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Awakening from sleep

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KEYWORDS
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Summary Awakening is a crucial event for the organism. The transition from sleep to waking implies physiological processes which lead to a new behavioural state. Spontaneous awakenings have varying features which may change as a function of several factors. The latter include intrasleep architecture, circadian phase, time awake, age, or disordered sleep. Despite its clear theoretical and clinical importance, the topic of awakening (in humans) has received little attention so far. This contribution focuses on major issues which relate to awakening from both basic (experimental) and clinical research. Recent knowledge on neurophysiological mechanisms is reported. The experimental data which provide in the human suggestions on the regulation of awakening are discussed, mainly those concerning sleep architecture and homeostatic/circadian factors also in a life-span perspective, since age is a powerful factor which may influence awakening. Clinical contributions will examine two main sleep disorders: insomnia and hypersomnia. Daytime functioning is shown in insomniac patients and compared to other pathologies like sleep apnea. A final section evokes links between some types of night waking and psychological factors.

INTRODUCTION

Awakening is a crucial event for the organism, separating sleep and wakefulness. The transition from sleep to waking implies physiological processes which lead to a new behavioural state. Transitions between sleep and wakefulness in humans encompass a wide spectrum of state changes, different in duration and characteristics: (i) ultrashort arousals in the range of seconds, (ii) short spontaneous awakenings from sleep in the range of minutes, and (iii) longlasting and consistent awakenings, often representing the termination of a full sleep episode.

In fact both terms, awakening and arousal, are used in the literature often with similar, even identical meaning. An epistemological discussion about the right to use one of these terms is beyond the scope of this review. However it could be remarked that "arousal" is mainly used in neurophysiology to indicate cortical events and in clinical domain for physiological events linked to respiratory pathology; awakening includes a behavioural component.

Non-provoked awakenings, either final or intranight, have varying features: their number, temporal

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placement, cognitive characteristics and the duration of the following wakefulness may change as a function of several factors. The latter include intrasleep architecture, circadian phase, time awake, age, or disordered sleep. Despite its clear theoretical and clinical importance, the topic of awakening (in humans) has received little attention so far.

The present cooperative effort is an attempt to raise the interest in this area of sleep research. It was inspired by a symposium at the 14th Congress (Madrid) of the European Sleep Research Society. We decided to focus this contribution on major issues which relate to awakening from both basic (experimental) and clinical research.

Firstly, an insight in the up-to-date neurophysiological mechanisms. Then the experimental data which provide in the human suggestions on the regulation of awakening, mainly those concerning sleep architecture and homeostatic/circadian factors. These aspects will be discussed also in a life span perspective. Age in fact is a powerful factor which may influence awakening. Clinical contributions will examine two main sleep disorders: insomnia and hypersomnia. Daytime functioning in insomniac patients will be discussed too and compared to other pathologies like sleep apnea. Difficulty in waking up will be illustrated and discussed linking pathologies to models of sleep regulation. Finally, a contribution from the mind, i.e. psychological factors in night awakening. This section will evoke links between some types of night waking and psychoanalytic theory.

THALAMIC AND EXTRA-THALAMIC MECHANISMS IN CORTICAL AROUSAL

Awakenings essentially constitute cortical arousal, but with a strong behavioral component. Here we shall focus on the former. Cortical arousal, also called activation, is revealed by electroencephalographic desynchronization and a general increase of electrical activity and excitability both in sensory and motor systems.

Cortical arousal has been studied in animal models, using chronic preparations, and it has been shown that they are controlled by various subcortical structures. The "activating system" is constituted by neurons located in the midbrain reticular formation (MRF) projecting to the thalamus and to the cerebral cortex [1]. In the thalamus, in many intralaminar nuclei (i.e. Centralis Lateralis), an increase of unitary activity, and a remarkable change of the discharge pattern, anticipate the EEG changes by tenths of seconds during transitions from slow-waves-sleep (SWS) to wakefulness (W) [2]. Transition to wakefulness is also marked, in many brain regions, by a widespread activation of c-fos and others immediate-early genes, which could be the molecular correlates of electrophysiological activation [3].

In the Ventralis Postero Lateralis (VPL), a specific sensory nucleus of the thalamus, the response to peripheral physiological stimulation during sleep shows three main components: a very brief and scanty excitatory response, followed by a long period of discharge suppression and by an excitatory rebound. The landmark of arousal is a strong increase of the excitatory response and a marked reduction of the inhibitory phase, eventually with disappearance of the rebound [4].

In all the thalamic nuclei sleep is signalled by oscillatory rhythmical activity, synchronizing diencephalon and cerebral cortex [1].

In acute experiments, in thalamic neurones intracellularly recorded, a disruption of the oscillatory neuronal activity was observed during EEG desynchronization [5]. Spontaneous oscillatory activities in the thalamic neurones are controlled by the level of polarisation of the membrane potential. As has been shown in *in vitro* preparations, all the thalamic neurones behave like synchronized oscillators when they are hyperpolarized. In contrast, a reduction of the membrane polarisation induces an abrupt blockade of rhythmical activity and increase of responsiveness to peripheral input [6]. This is the mechanism by which the ascending cholinergic pathways, originating from the mesencephalon, are able to induce desynchronization and arousal.

However, experimental evidence shows that cholinergic cells are also located in the preoptic-anterior hypothalamic and basal forebrain regions (BF-POAH) and project to the cerebral cortex. GABAergic neurones have been recently discovered within the BF in the same regions where cortically projecting cholinergic neurones were described [7]. Neurons located in these areas may influence cortical activities through direct projections as well as indirectly through sub cortical connections involving the medial and the dorsal thalamus. Dampening of the GABAergic inhibitory influences ascending from these regions to the thalamus and the frontal cortex could be one of the mechanisms of cortical arousal. The cholinergic and non-cholinergic preoptic-anterior hypothalamic and

basal forebrain neurones are also under the control of endogenous adenosine, as was clearly shown *in vivo* and *in vitro* preparations [8].

Recently, in the thalamic nuclei, in chronic animal preparations, has been described a very slow rhythmical activity, highly correlated with two major oscillatory components detectable in the peripheral activity of the sympathetic system, both in man and in animals. In the EKG these very slow rhythms can be observed as variability of R–R intervals and have been classified as low (LF; 0.04–0.15 Hz) and high (HF; 0.15–0.5) frequency in humans. The HF oscillation has been related to respiration, and is considered a marker of vagal modulation. The LF rhythm, related to vasomotor activity, was proposed as a marker of sympathetic modulation. The origins of these oscillations can be attributed to the medullary neurones, where they have been recorded in the areas involved in the regulation of cardiovascular system. In thalamic neurons these very slow rhythms are influenced by transitions of sleep–waking cycles. In most of somatosensory thalamocortical neurones, studied by means of the spectral analysis of the spontaneous firing, arousal is accompanied by a power shift from HF to LF as the main component in very slow rhythms domain, whereas coherence with the cardiac HF rhythms is lost [9]. In man a very slow oscillation of EEG spectral power has been recently described, in the minutes domain, and attributed to a brain stem generator triggered by the arousal systems [10].

What recalled above shows that many subcortical components are acting during cortical arousal. Thalamic activity is dependent not only by ascending influences from mesencephalon, but also from anterior hypothalamic and basal forebrain regions, which could also act directly on the cortex. Possibly, more caudal brainstem regions, usually considered to be involved only in peripheral regulations, could contribute to the overall changes of neocortical activity during arousal.

THE TEMPORAL DISTRIBUTION OF AWAKENINGS

Sleep and wakefulness are conceived as two distinct behavioral states which differ in body position, muscular and neural activity, and consciousness. The common research criteria to separate sleep and wakefulness are electrophysiologically defined. The combined information from the electroencephalogram (EEG), electrooculogram (EOG) and electromyogram (EMG) is used to separate behavioral states by quantifiable criteria. While these criteria allow to distinguish sleep and wakefulness objectively, they also show gradual steps of state transitions. There are atleast four different electrophysiological criteria to define transitions from sleep to wakefulness: (a) intrusion of alpha activity, or an increase of higher frequencies in the sleep EEG, (b) EEG defined arousals [12], (c) epochs of wakefulness [13], and (d) full awakening.

For young adults the percentage of time awake during night sleep, according to electrophysiological criteria, is generally less than 5%. Williams *et al.* [3] observed a mean value of 1.3% $\pm$ 1.1% for 10 males, and 0.5% $\pm$ 0.5% for 11 females. In spite of their rare occurrence, awakenings are events of major strategic importance since they allow the sleeper to scan the environment and to decide either to go back to sleep or to terminate sleep. Merica and Gaillard [14, 15], who analyzed the distribution of all stages in uninterrupted and interrupted cycles of healthy adults described a peak of wakefulness early in normalized, uninterrupted NREM-REM sleep cycles, while the distribution of wake episodes was irregular in a subset of interrupted cycles. This finding was replicated and extended in a study by Schulz and Bes [16] who analyzed a sample of 799 nights with a total of 3366 normalized NREM-REM cycles from 29 young, healthy subjects, whose sleep was recorded for multiple nights. Time awake peaked in the early part of the normalized cycles, i.e. immediately after the end of REM sleep. The height of the peak increased monotonically from cycle 1 to cycle 5. The peak value of time awake was less than 3% in the first cycle, 8% in the second cycle, about 10% in the third, about 12% in the fourth cycle, and 13–14% in the fifth cycle. Additionally, the area under the curve of the wake epochs increased in the first 20%-proportion of the normalized NREM-REM cycle from the first to the fifth cycle, while it remained on a steady low level for the remainder of the normalized cycle time. Thus, awakenings during sleep show a characteristic distribution with a local maximum immediately following REM sleep. Preferred transitions from REM sleep to wakefulness have also been reported by Muzet *et al.* as early as 1972 [17]. This in mind, it will be interesting to analyze the wake distribution in sleep cycles of patients with sleep disturbances to see whether their distribution pattern of wake episodes represents an exaggeration of the normal pattern, or whether their wake

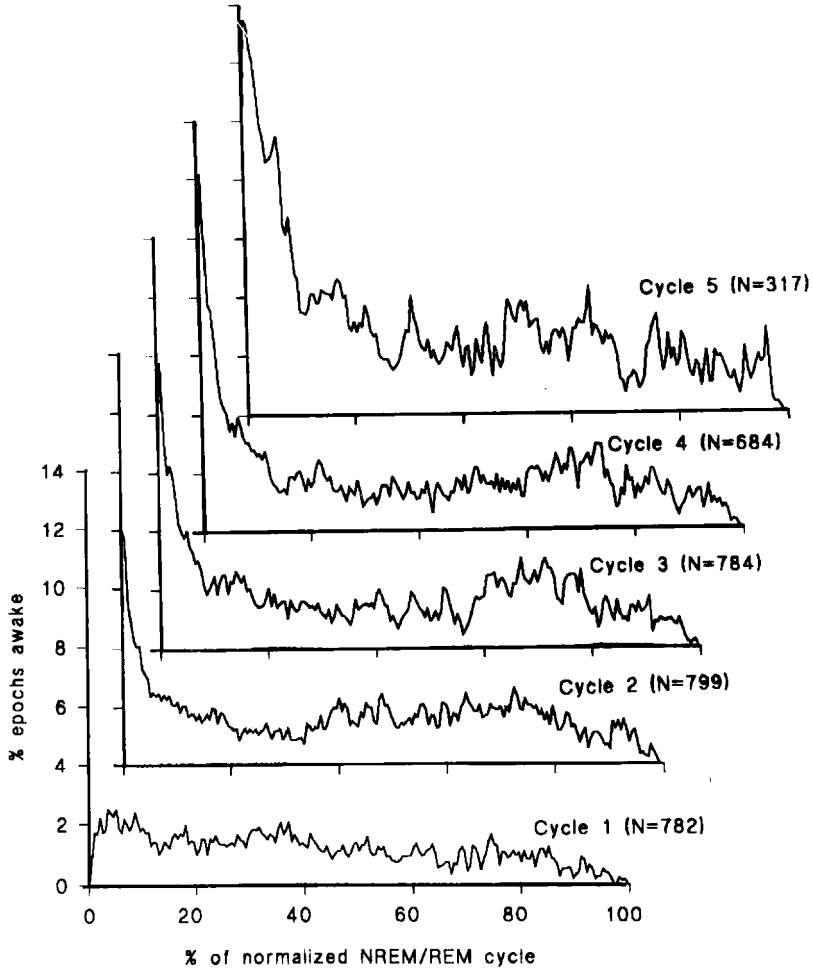

Figure 1

times follow a different pattern which is more irregular with a random distribution across NREM-REM cycles. In this case, one may speculate that the low rate and typical distribution pattern of wake episodes in subjects without sleep complaints has an adaptive value, which is compatible with the ongoing sleep process, while longer and irregularly distributed awakenings deteriorate sleep quality and possible also interfere with cognitive processes during sleep [18].

While the distribution of sleep interruptions by wakefulness can be analyzed from sleep which was recorded under normal conditions, sleep termination was preferably studied in polygraphic sleep recordings under experimental conditions without external *zeitgebers*. Under these conditions, where subjects determined the end of sleep by themselves, it was found that the final awakening preferentially coincided (a) with the rising slope of the circadian rhythm of deep body temperature and (b) with the REM sleep phase of the NREM-REM cycle [19, 20]. This indicates that the preferred time to wake up from night sleep is phase related to circadian rhythms and to the ultradian REM-NREM sleep cycle. In a later study, which was conducted under forced desynchrony conditions, Dijk and Czeisler [21] tried to assess separately the relative contribution of the circadian pacemaker and the sleep homeostat to the consolidation of sleep. While high sleep efficiency was maintained in the first half of sleep at all circadian phases, sleep consistency in the latter half of sleep depended on the phase relationship with the circadian core body temperature cycle. Sleep was severely disturbed when it coincided with the rising phase of the body temperature cycle, while wakefulness within sleep remained at very low levels when the second half of scheduled sleep coincided with the minimum of the circadian body temperature rhythm. This suggests that the homeostatic component of sleep regulation dominates in the first half of sleep, while the consistency of sleep in the second half of sleep mainly depends on circadian components, with a high rate

of intrusion of wakefulness into sleep or termination of sleep coinciding with the rising limb of the circadian body temperature cycle.

Another approach to study sleep termination in relation to preceding REM or NREM sleep was chosen by Campbell [22] who analyzed spontaneous sleep termination in subjects who were continuously recorded for 60 h under bed rest conditions. The analysis was confined to sleep episodes which were characterized by the presence of both REM and NREM sleep. Sleep termination data were compared to expectancy data which were either based on the overall REM and NREM percentages, or more conservatively on the proportions of REM and NREM sleep in the last third of each sleep episode. Both comparisons showed that the termination of sleep occurred significantly more often from REM sleep than would be expected by chance. Campbell found also that the mean duration of those REM episodes which were terminated by awakening was only half of those which were uninterrupted, suggesting that sleep termination did not follow a completed REM sleep episode but rather interrupted REM sleep. This author suggested that REM sleep as a state with high neural activity provides "optimal physiological conditions for the transition from sleep to waking" (p. 241). The preferred tendency to wake up out of REM sleep was also shown for babies (Schulz *et al.* [23]) and young adults (Langford *et al.* [24]) while it was not present in elderly subjects with a mean age of 69 years (Salzarulo *et al.* [25]). One may imagine different explanations for this age-dependent difference in the sleep stage association of sleep termination. Either sleep is shallow and fragile in elderly patients, thus diminishing differences in arousability between sleep stages, or sleep in elderly patients is less shielded against the intrusion of external disturbances which may lead to arousals and awakening independent of the ongoing sequence of sleep stages. A more recent study by Murphy *et al.* [26] could help to clarify these different views. The authors, who studied subjects in isolation from external time cues found again that younger subjects (mean age: 22 years) awakened preferentially from REM sleep while older subjects (mean age: 68 years) did not. However, those older subjects who had sleep efficiencies above the median were more likely to wake up from REM sleep than those with lower sleep efficiencies. The results confirm age-related differences in sleep termination and suggest that sleep quality is a mediator variable which interferes with the relationship between age and sleep termination, even under controlled external conditions. An irregular distribution of awakenings within the ultradian NREM-REM sleep cycle was also reported by Merica and Gaillard [14, 15] for a subset of interrupted cycles under normal environmental sleep conditions.

The transition from the sleep into the wake state can be measured by behavioral responses or by changes in the EEG power spectrum with a decrease of delta and theta power on the one hand and an increase of alpha power on the other (Ogilvie and Simons [27]). The authors assume that "*the loss of hypersynchronization, which begins rapidly at the point of waking and continues beyond it*, is the most likely explanation for the decreases in low frequency power" (p. 85) which is a hallmark of sleep termination. The speed of this transition has been studied in the context of the sleep inertia concept [28]. The clear cut changes in EEG frequency composition, which are related with the state transitions wake-sleep-wake, have also been used for the implementation of computerized methods to detect episodes of wakefulness during sleep or sleep termination [29].

A final aspect of sleep termination is the expectancy to wake up at a given time. Some people claim to be very accurate in timing self-awakening [30]. In an experimental study with actometric measures Moorecroft *et al.* [31] found some indication for the ability to self-awaken at a given time. An endocrinological study by Born *et al.* [32] shed some light on additional factors which seem to be associated with the expectancy to wake up at an anticipated time towards the end of nocturnal sleep. The authors studied the regulation of adrenocorticotropin (ACTH) release in association with sleep termination under three experimental conditions, an early planned awakening, a late planned awakening, and a surprise condition in which sleep was terminated earlier than expected by the subjects. The interesting finding was that the early awakening was preceded by a distinct increase of ACTH within the last hour before waking, while ACTH had a secretion surge only after sleep termination in the surprise condition, where subjects did not expect to be awakened at this time. Thus, the increase of ACTH some time before sleep termination may be one of the adaptive mechanisms, which prepare the organism to transit from sleep into wakefulness at the end of the subjective night.

In summary, sleep-wake transitions are dependent (a) on the circadian phase of the sleep episode with more intrusion of wakefulness and a greater chance for sleep termination in the rising phase of the body temperature cycle, and (b) on the phase of the ultradian NREM-REM sleep cycle with a high

probability to wake up out of REM sleep. This latter factor seems to become effective at least early in development or in situations where the sleeper is shielded against external influences, and *zeitgebers*, while its role may be negligible if sleep is fragmented or unprotected against randomly occurring external influences. The transition from sleep into the wake state is heralded by adaptive mechanisms such as an increase of ACTH, and it is accompanied by typical EEG changes with a decrease of slow wave (delta and theta) activity and an increase of activity in the alpha frequency band.

DISPLACED SLEEP AND IRREGULAR HOURS

If sleep architecture is one major regulator of awakenings, the second major regulator probably is the timing of sleep in relation to circadian phase and prior sleep. The effect is particularly visible in connection with irregular sleep/wake patterns and when comparing such patterns with the reactions to day work.

Most individuals with daytime work tend to use external means to wake up and terminate with some subjective difficulty and with considerable inertia in terms of performance [33]. Awakenings after staying up very late, as after, for example, night work, tend to be spontaneous and "easy", but premature, as compared to night sleep [34]. Sleep is often reduced to 5–6 h. However, even if sleep is prematurely terminated, it appears that it is not disturbed in the sense of an increased number of awakenings. At the opposite extreme, awakenings from sleep before an early start of work are mostly forced through external means, as well as perceived as difficult and unpleasant [35]. However, sleep length is often the same as after going to bed after night work. Awakenings after sleep subsequent to an afternoon shift tend to be mixed but to contain much spontaneous sleep termination.

Similarly, aircrew travelling westward across several time zones will experience premature awakenings [36] i.e. easy awakenings [37], whereas aircrew travelling eastward will experience difficult and forced awakenings [37].

The reason for the different patterns of sleep termination is the relative influence of circadian and homeostatic factors. However, the amount of data is rather scarce since few laboratory studies have permitted sleep to terminate spontaneously. Some information may be gained from awakenings under conditions of spontaneous circadian resynchronisation during isolation experiments. There, the terminating force seems to be circadian–most sleeps tend to terminate on the rising slope of the temperature rhythm, whereas the circadian trough is a zone of "forbidden" awakening [38].

In a study in which sleep was displaced to different times of the 24 h span (23:00 h, 03:00 h, 07:00 h, 11:00 h, 15:00 h, 19:00 h, and 23:00 h) with gradually increasing time awake, it was demonstrated that the circadian rise of rectal temperature was very closely related to sleep termination. However, when sleep was started close after the circadian acrophase (i.e. at 19:00 h) sleep duration exceeded 10 h and did not end until shortly after the circadian trough [39]. Recently, Dijk and Duffy [40] have demonstrated the sensitivity of sleep termination to the first tendency to circadian upswing, immediately after the circadian trough.

In a series of experiments in which circadian phase, time awake or previous duration of sleep have been varied, it was found that the time of day or circadian phase had very strong effects, terminating sleep around the circadian maximum [41]. These effects are, however strongly modified by prior time awake before the start of the sleep, as well as by the amount of prior sleep. Thus, sleep loss will cause a resistance to the circadian rise, delaying termination. This means that sleep will terminate as a compromise between the circadian and the homeostatic influence. This observation is often more dramatic when sleep is started on the circadian rise. Then 8, 4, 2, and 0 h of prior night sleep will cause sleep length to vary between 2 and 4, 5 h [42]. In this study sleep was not terminated until the amount of spectral power density in the delta band (0.5–2.5 Hz) had reached the low levels normally seen around the termination of night sleep. Thus, it appears that the circadian rise is permitted to terminate sleep only after the normal need for delta (stages 3 and 4) sleep had been obtained. During night sleep this level is reached a few hours before final sleep termination [43]. This may cause one to speculate that from a homeostatic point of view night sleep termination is unnecessarily late, very likely due to the sleep maintenance effects of the circadian trough.

Interestingly, the tendency to terminate sleep shows the same circadian pattern as does the tendency to initiate sleep. That is, during daytime sleep will be prematurely terminated, while attempts to start a sleep episode will involve a long latency. At night, sleep latency will be short, whereas sleep termination will be delayed [41].

Considering the difficulties of early rising and the circadian-homeostatic regulation of sleep termination, it is not surprising to see that also performance on awakening is considerably worse after awakenings at the circadian trough [44] and after extended wakefulness [45]. In particular, late night naps during continuous wakefulness involve pronounced inertia in terms of performance and subjective feelings of sluggishness.

The homeostatic and circadian regulation of the subjective ease awakening has an interesting bearing on other aspects of sleep quality. Thus, while it has been demonstrated that sleep termination is easier the closer to the circadian acrophase of body temperature [46], the feeling of being well rested is higher for awakenings close to the acrophase. Intraindividual correlation's showed that being well rested was largely related to the ease of awakening. That is, unless the awakening was easy, one awoke with the impression of not being well rested. The ease of awakening, furthermore, was closely related to the amount of stage Wake and lack of SWS, suggesting that poor sleep would often result in a feeling of being well rested, mainly because the awakening was easy.

The other leg of subjective sleep ratings, sleep quality, maintained a high correlation with sleep efficiency and SWS, which were the main predictors. Thus, we quite frequently found weak negative correlations between subjective sleep quality and being well rested. The two are clearly not the same thing. In fact, a good night's sleep seems to be dominated by SWS, but ended by a certain amount of poor sleep to facilitate the awakening. The relation between the ease of awakening and feeling of well-restedness is likely to break down in insomnia patients, where fatigue is a pronounced trait [47].

There is also a pronounced age effect in the ease of awakening and in feeling well rested after sleep [48]. Somewhat unexpectedly well-restedness improved with age, at least up to 65 years, which was the upper limit in this study of gainfully employed individuals. Again, this feeling was correlated with an ease awakening, and with disturbed sleep. As with insomnia patients the relation probably breaks down in the elderly, but this has not been the subject of investigation yet. In the study cited it was suggested that the beneficial effects were due to the greater degree of diurnal "morningness" that increases with age [49]. This effect, in turn, may be due to an increased sensitivity to the circadian upswing during the day [40]. Interestingly, the difficulties maintaining day sleep after night work increase with age [50], probably also reflecting a decreased ability of the sleep mechanism to resist the sleep terminating influences of the morning circadian upswing.

In summary, spontaneous sleep termination is mainly dependent on the combined effect of circadian and homeostatic influences. The subjective difficulty of awakening reflects the same factors – the circadian trough and sleep loss makes awakenings difficult and non-spontaneous.

AGE CHANGES

Across the life span, night sleep undergoes several age-related modifications, extensively reviewed in a recent meta-analysis [51]. These changes concern the vast majority of sleep parameters, e.g. sleep duration and the amount of REM and NREM sleep, and are particularly prominent during early development [52] and in elderly people [53, 54]. In healthy individuals age is also an important determinant of sleep continuity, which has a major effect on sleep quality and subjective performance during daytime [46, 55, 56].

However, the age-related characteristics of spontaneous awakenings during night sleep as an event *per se* have only recently become a topic of discussion. It is well known that the night sleep of the healthy adult, unless it is perturbed by pathologies (either medical or neuropsychiatric) or by life and environmental circumstances (time displacement of sleep), is characterised by very few interruptions [57]. This is not the case in the extreme ages, that is, infancy and old age.

All psychophysiological studies, regardless of differences in instruments (direct observation, actigraphy, polygraphy) or methodology (time criteria to define behavioral awakenings, ranging from 1 to 5 min), are consistent in finding that the frequency of awakenings in infants is higher than in young adults [58–60].

There have been attempts to look deeper into the developmental course of spontaneous nocturnal awakenings at early ages. Giganti *et al.* [61], in a preliminary study on pre-term infants, showed few changes in the number and duration of awakenings between 34 weeks and the term. After term a pronounced reduction in the number of night awakenings goes along with the increase in the duration of night sleep episodes [62]. This trend is particularly evident across the first year of life [58], with a particular evidence in the second semester [60]. By contrast, the duration of the awakenings, that is, the time spent awake before sleep re-onset, remains constant all along the first

year of life [60]. By the end of the first year of life, night sleep is already much less interrupted than at birth: thereafter, the decrease in the frequency of awakenings continues at a slower rate [63] until it reaches values not far from adulthood.

Williams *et al.* [13] suggested that the number of awakenings starts to increase again already at mid-age: they showed that both women and men in their forties woke up during night sleep more often than women and men in their thirties. This evidence was confirmed in a study on 400 adults aged from 20 to 70 based on sleep logs and actimetry [64]. Also, a slight trend to an increase in the frequency of awakenings was found in a sample of Japanese workers in the age range between 19 and 64 years [65].

Several investigations have reported that in elderly individuals the number of awakenings increases again [66–68]. Awakening at night is one of the most common complaints in subjective sleep diaries of the general population elderly people [69, 70], and is widely reported also by healthy old subjects.

Thus, if we only take into account the number of awakenings, as an index of the sleep consolidation process, we may describe a curvilinear trend with a steep descending slope in the first year of life, a low plateau level across childhood/young adulthood and an ascending slope thereafter, slowly rising in late adulthood and progressively becoming steeper with age.

As a result, infants and elderly subjects tend to wake up with similar frequency during the night: however, it would be hazardous to interpret the two ages as similar to each other.

First of all, a longer duration of the wakefulness following awakenings has been found in old subjects [71, 72]. In an assessment on 25 individuals aged between 60 and 75, whose mean number of night awakenings was 3.9, our group detected a particularly impressive latency to sleep re-onset, much longer than in infants and young adults, also resulting in a significantly higher amount of intra-night wakefulness [25].

Secondly, a peculiarity of the frequency of awakenings in older persons concerns the appearance of wider gender differences. In a study by Webb [73] on healthy individuals between the ages of 50 and 60 years, women reported more frequent awakenings, inconsistent with the evidence of the objective recordings showing twice the level of sleep interruptions in men.

It is worthwhile noticing that in a study over the adult life-span (20–70 years), Hume *et al.* [74] found no "age-gender" interaction for any sleep measure but sleep onset and wake-up time. Awakenings features were not evaluated in Hume *et al.* study, but Webb's data [73] indicate that they might have turned out to be influenced by such an interaction.

Another interesting example of the different psychophysiological features of infants' and elderlies' awakenings regards the state of sleep, which precedes them. In infancy, most of the awakenings emerge from REM sleep [23], although the difference in the likelihood of awakening from the two states is reduced after the sixth month [60]. It has been proposed that also in the young adult REM sleep would have a "gating" role for both final awakening [19] and awakenings during sleep [75]. In the elderly, instead, no preferential association was observed between REM sleep and awakenings, whereas awakenings from Stage 2 were more common [25]. For this reason, both in infants and in the aged, there is a coincidence between the sleep state following sleep onset and the one preceding awakening: however, this is REM for the former and NREM for the latter. Also, the time distribution of the awakenings have a peculiar feature in infants, with the gradual build up of a periodicity which is around 100 min by the end of the first year of life [60].

It is plausible that the changes in the pattern of awakenings, from infancy to adulthood, up to the elderly, may reflect different psychophysiological processes. During early development, the high number and the short duration of awakenings are due to an inability to sustain prolonged and stable states [76] i.e., infants wake up several times per night as a reflection of their polyphasic sleep-wake rhythm, but rapidly fall asleep again since they are unable to sustain wakefulness.

Together with the evidence that successive sleep bouts have a similar internal architecture [77], the rather stable features of night sleep interruptions in infants suggest that they may represent "final awakenings" of each sleep bout. The consolidation with time of both night sleep and day wakefulness [62, 78] could be interpreted as due to the interaction of the emerging homeostatic factors and of the circadian drive.

Elderlies' awakenings, instead, seem to be the expression of a disorganisation of sleep. First, the occurrence of frequent awakenings neither preferentially associated to REM sleep nor to NREM sleep, is likely to imply a marked difficulty in sleep maintenance. In addition, the impressingly long time spent awake after each awakening speak also for an impairment of the sleep re-onset process. Age-related changes in circadian rhythms have been often invoked to explain

the marked increase in the drive to wakefulness during night sleep. These circadian modifications, possibly connected to the changes of many biological rhythms (core body temperature, GH, testosterone, prolactine, progesterone and cortisol secretion), as well as to morphological and functional changes shown in the suprachiasmatic nuclei and in the pineal gland [79], include the decrease in amplitude, the phase advance and the shortening of the period. The latter has been widely documented for body temperature [80, 81], but is not univocally reported with regard to the free-running rest-activity rhythm. If animals and early humans studies have indicated a shortening with age, Dijk and coworkers, studying circadian sleep regulation in the elderly by means of a number of experiments based on the "forced desynchronization" protocol [40, 82], did not find any shortening of the circadian period for the sleep-wake rhythm. Instead, a reduced strength of the circadian signal favouring sleep in the early morning hours was identified. The Authors hypothesize that a factor mediating this reduction is the empoverishment of sleep spindle activity, which is supposed to act with a sleep-maintaining role [83]. Furthermore, the propensity to awaken from sleep advances relative to the body temperature nadir in older people, a change that is opposite to the phase delay of awakening relative to internal circadian rhythms associated with morningness in young people. As a consequence, older people appear to have great difficulty in sustaining sleep after the temperature nadir.

Also homeostatic changes seem to contribute to the age-related changes in awakening features. The modified sleep behaviours over the 24 h, with frequent napping and reduced physical and mental activity, could cause, according to the homeostatic component of the two-process model of sleep regulation [84], a reduction of the sleep pressure in elderly compared to young subjects. This might partly explain the longer sleep latency, the decreased SWS, the higher degree of sleep fragmentation, and above all the difficulties falling asleep again after each awakening.

Although both the circadian and the homeostatic regulation seem to be affected by elderliness, we can agree with Wauquier and Van Sweden [85] that it is not yet possible to indicate which one between process C and process S is primary or secondary. Furthermore, irrespective of changes in sleep regulation, the higher propensity to awakenings of elderly people may as well be the result of anatomical and functional deficits impairing their capability to generate and coordinate stable sleep patterns.

INSOMNIA

Insomnia has been historically defined by patterns of inappropriate wakefulness which occur during the sleep period. Patterns of arousals, awakenings, and wakefulness may also help define patients with insomnia versus excessive sleepiness clinically [86].

Insomnia may be primary or secondary to many medical conditions [87]. Primary (or psychophysiological) insomnia is defined as difficulty falling asleep or maintaining sleep not secondary to any other medical problem or sleep disorder. As such, the defining factor is increased wakefulness. Insomnia is commonly defined as either a sleep onset problem or a sleep maintenance problem. However, little work has systematically looked at patterns of wakefulness and arousal in insomnia patients. In the discussion which follows, awakenings, arousals and wakefulness during sleep are all defined based upon EEG criteria. Unless noted otherwise, awakenings were based upon 30 s epoch scoring using Rechtschaffen and Kales criteria, wakefulness consists of all wake time after the first sleep onset, and arousals were scored based upon the ASDA criteria [88].

Early studies which looked at awakenings in patients reporting insomnia found that the number of awakenings (1-min criterion) was increased [89]. However, such studies predated standard polysomnographic screening of insomnia patients for periodic limb movements and sleep apnea. The inclusion of even a few patients with sleep apnea or periodic limb movements in a group of psychophysiological insomnia patients would result in the appearance of many more arousals and awakenings [86]. As a result, it is still common for reviewers to conclude that patients with primary sleep maintenance insomnia show both an increased number of awakenings and longer duration of awakenings [90]. However, more recent data do not support increased total awakenings in patients with psychophysiological insomnia [91–93].

In three studies done with groups of age, sex, and weight matched primarily sleep maintenance psychophysiological insomnia patients and normal sleepers [91–93], consistent significant increases were found for sleep latency and wake time during sleep in the insomnia patients as compared to normals as expected. Of interest was the fact that the number of awakenings was not significantly greater in the insomnia groups compared to their matched normals. Similarly, a study of geriatric insomnia patients and matched geriatric normal sleepers reported the same result [94]. The arousal index was actually nonsignificantly greater in

the normal groups than in the matched insomnia groups in two of the studies, although no significant differences in arousal index were found in any of the experiments. This implies that insomnia patients have longer awakenings. When the data were examined, it was found that the insomnia patients did have longer awakenings (about 3 min on average) as compared to normal sleepers (about 1.4 min). This indicates that sleep maintenance is not the problem in psychophysiological insomnia. Rather, these insomnia patients always have difficulty falling asleep whether it be at bed time, during a daytime nap, or after an awakening during the night.

In addition to number of awakenings, the distribution of wakefulness across the night in matched groups of insomnia patients and matched normal sleepers was examined in one data set [92]. Obviously, the insomnia patients had more wake time than the normal sleepers. The increased wake time was relatively evenly distributed throughout the night in the normal sleepers but was relatively increased in the insomnia patients in the first two-thirds of the night. The patients with insomnia had 48% of their total wake in the first third of the night (normals had 40%); 34% of their total wake in the second third of the night (normals had 28%); and 18% of their total wake in the final third of the night (normals had 33%).

Total sleep time is reduced in patients with psychophysiological insomnia (it averaged about 6.4 h in the studies cited above compared with 7.3 h in matched normal sleepers). Patients with other sleep disorders who have similar reductions in total sleep time typically are sleepy during the day. One difference is that patients with either obstructive or central sleep apnea or periodic limb movements during sleep have a very different pattern of arousals and awakenings during the night. For example, a group of patients with periodic limb movements had a total sleep time of 6.7 h but had 28 awakenings and an arousal index of 30 (compared to an arousal index of 16 in the insomnia studies cited above) and excessive sleepiness [95].

A random group of 10 patients with sleep apnea were selected from our clinic population (with the constraint that age would be about the same as the insomnia patients) so that patterns of arousal and awakening in obstructive apnea patients could be compared with those patterns in patients with psychophysiological insomnia. Sleep and arousal data averaged from the three insomnia studies discussed above and from the patients with sleep apnea are presented in the table. It can be seen that there are a number of significant differences in sleep in these two groups. Of particular interest is that the sleep apnea patients did not differ significantly from the insomnia patients in sleep latency or in wake time after sleep onset although apnea patients report significant sleepiness during the day while the insomnia patients have great difficulty falling asleep during the day. One of the largest differences between the groups was in the arousal index. Sleep apnea patients also had greatly increased awakenings, but this difference was not significant due to very large variability. Patients with sleep apnea have many shorter awakenings and frequent arousals, compared to insomnia patients (awakenings averaged about 1.5 min in sleep apnea patients and arousals averaged about 1 per min throughout the night).

The high rate of arousals and awakenings produces sleep fragmentation and decreases the restorative function of sleep [96]. Because patients with psychophysiological insomnia have an arousal index that does not differ from that seen in normal young adults, they are less prone to suffer from nonrestorative sleep. In fact, in one study, the pattern of awakenings and arousals seen in actual psychophysiological insomnia patients was produced in normal young adults for 1 week (by using tones to awaken or arouse the normals at the same times that the insomnia patients had awakenings or arousals) with relatively little impact upon the normal sleepers [92]. As such, the pattern of longer awakenings with infrequent arousals found in insomnia patients appears to preserve sleep restoration in comparison with the more frequent arousal pattern seen in patients with sleep apnea.

One other summary paper reported awakenings and stage shifts in normal sleepers, insomnia patients, and patients with sleep apnea [97]. Comparisons to the other studies are difficult because sleep stage data were not presented, 1 min scoring epochs were used, and subjects in the insomnia and apnea groups were older than the normal group. The results differed primarily in that Declerck *et al.* [97] found very few awakenings in their normal sleepers. Their very low number of awakenings probably resulted from the fact that they used a 1-min scoring epoch (and normal sleepers typically have short awakenings while insomnia patients have long awakenings) and the fact that their normal sleepers appeared to be younger than the insomnia patients. Declerck *et al.* [97] found a similar number of awakenings in their insomnia patients and in their sleep apnea patients. They do not present data on the severity of apnea in the apnea patients, but since awakenings were also shorter in apnea patients than in

insomnia patients, the length of the scoring interval could also account for this finding.

In summary, insomnia is defined by increased wakefulness during the night. Patients with insomnia have more difficulty falling asleep as a characteristic trait. As such, psychophysiological insomnia patients take longer to fall asleep after awakenings during the night and therefore accumulated more wake time during the night. However, recent data suggest that these patients may not have increased awakenings and arousals during the night as do patients with sleep apnea or periodic limb movements [91, 93].

IMPAIRED AWAKENING IN SLEEP DISORDERS MEDICINE (INSOMNIA EXCLUDED)

Most healthy subjects can move, think and react appropriately within seconds or at most minutes after the cessation of sleep, regardless of whether awakening is spontaneous or provoked. However, there are different instances of pathological difficulties achieving normal awakening: either after provoked awakening at a time which is generally considered as normal, for instance at the end of the night, between 6:00 and 9:00 a.m.; or after provoked awakening during naps supposed to be refreshing; or after spontaneous arousal in the first third of the night. This chapter will summarize clinical features and results of laboratory tests in each of these situations.

Difficulty achieving normal awakening after provoked awakening at the end of night sleep

Idiopathic hypersomnia

Idiopathic hypersomnia has been first described by Roth *et al*. [98] and Roth [99, 100]. It can be either polysymptomatic or monosymptomatic. The polysymptomatic form is the best identified one with a prolonged major sleep episode, great difficulty waking up in the morning or at the end of a nap, constant or recurrent sleepiness and unrefreshing naps. In comparison the monosymptomatic form is not as well characterised with a major sleep episode of normal duration, no difficulty waking up, constant or recurrent sleepiness, refreshing or non refreshing naps. The great difficulty waking up in the morning or after a nap, also referred to as sleep drunkenness, is typical of the polysymptomatic form. Subjects do not awaken to the ringing of an alarm clock and if the ringing is prolonged they turn it off and return to sleep so that they have to be awakened by family members or friends. Awakening procedure has to be vigorous and repeated. Once out of bed subjects are still confused, very slow, unable to react adequately to external stimuli and it may take up to several hours before they can function adequately. Investigation of these subjects has somewhat turned short in the past. The multiple sleep latency test (MSLT) seems irrelevant or at least insufficient for several reasons. Awakening the subject early in the morning for the MSLT precludes documentation of the prolonged night time sleep, and the MSLT procedure precludes the observation and recording of prolonged, unrefreshing daytime sleep episodes. Moreover the mean sleep latency is not strikingly reduced as it is in narcolepsy or severe sleep apnea syndrome. Hence the need for more adequate investigations.

Continuous polysomnography has the advantage of documenting the total duration of spontaneous sleep and thus of giving a more realistic picture of sleep behaviour in these subjects. Along this line 19 subjects with the polysymptomatic form of idiopathic hypersomnia, 11 females and 8 males, aged 18–57 (median 27) underwent polysomnography. Night 1 was a conventional night with lights off at 22:30 and lights on at 7:30, followed by a MSLT; night 2 and day 2 (18:30–18:30 the next day) served for continuous polysomnography with the subject free to lie in bed, sit at a table or make a few steps in the room at his own convenience.

Results are disclosed on Table 2. From these results it is clear that subjects did not show a severe propensity to fall asleep (mean sleep latency $= 10.4 \pm 3.8$). On the other hand total sleep time on night 2 and on night 2 and day 2 was extremely prolonged thus showing an enormous propensity of these subjects to sleep or an inability to terminate sleep. Yet this procedure investigated sleep rather than awakening hence the need to resort to other strategies.

According to the two-process model of sleep regulation the difficulty to achieve normal awakening could be the result of any combination of prolonged decline of process S, delayed or insufficient rising of process C or abnormality of process W.

To date the homeostatic process in hypersomnia patients has not yet been investigated. Results of a recent study of both melatonine and cortisol secretion in idiopathic hypersomnia are indicative of a phase delay of melatonine and cortisol rhythms in this condition [101]. Finally Sangal and Sangal [102] used

cognitive evoked potentials (P300) measures and showed that subjects with idiopathic hypersomnia had longer auditory P300 latency than normals and smaller auditory P300 amplitude than narcoleptic patients, e.g. cognitive evoked potential evidence of cognitive dysfunction.

Delayed sleep phase syndrome

Delayed sleep phase syndrome is a disorder in which the major sleep episode is delayed in relation to the desired clock time [103]. It is characterized by sleep-onset and wake times that are much later than desired, little or no difficulty in maintaining sleep once sleep has begun, extreme difficulty awaking at the desired time in the morning, and a relatively severe to absolute inability to advance the sleep phase to earlier hours by enforcing conventional sleep and wake times.

When patients are recorded at a conventional time (23:00–7:00) the sleep latency is prolonged and the patients experience difficulty in awakening. A multiple sleep latency test performed after such a sleep period can show shorter sleep latencies in the morning naps compared to the afternoon naps [11].

Difficulty achieving normal awakening after provoked awakening during naps supposed to be refreshing: the example of narcolepsy

Narcolepsy is characterised by a set of clinical symptoms including abnormal sleep features, excessive daytime sleepiness, overwhelming episodes of sleep, hypnagogic hallucinations, disturbed nocturnal sleep and manifestations of paroxysmal muscle weakness, cataplexy and sleep paralysis. Characteristically patients wake up refreshed at the end of overwhelming episodes of sleep and there is a refractory period of one to several hours before the next episode occurs. Because of this feature short daytime naps evenly distributed throughout the day are recommended as a therapeutic measure.

However one study [104] found evidence for sleep inertia following brief episodes of drowsiness and light sleep. A later study of scheduled naps and performance [105] was designed both to investigate the efficiency of napping strategies in narcolepsy and to investigate sleep inertia effects associated with daytime naps. This study included five short naps spaced equidistantly throughout the waking period or a single long afternoon nap scheduled 180 degrees out of phase with the nocturnal midsleep time. Most interestingly short naps were accompanied by sleep inertia in narcoleptics with the exception of the first short nap which was not followed by sleep inertia. Sleep inertia was maximum after arousals from stages 3 and 4 NREM sleep. Conversely sleep inertia was completely absent following the single long nap.

Difficulty achieving normal awakening after spontaneous arousal in the first third of the night

Arousal disorders: confusional arousals, sleep walking and sleep terrors are three different parasomnias grouped together because impaired arousal from stages 3 and 4 has been postulated as a common cause [106]. Confusional arousals occur during and following arousals from stages 3 and 4 NREM sleep, most commonly in the first third of the night. Sleep walking consists of a series of complex behaviors initiated during stages 3 and 4 and sleep terrors manifest as a sudden arousal from stages 3 and 4 accompanied by autonomic and behavioral manifestations of intense fear. Pathophysiologically these entities represent incomplete awakenings from sleep, most commonly deep NREM sleep, leading to intensification of the normal period of sleep inertia before full wakefulness is evident.

In conclusion, difficulty achieving normal awakening is a feature of different sleep disorders. However not a single mechanism seems to be involved. In idiopathic hypersomnia the great difficulty waking up comes after a very long period of sleep, and may be explained in terms of either abnormal homeostatic or circadian process of sleep. In the sleep delayed phase syndrome the difficulty waking up is clearly related to an abnormality of the circadian rhythm of sleep which is phase delayed and the time of provoked awakening does not correspond to the normal time of awakening for these subjects. In narcolepsy the difficulty waking up is a typical manifestation of sleep inertia, maximum after arousals from stages 3 and 4 NREM sleep, but also present after arousals from stage 2 NREM sleep. In NREM sleep parasomnias, the so-called disorders of arousal, the difficulty coming to complete awakening is obviously linked with a spontaneous and incomplete awakening from stages 3 or 4 and sets the stage to abnormal autonomic nervous system changes and skeletal muscle activity.

Oneiric activities versus dreams in nocturnal awakenings

The sleep disorders clinic can in a sense, be viewed as a clinic of nocturnal awakenings. Within the framework

of sleep disorders, nocturnal awakenings (or sleep-stallings) vary greatly. To examine sleep disorders from the angle of nocturnal awakenings one needs to consider the physiological components of sleep as well as the mental processes which accompany them. We will concentrate on the adult patient's mental sleeping content. We will choose for our case two opposed groups of awakenings: nightmares due to anxiety or post-traumatic dreams, and night terrors and sleep-walking. Here we refer to a review of the literature and to our clinical personal experience since 1971 with patients treated at our sleep disorders center.

In this chapter we intend to show that dealing with patients with these sleep disorders is dealing with various types of psychic activities: some are dreams (a specific form of thinking), some are not dreams, which we will call "oneiric" for lack of a better word. *Oneiric* experiences, as we will see, are psychic activities which do not follow the classical *Freudian* dream model.

A simultaneous examination of the way in which psychoanalysts take interest in sleep and in the sleeping mind, and of the clinical approach of sleep medicine could be useful. Clearly, a study of the psychoanalytical point of view of the sleeping mind must also take into account current knowledge on sleep neurophysiology [107, 108] as well as on mental processes during sleep and upon awakening from different stages [109, 110]. As our subject here is sleep pathology, we will only recall in a few words that experimental and cognitive psychology investigations, on dream-sleep-memory relationships, have shown that mental activity continues throughout all sleep stages, all night long [111, 112]. Psychophysiological research findings indicate that dreaming occurs in all sleep phases and not only in REM episodes [113–118]. The mental activities of sleep varies within sleep stages and with the time of night. With different rates of recall, and under diverse guises, dream reports can be obtained througout all sleep stages after awakening the subject.

The classical Freudian dream work mechanisms. Freud's works have been reconsidered in the light of present-day neurobiology [119, 108]. They have come under hard criticism. Yet for example, the creation of *Neuro-Psychoanalysis*, "An interdisciplinary Journal for Psychoanalysis and the Neurosciences", shows how interesting and lively is the discussion.

We will intentionally simplify the summary of the psychoanalytical arguments. The freudian theory, a cognitive description of the psychic processes, taught us that dream is the product of a work of transformational processes of thoughts, which use different mechanisms (displacement, condensation, pictorial representation . . .). Freud calls "dream work" the psychic mechanisms of transformations through which is performed the passage of the *latent content*, the thoughts of the dream, to the *manifest content*, the recall (or the report) of the dream after the night [120]. Freud distinguishes between three mental systems: Conscious, Preconscious and Unconscious, with shields – protective fields – separating them. His topographic-economic model is a logical outcome of the application of the method of free-association to the analysis of dream experiences [120, 121]. This method followed a fundamental rule: the patient had to say what was passing through his mind, however absurd, immoral or painful it seemed.

We would picture the situation which leads to the formation of dreams as follows: Dreams accomplish a function of guarding sleep. Dreams allows the sleeper to continue sleeping while playing with a pair of opposites: the wish to sleep versus unconscious wishes (latent thoughts). The dream finds its energy, its source, from the strength of unconscious wish. The conflict is between the wish to sleep and the wishes or affects which threaten to waken the sleeper. Dream is the guardian of sleep, but to be this guardian it must also guard itself: protect the global sleep. If the dream is disturbed, the dream disrupts sleep. Thus, the hallucinatory reinterpretation, distorting and deforming elaboration, builds up a façade to the dream. Through the work of the dream, the psychical activity of the sleeper changes and transforms itself, but does not stop. The censorship holds the dream, which the quietude of sleep and prevent the irruption of anxiety.

Out of this model, we will use only the description of the mechanisms of dream formation, in other words the explanation of the dreaming production and we will stay away from dream interpretation.

As we saw above, the mind never rests during sleep. However, this does not mean that mental events during sleep are always organized to form a dream. The dream is not the sole psychic activity of the sleeper. Thus, within the field of clinic of awakenings, *dreams* (here illustrated by *nightmares*), and *oneiric activities* (*night terrors and sleepwalking* serving as examples) need to be carefully identified [122]. The use made of the word *oneiric* refers to mental activities experienced during sleepwalking or night terrors, which are well-known nosological entities in the field of sleep medicine.

In dream-anxiety attacks and post-traumatic nightmares, *true dreams are experienced*. The *nightmare*, a frightening dream with a feeling of a lived-in situation that awakens the sleeper, generally arises from REM

sleep or from stage 2 of the end of the nigh. Awakened by a nightmare, the patient is fully awake and completely conscious with immediate dream recall. "Exiting" from sleep does not pose any problem [123, 124].

Traumatic nightmares and sleep disturbances are clinical effects of major stressing events [125]. The dream replays the traumatic event over and over again, with a heavy emotional load and a corporal participation, causing awakeness in terror, with consciousness, and without amnesia. *Post-traumatic nightmare*s, occur mainly outside of REM sleep, sooner (1:00–3:00 a.m.) than typical anxiety dreams [126–128].

Dreaming is one of the most complex forms of life and should not endanger sleep, but preserve it [120, 121]. However, a nightmare, a proper dream, fails to contain the emotional surge and to maintain, at the same time, the continuity of sleep and the sleeping psychical life [122]. From Freud's structural model of sleeping mind, nightmares are a failure of the normal pattern of dream, located at the border between Unconscious and Preconscious systems. The dreamed psychic situation becomes incompatible with sleep. The dreamer cannot "keep" his hallucination and is no longer capable of continuing to use dream mechanisms. Awakening ends dreaming and the sleep episode.

Sleep terrors and sleepwalking are much less frequent (but similar) in adults than in children. These disorders are related to a disorder of arousal [106, 129]. They occur at precise times, out from the deepest NREM sleep (a shift from stage 4 to arousal), early at night, with increased motor tone or motor activity. Sleeep is pertubed but not to the extent of full awakening. There is a severe cognitive dysfunction and no conscious awakening. In other words, sleep will not give way to wakefulness (the ability of the sleepwalker to fall asleep soon after an episode, without reaching alertness at any point, is striking).

Adult sleepwalkers usually have some vague memories, the contents of which usually concerns a theme of imminent catastrophe with a need to escape, or a suggestion to move [130]. In sleep terror, mental content report, hard to verbalize, is made of a single unelaborated scene which lacks human beings; generally there is a lone terrifying vision accompanied by intense anxiety [131].

As Jouvet wrote [132]: " . . . sleepwalking is a good example of lack of psychoneural correlation which could call the neurobiologist to more humility", adding further: "Neurobiology (and specially clinical neurophysiology) must admit that the relations between sleep and conscience are ambiguous".

The main point is that the intrapsychic state of the sleeper suffering from one of such arousal disorders does not allow the same work of psychic elaboration as with classical dreams [122, 133]. The structural organization of mental experiences, although assessed on an intuitive basis of clinical observations, seems to indicate that the cognitive features of mental production (less effective information processing) vary with respect to the situation of a nightmare production.

Seen from the angle of psychoanalytical processes, the hallucinatory mechanism is short-circuited; sleep terrors and sleepwalking episodes are the result of an extensive rupture of the protective barrier mechanisms (psychological formations seen as a number of filters) into and out of the Unconscious [134–136]. There is absolutely no dream-work involved in these disorders. They are not dreams, but oneiric activities. Such oneiric activities are not experienced as a dream.

It seems that, in the case of a nightmare, dream-anxiety attacks or post-traumatic nightmares, the dreamer cannot continue his hallucination and cannot escape from awakening, when in sleep terror or in sleepwalking the sleeper cannot escape from sleep; the work of psychic elaboration here follows other standards than classical dreams. Both cases end in awakening, but the dynamics of each are completely different: their mechanisms are diametrically opposed. Most likely, these two types of disturbances are even incompatible: they are both very rarely found together in the same patient.

Practice Points

1. Human subjects awake preferentially at the end of REM sleep and the preparedness to awake increases with the rank number of the sleep cycle and with higher position of the circadian morning upswing of the body temperature rhythm. Elderly awake from REM as well as from NREM sleep and earlier since the nadir of the temperature.
2. Awakenings after day sleep finished in the early morning is usually the most difficult and those during the day time the easiest.
3. Insomnia patients differ from normals in the amount of total wake – not the number of awakenings.
4. Sleep inertia is abnormally strong in subjects with the polysymptomatic form of idiopathic hypersomnia.

5. Being well rested is to a large extent a matter of ease awakening and reduced stage 3 and 4 sleep, and carries very little relation to subjective sleep quality.
6. Features of awakenings may have a different impact on objective and subjective sleep quality according to age.
7. Excessive propensity to fall asleep and inability to terminate sleep are two different features of hypersomnia.
8. Sleep quality and dream activity are indissociable.

Research Agenda

1. The distribution of spontaneous awakenings within NREM-REM cycles should be studied in patients with sleep disorders.
2. The sleep periods immediately preceding spontaneous awakenings should be investigated in order to identify the sequences of physiological events taking part in the awakening process.
3. Hypothalamic–mesencephalic interactions during awakening should be investigated.
4. More research is needed on life conditions effects on physiological activities leading to awakening in babies and in elderly subjects.
5. The excessive propensity to fall asleep and the inability to terminate sleep need closer study, both from a clinical perspective and to understand sleep inertia in more general terms. Cognitive ERP(300) may be one important instrument in this work.

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