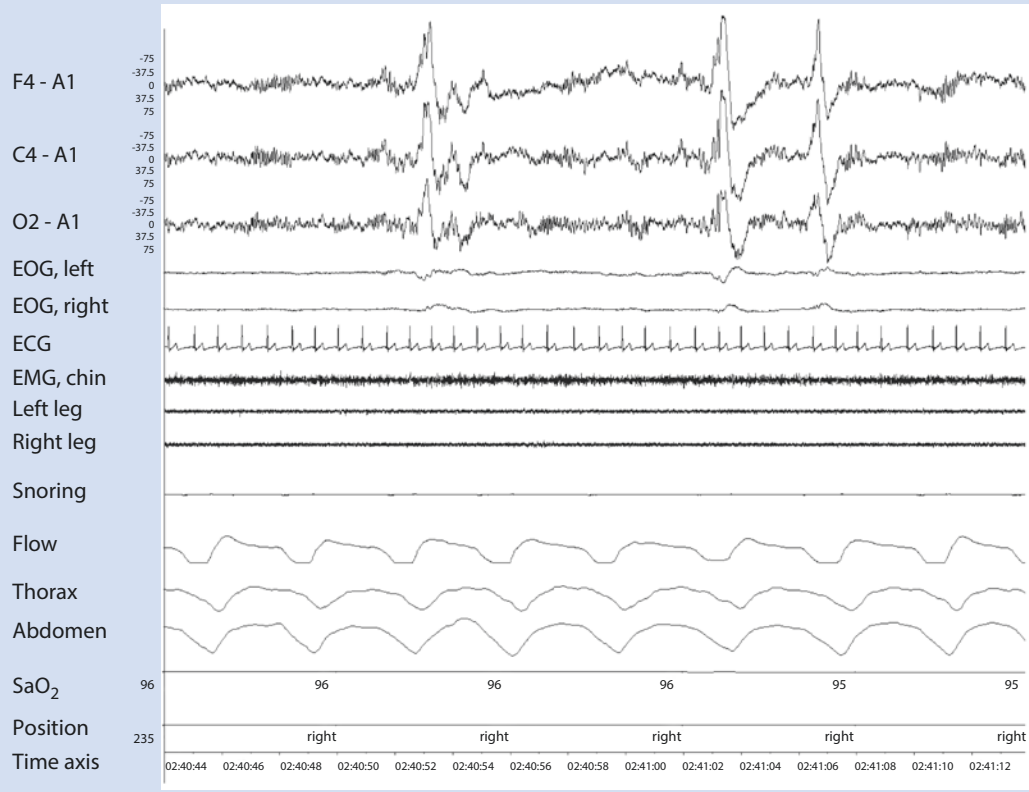

Fig. 1.3 Typical stage N2 within a 30-s epoch of polysomnography in a 40-year-old man. The EEG is similar to that of stage 1 (theta rhythm with low amplitude and mixed frequency); additionally, sleep spindles can be observed with a typical frequency between 12 and 14 Hz (maximum, 11–16 Hz) and K complexes

a sleep duration between 7 and 9 h is considered as healthy. Variations in duration of sleep between 4 and 12 h, however, can be observed, and there is no reason to directly classify them as pathological.

Correlations between duration of sleep and life expectancy are discussed, but because of the methodical limitations of single studies, no clear statements can be given. There are hints that an average duration of sleep of more than 9 or less than 6 h is associated with a slightly reduced life expectancy. However, it must be taken into account that the average genetic sleep quantity was taken as the basis for the risk estimation in those studies. According to this assumption, deviations of more than 1–2 h from the individually genetic sleep quantity would have to be evaluated as pathological.

For the assessment of sufficient sleep quantity at night, it is less the absolute quantity that is decisive but rather the alertness of the individual during the day.

1.4 Physiological Alterations During Sleep

Times of rest and activity alternate cyclically in nearly all creatures. Conditions of rest similar to sleep are already found in the lower vertebrates, although sleep with clear REM and non-REM phases is only found in birds and mammals.

Sleep is a particularly intense phase of rest with high vulnerability, such that its evolutionary advantages must have been highly superior to the disadvantages. In contrast to wakefulness, it is characterized by a nearly nonexistent motor activity and a very low responsiveness to internal as well as external stimuli. On the other hand, it is a complex, highly active condition, which is seen in the determined sequence of non-REM and REM sleep with its partly high neuronal activity and modulation of nearly all body functions during sleep. If sleep is interrupted, consciousness and

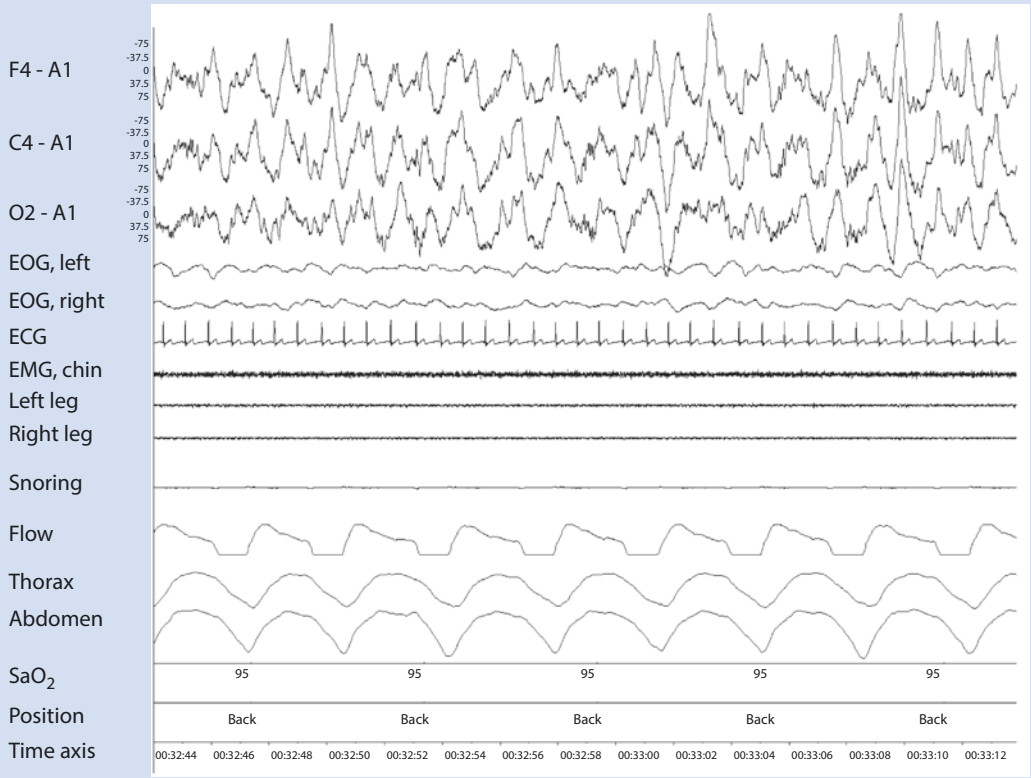

Fig. 1.4 Typical stage N3 (deep sleep) within a 30-s epoch of polysomnography in a 40-year-old man. In the EEG, delta waves are found in more than 20% with frequencies between 0.5 and 2 Hz (slow waves)

body functions return completely to the level of normal wakefulness within a very short time. However, sleep is subjectively only perceived when it lasts for 10 to 20 min without interruption, that is, without significant awakening or arousal (see ▶ Sect. 2.7.2.2).

Practical Tip

Based on motor activation, electric brain activity, cerebral neurotransmitter activity, and autonomous activity, three conditions can be differentiated: wakefulness, non-REM sleep, and REM sleep.

- Wakefulness is characterized by a high motor and cortical activation.
- During non-REM sleep, motor and cortical activation are greatly reduced.
- During REM sleep, minimal motor activation is associated with a high cortical activity.

Manifold physiological changes during sleep generally concern all functional systems (Table 1.2). Although many of those alterations have already been described in detail, very little is understood regarding pathogenetic processes. During non-REM sleep, anabolic processes are enhanced compared to wakefulness; especially, the inexact regulation of many body functions during REM sleep is apparent compared to non-REM sleep. The changes of the cardiovascular system, thermoregulation, and hormone secretion are specifically elucidated. Regarding changes in breathing, see ▶ Sect. 4.1.

1.4.1 Cardiovascular System During Sleep

Naturally, people sleep in a lying position. The increased venous backflow from peripheral vessels leads to increased filling of the right atrium and thus increased right ventricular stroke vol-

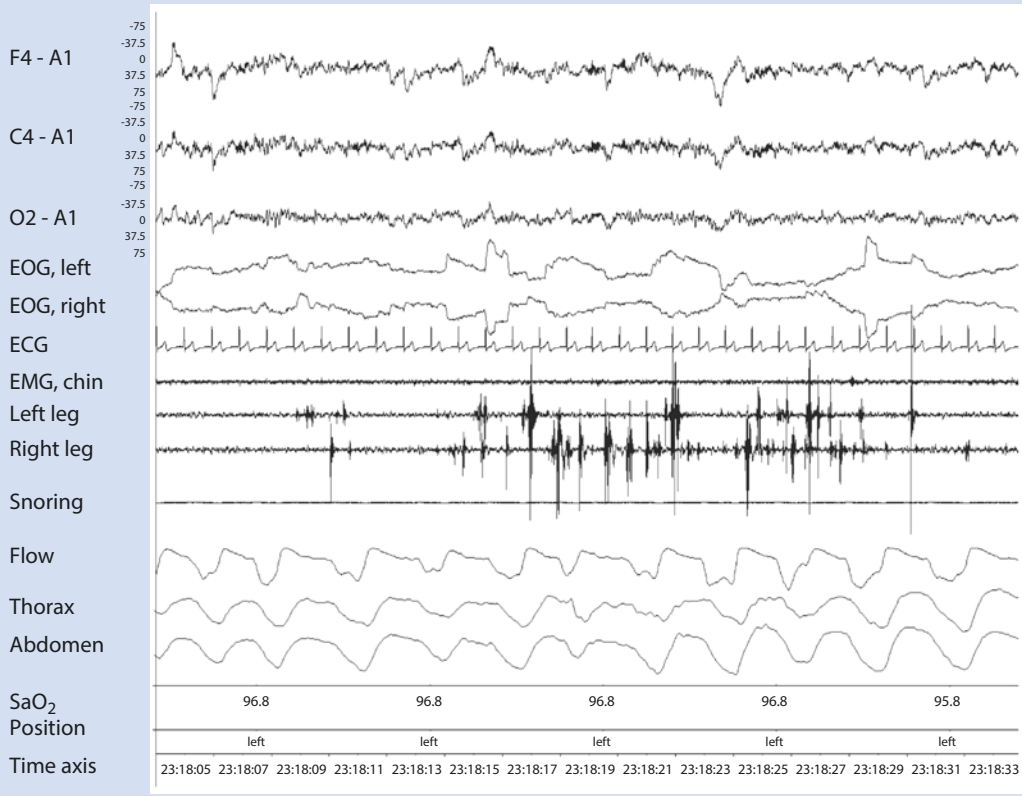

Fig. 1.5 Typical stage R (REM) within a 30-s epoch of polysomnography in a 40-year-old man. In the EEG, an alpha-theta rhythm is found similar to stage 1. In the EOG, rapid conjugated eye movements are observed. In the EMG, typical phasic muscle twitches are seen

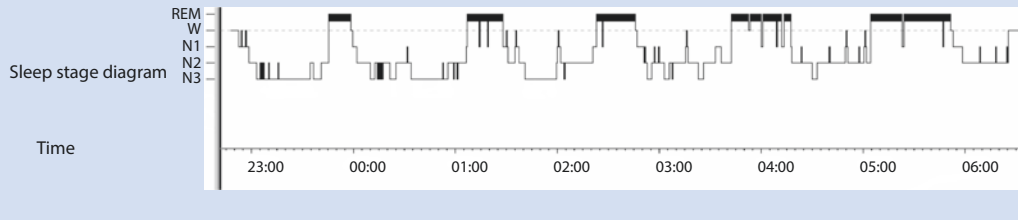

Fig. 1.6 Typical sleep profile of a healthy young man. Five sleep cycles have passed. It is clearly seen that the deep sleep is greatest in the first third of the night. In the last third of the night, increased REM sleep is observed. Further explanations are found in the text

ume. As a consequence, the atrial natriuretic peptide is increasingly and renin decreasingly secreted. During sleep, this position-related diuretic effect is reversed so that finally no volume deficit occurs.

When falling asleep, the sympathetic tone is reduced and the parasympathetic tone raises. Overall, this leads to an increasing reduction of the cardiac output from light sleep over deep sleep to REM sleep. The decreasing heart rate and left ventricular stroke volume are assumed to be responsible for this effect. In connection with the decreased total peripheral resistance, the systemic arterial blood pressure decreases during non-REM sleep with increasing sleep depth. However, so far no consistent explanation exists for the

Table 1.2 Physiological changes during sleep

Parameter	Transition from wakefulness → non-REM	Transition from non-REM → REM	Difference wakefulness → sleep
Cardiovascular system	–		
– Heart rate	10–20% ↓	↑ to ↓, variability ↑	10–20% ↓
– Conduction system	AV transition ↓	AV transition ↓	AV transition ↓
– Stroke volume	5–10% ↓	Variable	↓ to →
–Cardiac output	↓	↓	Up to 25% ↓
– Total peripheral resistance	↓	↑ to →	15–20% ↓
– Systemic arterial blood pressure	↓	↑	10–20% ↓
– Pulmonoarterial pressure	↓	?	2–4 mmHg ↑
– Cerebral blood flow	↓	↑	↓
Gastrointestinal tract	–		
– Swallowing rate	↓	?	↓
– Gastrointestinal mobility	↓	↓ to →	↓
– Salivary secretion	↓	?	↓
Gastric acid secretion	↑ to ↓	?	↑ to ↓
– Sphincter pressure (esophagus, anus)	→	?	→
Urogenital system	–		
– Urine production	↓	↓	20–50% ↓
– Urine osmolality	↓	↓	↓
– Erection (penile and clitoris)	↓	↑	→

proven increase of the blood pressure, the total peripheral resistance, and the heart rate during REM sleep to a level of sleep stage N2.

1.4.2 Thermoregulation

Body temperature as a key variable of the circadian rhythm varies as much as 1 °C during 24 h. It reaches its maximum directly before going to bed and decreases during nighttime to its minimum in the early morning hours (Fig. 1.7a). On one hand, the greatest sleepiness is associated with minimal temperature; on the other hand, it is most probable to reach REM sleep about 30–90 min after the temperature minimum. During REM sleep, mammalians show a poikilotherm behavior; in this sleep stage, they are able to control only their core body temperature: neither sweating for heat loss nor trembling for heat generation is sufficiently possible. In particular for infants, this phenomenon bears the risk of hyperthermia or hypothermia. During non-REM sleep, the body temperature may be controlled in the same way as in the stage of wakefulness, even if it occurs in a slightly reduced way.

1.4.3 Hormone System and Sleep

Many endocrine systems are determined by a more or less strict circadian rhythm. The effects of sleep and the circadian rhythm on hormone

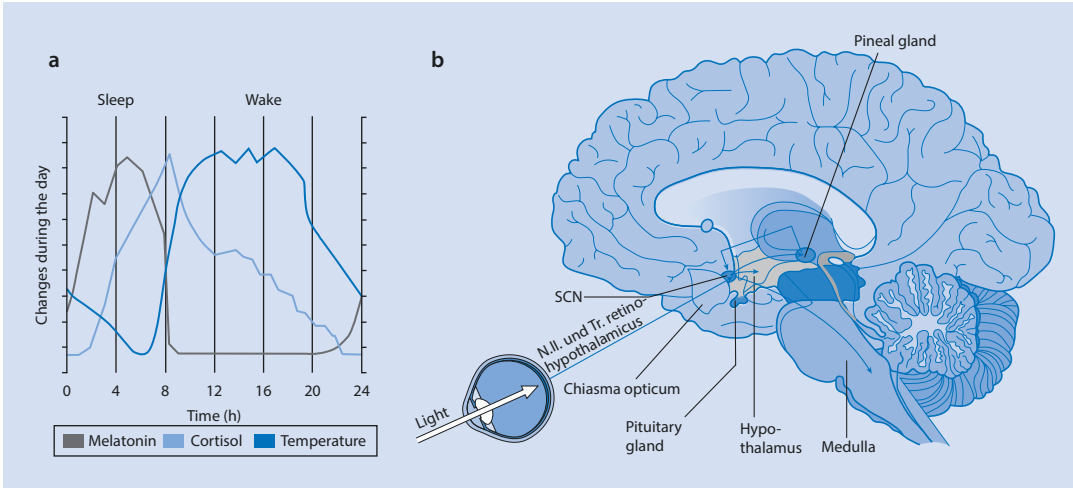

Fig. 1.7 **a** Circadian course of the body temperature and selected hormones. **b** Significant anatomical structure of the sleep–wake regulation (**b** modified according to Birbaumer N, Schmidt RF (2006) *Biologische Psychologie*, 6th Edition, Springer, Berlin)

secretion typically overlap, and it is not easy to separate one from the other.

However, it was possible to prove that the release of growth hormone is enhanced particularly by deep sleep, which is apparent in a maximal blood level about 1 h after falling asleep, independent from the time of falling asleep (Fig. 1.7a).

Similarly, prolactin release increases during sleep and decreases rapidly after waking up.

In contrast, the hypothalamic-pituitary-adrenal axis (HPA) is difficult to stimulate during deep sleep, which leads to a low cortisol value at the beginning of sleep. Only with increasing duration of sleep and the decreasing part of deep sleep does the concentration of cortisol increase.

The ACTH concentration clearly increases about 1 h before awakening and reaches its maximum directly after waking up. The time of the maximum value seems to depend rather from the time of the anticipated awakening than from the real time of awakening. Further, there are hints that the course of the cortisol level is relevant for sleep-associated memory formation.

Also, the regulation of body weight seems to be influenced by sleep. Concentration of the appetite suppressant leptin increases with increasing duration of sleep whereas the level of the appetite-stimulating ghrelin decreases.

Interactions with sleep are described for different cytokines; for example, increased sleepiness is induced by interleukins and tumor necrosis factor, which is important in the context of infections and cancer diseases.

1.5 Circadian Rhythm

All biological processes are subject to a rhythm, wherein the rhythms of 1 day ("circadian") are most obvious. From single-cell organisms to humans, rhythms are already present on the cellular level in the form of so-called clock genes. In mammalians, they are coordinated by the suprachiasmatic nucleus (SCN) in the hypothalamus, which is the master timer (called Zeitgeber) or pacemaker. In humans, the endogenous rhythm of the SCN amounts on average to a bit less than 25 h, which could be detected in volunteers who spent several weeks in a bunker without any contact with the outside world. The endogenous rhythm is only synchronized to 24 h by further zeitgebers. Besides social factors (time of the day, working times, etc.), this is mainly the change between light and dark (Fig. 1.8).

Besides the rods and cones that are responsible for eyesight, special ganglion cells are found in the retina that contain the photosensitive protein melanopsin. The axons of those retinal ganglion cells are directly connected with the SCN via the retinohypothalamic tract. If melanopsin is missing, synchronization is still possible via rods and cones, although less precise, because they dispose themselves of synapses to the ganglion cells.

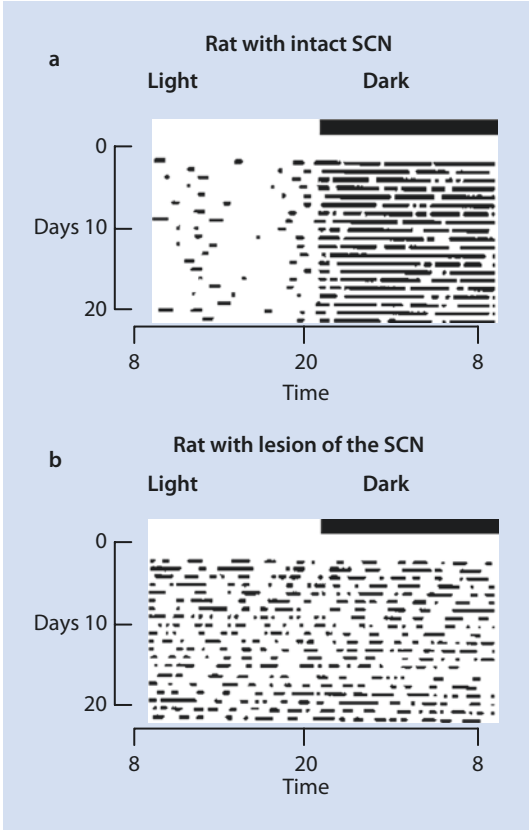

Fig. 1.8 **a**, **b** Activity profile of a rat with intact suprachiasmatic nucleus (SCN) (**a**) and after lesion of the SCN (**b**). As nocturnal animals, healthy rats show high activity during nighttime and long resting phases during daytime. After lesion of the SCN, their rest–activity pattern completely lost its circadian rhythm

Without retinal ganglion cells, synchronization with light–dark alternation is no longer possible (Fig. 1.7b).

In the ventrolateral area of the SCN, the neurotransmitters vasoactive intestinal peptide (VIP) and neuropeptide Y are especially relevant. Synchronization of the cells of the SCN is then mediated via vasopressin-controlled efferences to subordinate systems of the hypothalamus and other brain structures. In this context, in particular the epiphysis (pineal gland) must be mentioned. Its melatonin secretion is inhibited by light, which leads to a feedback for the SCN with regard to the day–night alternation. In nocturnal as well as in diurnal mammalians, the maximum melatonin level is measured at night. The relevant markers of the endogenous rhythm are the core body temperature and the cortisol level (Fig. 1.7a). This rhythm is missing in VIP-deficient mice, for example.

1.6 Sleep Regulation

As a model, sleep is described by three basic mechanisms:

- A *homeostatic process*, wherein the previous sleep and wake times determine the pressure to sleep
- A *circadian process* that defines the circadian oscillating degree of wakefulness
- An *ultradian process* that controls the alternation of REM and non-REM sleep within the sleeping period

The first two processes determine the time and duration of sleep and influence the ultradian process.

In 1982, Borbély developed the "two-process model" for the aforementioned ideas with the process S (homeostatic) that approaches asymptotically a maximum during wakefulness and is then reduced during sleep, and the process C (circadian) as the degree of wakefulness that tends to its lowest values in the evening (Fig. 1.9).

Simply put, the *process S* can be compared with the intensity of the delta waves (delta power) because delta power depends on the previous wake time more than the duration of deep sleep. Recent investigations show an accumulation of adenosine and the associated receptors in the basal forebrain during wakefulness and an increasing degradation with increasing duration of sleep. Adenosine itself triggers the ventrolateral preoptic region (VLPO) that is discussed as the "door to sleep" because it blocks cholinergic, adrenergic, serotonergic, and histaminergic arousal systems (see the following chapter) and thus induces non-REM sleep.

For *process C*, the SCN is responsible for sending arousal signals that continuously increase until the early evening hours. Afterward, they decrease rapidly, which relevantly increases the individual's readiness to sleep.

To describe the *ultradian rhythm* of non-REM-REM sleep cycles, by 1975, Hobson and McCarley had developed their model of reciprocal interaction of aminergic and cholinergic neurons in the mesopontine crossing of the brainstem. Based on recent neurophysiological examinations, this

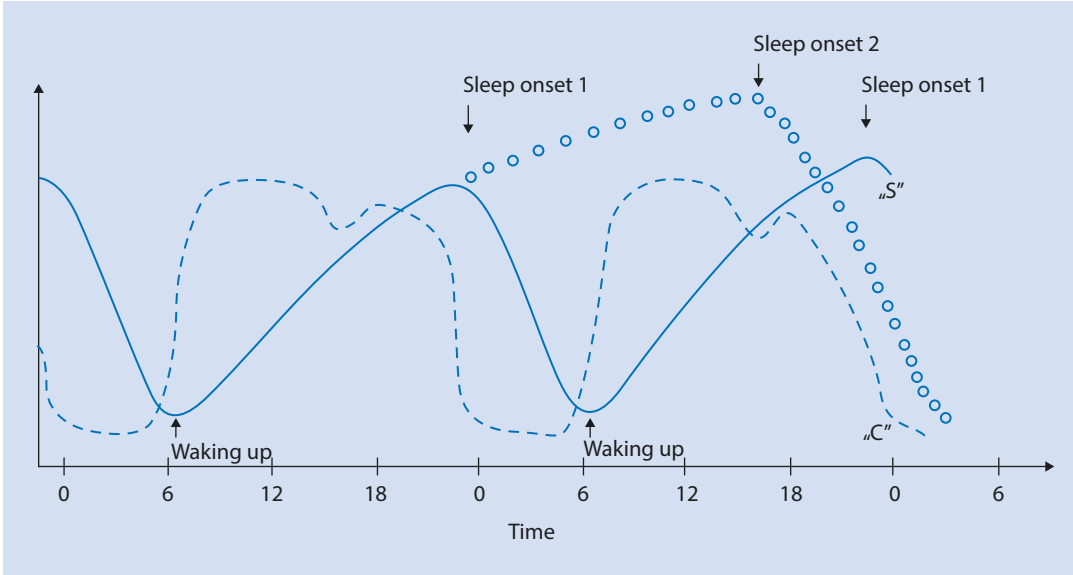

Fig. 1.9 Model of sleep regulation according to Borbély. *C* circadian degree of wakefulness, *S* endogenous "sleep substance" accumulating in the wake phase. Sleep onset occurs when *C* is low and *S* is high (sleep onset 1). *Dotted line* is the course of *S* when sleep was missed for 1 night; sleep onset then typically occurred in the afternoon (sleep onset 2)

model was modified but generally confirmed: a dopaminergic (tuberomammillary nucleus), serotonergic (raphe nuclei), and adrenergic (locus coeruleus) activity that decreases from wakefulness via non-REM sleep and is almost completely suppressed during REM sleep is opposed to a high cholinergic (laterodorsal tegmentum, pedunculopontine nuclei) activity during wakefulness as well as during REM sleep. Accordingly, pharmaceuticals with a cholinergic or anticholinergic profile mostly have significant impacts on the parameters of REM latency, percentage, and density.

The condition of wakefulness is furthermore actively maintained by predominantly glutamatergic, besides also cholinergic, neurons of the ascending reticular activating system (ARAS) in the brainstem. An electrophysiological correlate of the diffuse tonic and phasic activation is the low-amplitude, high-frequency activity in the EEG. Sleep is induced by an active GABAergic decline of the tonic activity level of the ARAS during wakefulness. GABA is the most important and most broadly distributed inhibiting transmitter in the CNS. It binds to $GABA_A$ and $GABA_B$ receptors, whereof the $GABA_A$ receptors mediate the relevant sedating and sleep-promoting as well as anxiolytic and muscle-relaxing effects.

Although serotonin shows activating and even mood-lifting effects during the daytime, it is significantly responsible for the overall development of sleep and especially for deep sleep regulation. The serum concentration of serotonin during sleep correlates directly with the percentage of deep sleep. The peptide hormones hypocretin 1 and 2 (orexin A and B) originate from a precursor protein exclusively produced in maximally 100,000 neurons of the dorsal, lateral, and posterior hypothalamus as well as the perifornical nucleus. Hypocretinergic neurons seem to have a mainly excitatory effect on systems stimulating wakefulness. Their activity continuously increases during the day with a maximum in the evening.

1.7 Functions of Sleep

Simply put, the condition of wakefulness is considered as a temporary hyperactive catabolic phase serving as time for food intake and reproduction. Different functions are assigned to sleep; the most important of these are explained in the following paragraphs.

The *function of recovery* seems to be clear for everybody from their own experience. This concept is supported by the increased level of growth

hormone directly after sleep onset, the restoration of cerebral glycogen as well as enhanced delta power, and the prolonged sleep phase after sleep deprivation. Opposed to these are the reduced protein synthesis during sleep, the unchanged duration of sleep despite physical stress, and the unchanged mitotic rate during sleep.

Another hypothesis states that sleep has the function of *saving energy*. Energy consumption actually decreases during sleep by about 10%, and body temperature is reduced. The evidence of neurons in the anterior hypothalamus that contribute to thermoregulation as well as sleep regulation supports the concept that sleep and thermoregulation are closely linked.

In addition, sleep is considered as being relevant for a *well-functioning immune system*. This idea, however, is generated exclusively from investigations with sleep-deprived laboratory animals or patients. Sleep deprivation led to an increased susceptibility for infections and a reduced vaccination response. In cases of extreme sleep deficit, an animal experiment with rats even revealed a collapse of the immune system with fatal outcome.

The *ontogenic theory* attributes an important function to REM sleep for the differentiation of the brain, especially during the first months of life. In terms of this model, the atony of the skeletal muscles during REM sleep allows stimulation of the brain without the necessity of movements that would have to be actually performed. In the fetal stage, for example, breathing movements are neuronally executed during REM sleep. Furthermore, certain behavioral patterns that are necessary to conserve the species are regularly trained and presented to a potential mating partner: these include the erection of men that is closely linked to REM sleep and the increased vaginal blood flow of women. During REM sleep, primarily processes occur that are associated with psychic well-being and intellectual performance (see ► Sect. 1.8). REM deficiency in children may lead to later developmental problems, behavioral disorders, permanent problems with sleep, reduced brain mass, and an extraordinarily high neuronal cell death (see ► Chap. 11).

The *consolidation of memory and acquired knowledge and skills* during sleep is scientifically proven. In 1924, it could already be confirmed that simple learning tasks (declarative learning) that were offered immediately before a sleep period were better retained than tasks before a wake period of the same duration. In particular, studies of recent times reveal the probability of a correlation between non-REM sleep and the declarative memory. REM sleep, however, seems to have a key role for procedural memory (e.g., riding a bike) and emotional memory (emotion-related content). These findings are not only academically relevant, but they may also confirm the impaired memory that is a frequent complaint of patients with sleep disorders.

1.8 Dreaming

1.8.1 Definitions

In everyday language, the term dream is used with many meanings, in such expressions as being a dreamer, dream house, or the woman of my dreams. Approaching the phenomenon of dream from a scientific perspective requires clear definitions for dreaming as process as well as for dreams (dream reports):

- *Definition I*: Dreaming is subjective experiencing that occurs during sleep.
- *Definition II*: *A dream or a dream report is the recollection of subjective experiences that occurred during sleep after waking up.*

The term 'subjective experiences' intends to elucidate the fact that dreaming is a holistic experience with sensory impressions, emotions, and thoughts, that is, we experience ourselves in dreams in the same way as in the state of wakefulness. Sleep physiology (EEG, eye movements, heart rate, etc.) can be assessed and measured, but the subjective experiences can only be accessed by means of interviews after awakening. For sleep and dream research, it is important to distinguish both levels, the physiological and the psychological level.

The second definition illustrates one aspect very clearly. Dreaming is not directly accessible, either for the dreamer nor for the researcher. Two transitions have to be made to obtain a dream report: first, the individual has to awaken (sleep–wake transition), and, second, the individual has to recall what happened before waking up (dimension of time). So, the question has to be asked to what extent the dream report reliably reflects the experiences that occurred during sleep.

Table 1.3 Different types of dreams

Term	Definition
REM dreams	Recalling the subjective experiences that occurred during REM sleep
Non-REM dreams	Recalling the subjective experiences that occurred during non-REM sleep
Sleep-onset dreams	Recalling the subjective experiences that occurred during non-REM sleep stage 1
Nightmares	REM dreaming with strongly negative emotions that typically cause awakening
Night terror (pavor nocturnus)	Abrupt arousal from slow wave sleep associated with panic, might be accompanied by non-REM dreams
Posttraumatic replications	REM or non-REM dreams that realistically replicate a traumatic event
Lucid dreams	REM dreams associated with the awareness that the current experiences are dream experiences

Dreams can be classified into different groups (Table 1.3).

In the first sleep lab studies on dreams, the participants were woken up from REM sleep, and the researcher received reports about vivid and colorful dreams with very high probability (more than 80%). After awakenings from non-REM sleep, however, dreams were reported very rarely. In 1962, David Foulkes highlighted the fact that the definition of dreaming play a major role in this context: He did not ask specifically about vivid dreams but generally about what went through the participant's mind before the awakening. Applying this approach, he obtained report rates of more than 50% even for non-REM awakenings. Even if non-REM dreams are often shorter, less emotionally intense, and more comparable to thoughts than REM dreams, the distinction is not clear-cut. About 25% of non-REM dreams cannot be differentiated from REM dreams based on their content.

Sleep-onset dreams occur in non-REM stage 1 and are typically forgotten when the sleeper is not awakened by noise during the process of falling asleep. Mostly sleep-onset dreams are a continuation of the thoughts one has prior to sleep onset; sometimes these thoughts can become very bizarre. However, there are also many people who experience single images and also sequences of images during sleep onset, so that the distinction to REM dreams is not clear-cut.

The classification of dreams based on sleep stages emphasizes the current view that dreaming takes place during the entire time of sleep. The brain and consciousness never sleep.

The following three dream phenomena are associated with fear: nightmares, night/sleep terror (pavor nocturnus), and posttraumatic replications.

Nightmares are REM dreams in which the strong negative affect causes awakening. Nightmares are differentiated from distressing or "bad" dreams that also contain strong negative emotions such as fear, disgust, or grief but that do not result in awakening (see ▶ Chap. 7).

In the context of *night terror* or sleep terror (pavor nocturnus), the individual abruptly arouses from slow wave sleep with intense panic, but the person is not really fully awake and often cannot recall the incident (see ▶ Chap. 7).

Posttraumatic replications originate from traumatic events such as sexual abuse or war experiences and may occur during REM or non-REM sleep. Even during daytime, such posttraumatic repetitions may appear, these are called "flashbacks." These three dream phenomena (nightmares, night terrors, posttraumatic replications) are forms of parasomnias (see ▶ Chap. 7).

During *lucid dreams*, the dreamer is aware of the fact that s/he is dreaming. This state is highly interesting to researchers but also for the individual himself/herself because of the manifold possibilities to influence the dream according to one's own intentions.

In other states of consciousness, dreamlike imagery is experienced, for example, under anesthesia or in the context of near-death experiences. Even during wakefulness, dreamlike phenomena may occur; these are called daydreams or mind-wandering.

1.8.2 Dream Recall

Although it is currently assumed that every individual dreams every night, recalling the events

experienced during sleep after waking up varies a great deal. Some people are able to report a dream nearly every morning, whereas others state that they have not dreamt for many years or - to be correct - that they do not remember any dream for a long time. The basic factors for those inter-individual differences in dream recall are not yet fully understood.

Regarding dream recall, a stable gender difference have been found. The findings that women showed a higher rate of dream recall than men could be explained by a study showing that girls talk more often about their dreams during childhood and adolescence compared to boys, which might indicate a gender-specific dream socialization; that is, talking about dreams and the interest in dreams has been promoted in girls but not so much in boys. Findings showing that dream recall decreases with age in cross-sectional studies have to be viewed with caution because there are no longitudinal studies (investigations of a individuals from young adulthood to older ages), and a high constancy of the dream recall over this period can be expected from retrospective studies.

Regarding personality factors, most studies did not find correlations between dimensions such as repression, extraversion, and anxiety and dream recall frequency. Similarly, cognitive factors such as general intelligence are not relevant with regard to dream recall. Personality dimensions such as "thin boundaries" that are related to creativity and vivid fantasy life had a significant but small influence. The fact that the ability to recall dreams can be significantly increased with simple means (preparing pen and paper, focusing on dream recall when waking up) indicates that trait factors may only explain a small portion of the inter-individual differences in dream recall.

Regarding sleep parameters, it was found that people who have poor sleep quality and often awaken at night remember their dreams more frequently. Also, insomnia patients have a higher frequency of dream recall than healthy individuals. This difference is plausible: the higher the frequency of nocturnal awakenings, the greater the chance to recall a dream.

Today, empirical findings are best fit in with the arousal-retrieval model of dream recall. Two steps are important in this context: first, one has to be awake after the dream experience so that it can be stored into the long-term memory, and, second, the awakening process should contain few interferences, and the dream should have a significance and/or emotional intensity so that it will be well remembered.

Practical Tip

Tips to increase dream recall

- Prepare pen and paper in the evening on the night table before going to bed.
- Make up your mind before falling asleep to recall a dream in the morning.
- After waking up, take some time, think back and rehearse all that you can recall (like learning a poem by heart).
- Take at least some notes of the dream actions.
- Record your dreams regularly.

Table 1.4 Reality character of diary dreams ($n = 365$)

Category	Incidence
Possible in wakefulness, normal everyday experiences	29.3%
Possible in wakefulness, but unusual elements	39.5%
One or two bizarre (impossible) elements	27.4%
Several bizarre elements	4.1%

1.8.3 General Characteristics of Dreams

In more than 90% of dreams the dream-self is involved in the dream action, i.e., most dream experiences are holistic in a similiar way as we experience wakefulness. Dreams that the dreamer watches like a movie and in which the dream-self remains totally passive are very rare.

Regarding the reality character of dreams, the general public often assumes that most dreams are bizarre, that is, contain elements that are not possible in the physical reality of our waking world. This concept is probably explained by the fact that in most cases only exciting, interesting and/or extraordinary dreams are shared with others or

published. An content analysis of dreams that had been recorded for 2 weeks by participants on a regular basis (see Table 1.4), however, showed that only about 30% of the dreams actually contain elements that are impossible in waking life. In this context, the definition of bizarreness is of importance. Some authors already consider abrupt scene shifts or inconsistencies (the apartment from one's childhood is located in another city) as bizarre, so that according to this definition nearly all dreams contain bizarre elements.

In laboratory dreams as well as diary dreams, healthy individuals showed a balanced proportion of positive and negative dream emotions. However, in the laboratory, more neutral dreams occur, i.e., lab dreams are less intensive than home dreams.

The common view that dreams are predominantly negative is probably explained by the fact that negative dreams, in particular when they are recurring, are more easily recalled even after several years. Further, positive dream emotions are less frequently described explicitly in the dream report, so that studies that do not assess the dreamers' subjective ratings but only analyze the dream reports are subjected to bias, that is, a preponderance of negative emotions is then found.

All dreams contain visual perceptions. In individuals who are congenitally blind, these visual perceptions in dreams are completely missing. Visual dream content, even decades after the loss of sight, can be found in individuals who lost their vision after the age of 7.

Auditory perception also plays an important role in dreams, whereby language is more prominent than noises.

Kinesthetic experiences (sensations that originate from movement) occur now and then, for example in the context of flying dreams, but also in the context of other types of movement. Tactile, gustatory, and olfactory experiences and pain only rarely occur in dreams.

1.8.4 Correlation Between Wakefulness and Dream

Before addressing possible functions of dreams in the next paragraph, the question if and how waking-life experiences influence the dream content is discussed. To study this topic, different methodical approaches have been applied.

For determining temporal references of dream elements, the participant is asked - typically after reporting or recording the dream(s) - when a certain event that occurred in the dream had happened in waking life the last time, for example, seeing one's mother. Even if such studies frequently showed a very plausible exponential decrease with increasing time interval to the matching waking-life experience (comparable to other memory processes), the results have to be evaluated with caution. The main problem is that it is nearly impossible for participants to remember all waking-life events and thoughts of the last days, weeks, or years. Another difficulty is that many events take place over and over again in waking life. For example, the mother in the dream might be associated with the telephone call from the previous evening with her but also might be linked to a childhood memory. These types of studies may provide interesting ideas for hypotheses, but the findings have to be confirmed by experimental and field studies.

For experimental manipulation, the pre-sleep experiences of the participants are influenced, for example, by showing movies, reading stories, or letting the participant carry out specific activities. In many studies films were used in the evening before the participant went to bed in the sleep lab. Overall, the studies on experimental manipulation showed that specific film elements were rarely found within subsequent dreams, but the emotional quality of dreams were affected by the experimental conditions, i.e., a stressful film was followed by dreams with more negative emotions.

Because experimental manipulation did not show large effects on dreams, *field studies* tried to investigate the effects of real stressors and life events on dreams. Field studies are performed outside the artificial lab environment and assess waking-life events and dreams by means of diaries, questionnaires, or interviews. Daytime events and dreams can be assessed on a day-to-day basis (or from night to night) to test how many days it will take until a specific event actually show up in the dream. This approach can be used to assess intraindividual fluctuations of dream content over time.

Life events such as divorce and pregnancy have shown clear influences on the dream content of the individuals. The strong effects, are especially obvious in traumatic events such as sexual abuse, war experiences, or natural disasters. Our

own data indicated that participants who had experienced the Second World War reported, even in 2000 more frequently war dreams than younger participants. The field studies demonstrated impressively that dramatic and stressing life events have a strong and sometimes long-lasting influence on dreaming.

In summary, the empirical results support the *continuity hypothesis* stating that dreams directly reflect the waking life. However, further research efforts are necessary to exactly assess the factors such as emotional intensity of waking-life experiences, personality of the dreamer, etc. that moderate the relationship between dreaming and waking.

1.8.5 Function of Dreams

The question arises if dreaming defined as subjective experiences during sleep has a function that goes beyond the function(s) of sleep (see ▶ Sect. 1.7). Memory consolidation during sleep, for example, takes place on the cellular level and system level so that it is not very likely that dreams are involved in these processes; they probably just reflect those processes. Practicing simple motor abilities during lucid dreams such as throwing darts with the nondominant hand, showed a positive effect on performance on the next morning. This effect is comparable with the effect of mental training carried out in the waking state, which has already been applied in sports for many years. Research still has to demonstrate the function or positive effects of dreams on wakefulness in an experimental setting. One problem is that dreaming can only be accessed via the dream report (recall of the dream experience after waking up); possible positive effects may be explained by sharing the dream or reflecting on the dream content and is not necessarily causal to the dream experience itself. Unfortunately, one cannot study the effects of unrecalled dreams on waking life. Over the years, many functions of dreaming have been proposed, for example, the dream as the guardian of sleep (Sigmund Freud). Today, many researchers assume that dreaming has a problem-solving function because elements from memory (waking-life experiences of the past) are mixed with new input of current wakefulness within dreams in a creative way—a kind of brainstorming at night. Research efforts are still needed to answer the question of the function of dreaming.

1.9 Questions

1. Please describe and define the sleep stages according to the AASM criteria.
2. Which physiological changes during sleep do you know?
3. Please describe the sleep–wake regulation taking into account chronobiological aspects.
4. Which findings indicate that dreaming takes place during the entire sleep?

Further Reading

1. American Academy of Sleep Medicine. International classification of sleep disorders, vol 3. Aufl. Darien: American Academy of Sleep Medicine; 2014.
2. Berry RB, Brooks R, Gamaldo CE, Harding SM, Lloyd RM, Marcus CL Vaughn BV, for the American Academy of Sleep Medicine. The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications, version 2.6. www.aasmnet.org. Darien: American Academy of Sleep Medicine 2016.
3. Czeisler CA, Gooley JJ. Sleep and circadian rhythms in humans. Cold Spring Harb Symp Quant Biol. 2007;72:579–97.
4. Dijk DJ, Lockley SW. Integration of human sleep-wake regulation and circadian rhythmicity. J Appl Physiol. 2002;92:852–62.
5. Moore RY. Suprachiasmatic nucleus in sleep-wake regulation. Sleep Med. 2007;8(suppl 3):27–33.
6. Peter H, Penzel T, Peter JH. Enzyklopädie der Schlafmedizin. Heidelberg: Springer; 2007.
7. Schredl M. Researching Dreams: The Fundamentals. Cham: Palgrave Macmillan; 2018.
8. Walker MP. Why we sleep - The new science of sleep and dreams. New York: Scribner, 2017.