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PSYCHOLOGY, PHYSIOLOGY AND CLINIC OF THE AWAKENING

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Abstract

Although sleep has been received a great interest by scientists, the transition from sleep to wakefulness has been scarcely investigated. The criteria to define awakening and to distinguish it from other similar events are a debated topic. Number and duration of awakenings modify across the life span. Also the sleep state preceding the awakening changes through the life.

Pathology is among the factors that contribute to modify awakenings: Parkinson's and Alzheimer's diseases were found to increase their frequency. Behavioural events, mood changes and mental processes accompanying the awakening are mentioned. Sleep inertia and cognitive performances after the awakening differ as a function of prior sleep duration, sleep state preceding the awakening, time of day and type of the task.

Some individuals refer to be able to awake spontaneously at predetermined time: this ability was objectively investigated through polygraphic and actigraphic recordings. Psychological and physiological factors underlying this ability were suggested and remain to be further investigated.

Concepts

Every one each day has a subjective experience of awakening. This event in the past decades received by scientists relatively scarce attention as compared to sleep.

What is awakening? According to RECHTSCHAFFEN and KALES contiguous epochs scored awake with less than 10 seconds intervening sleep were counted as one "awakening"; awakenings were not scored on the basis of submental EMG changes alone. More recently a new terminology was introduced concerning a "similar" condition: arousal. Criteria which should distinguish the two have been discussed (ÅKERSTEDT et al. 2002, SALZARULO and FICCA 2002). We take this distinction: awakening is a "true" change of state, whereas arousal is a short lasting "instability" of the central nervous system (CNS) activity. It is interesting to observe that there could be some continuity between the two, at least temporal. For example, some authors (THACH and LIJOWSKA 1996) proposed for infants studies the term "arousal" involving physiological events (sighs and trashing) necessarily preceding a "full arousal" indicated as "awakening". Also CHUGH and colleagues (1996) in the adult see arousal as a phenomenon preceding the awakening. As a support to the separation between arousal and awakening SCHER et al. (1992) suggest different mechanisms involved in each. An interesting source of information contributing to clarify the differences (or similarities) between the two could come from the analysis of the developmental trend of awakening and that of arousal. Do they show similar or different changes with age? Whereas modifications of number and duration of awakenings across the life span have been well documented in the literature (FICCA et al. 1999, FAGIOLI et al. 2002, WEBB and CAMPBELL 1980, GARMA et al. 1981), unfortunately changes of arousal were scarcely investigated.

Since awakening implies the transition between two different states (sleep and wakefulness), as a consequence it is necessary to clearly identify the specific features of the two. If states are not identified, or only one is present, there is no transition but only the end of a state.

Which are the criteria to define and to distinguish sleep and wakefulness? In which cases these states do not exist?

Before 24-28 weeks of postconceptional age infants are in a condition called “indefinite sleep” (DREYFUS-BRISAC 1974) characterized by continuous motility. Progressively, physiological and behavioural activities synchronise to coalesce into different states lasting for a certain time. Namely, between 27 and 30 weeks of postconceptional age, throughout EEG and rapid eye movemets recordings (CURZI-DASCALOVA et al. 1993) and the observation of behavioural variables as eyes’ opening/closure and body movements (PARMELEE and STERN 1972), it is possible to distinguish different behavioural states: active sleep and quiet sleep. Periods in which physiological and behavioural activities are poorly organised in pattern, are named “indeterminate sleep”.

PRECHTL and co-workers (PRECHTL 1974, NIJHUIS et al. 1984) taking into account eye movements, body movements, and hearth rate consider 36-38 weeks of postconceptional age the time for the emergence of behavioural states.

When waking state does firstly appear? HOPKINS (2002) complains that the early development of the characteristic of waking state is a “neglected topic”. According to behavioural criteria, STEFANSKI and colleagues (1984) identify waking state in preterm infants from 30 weeks of postconceptional age on, whereas taking into account physiological and behavioural criteria CURZI DASCALOVA and MIRMIRAN (1996) identified waking from 35 weeks of postconecptional age on.

In infants, observed after term age , two kinds of wakefulness were identified: of "necessity" (a primitive kind of waking) and of "choice" (KLEITMAN 1963). More recently WOLFF (1987) distinguished in infants, observed during the first six months of life, three types of wakefulness: "waking activity", "alert inactivity" and "alert activity" which differ across development. According to HOPKINS (2002) at two months wakefulness becomes a real "behavioural state", which implies that a "true" awakening could be detected from that age on.

For the elderly the characteristics of waking were less investigated, while we know that in same cases particular EEG features make difficult to catch the transition between sleep and waking (LAIRY et al. 1962).

Animal data

As previously mentioned, both cortical arousal activation and behavioural components contribute to the awakening. Cortical arousal is detected by electroencephalographic desynchronization and implies also a general increase of electrical activity and excitability of sensory and motor system. Information about structure (mainly subcortical ones) regulating cortical arousal were collected in animals. In particular, the "activating system" includes neurons located in the midbrain reticular formation projecting to the thalamus and to the cerebral cortex (STERIADE et al. 1993). In the thalamus the role of intralaminar nuclei during transition from sleep to wakefulness previously shown by GLENN and STERIADE (1982), was recently confirmed by MARIOTTI et al., (1998). At the awakening also c-fos and other immediate-early genes are activated, probably representing the molecular correlates of electrophysiological activation (Cirelli and Tononi 2000).

How often, when do we awake and how

The number of night awakenings modifies across the life span (Figure 1).

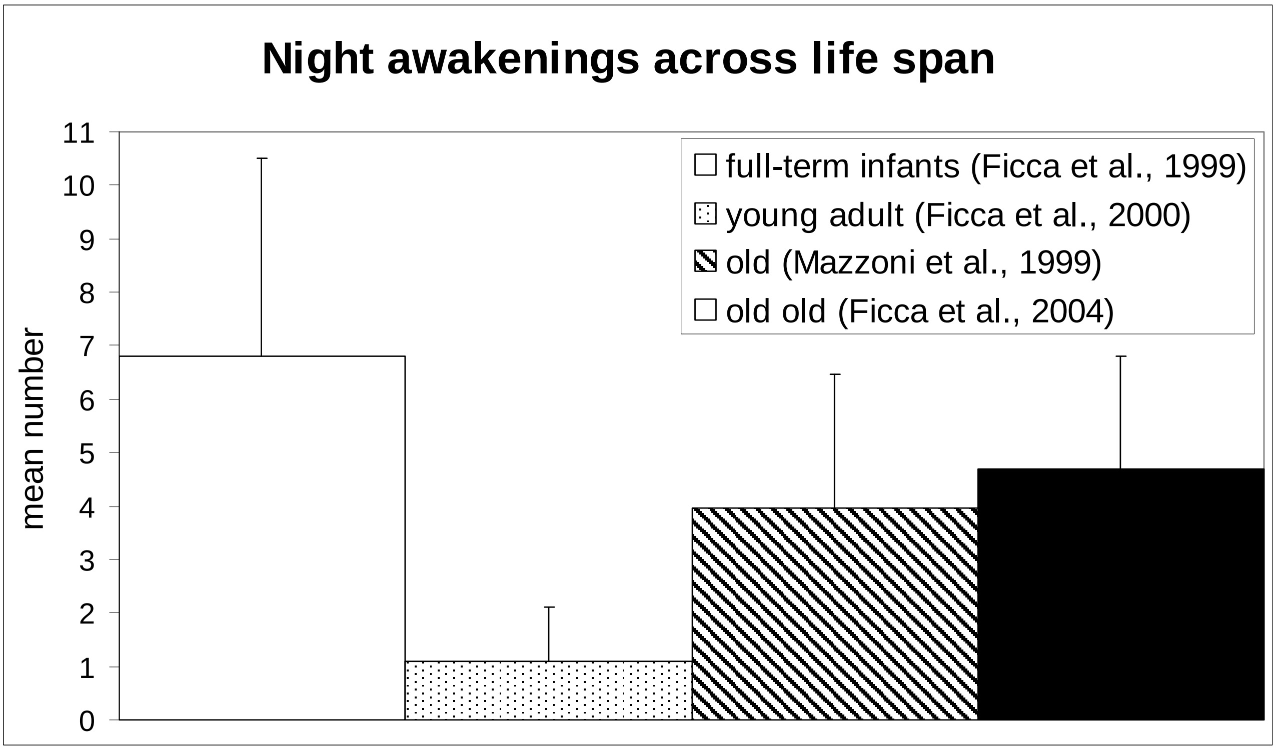

Figure 1: Number of nocturnal awakening across life span

Early after birth the number of night awakenings is high: from 4 to 14 according to different studies using different methodology to detect them (Fagioli et al. 2002). During the first year of life the number of nocturnal awakenings progressively decreases; in young adult there is about one awakening per night. Nocturnal awakenings increase again in the elderly who awake about 4-5 times for night. Although in both infants and elderly the number of awakenings is higher than in the young adult, it is important to remark that these modifications reflect different physiological processes. During early development frequent sleep-wake transitions reflect the immaturity of CNS to maintain for long period a behavioural state, while in the elderly night awakenings reflect the fragility of sleep and the inability of CNS to sustain a stable condition, due to a condition of "functional uncertainty" (SALZARULO et al. 1997).

According to age, "when" is changing across the 24-hour in relation to both the number of sleep episodes over 24 hours and the trend of other physiological activities, like temperature.

The model by BORBELY et al (BORBELY 1982, DAAN et al. 1984, ACHERMANN and BORBELY 1990) for the adult is able to foresee the one/day awakening in the morning. According to this model, the time of sleep onset and that of sleep ending are the result of the interaction between a homeostatic and a circadian component (called S Process and C Process respectively). The S Process is the expression of sleep pressure and progressively increases during waking period, whereas C process fluctuates during the day with a maximum in the afternoon and a minimum in the early morning and it is well represented by body temperature time course. When the increasing S process meets the decreasing C process subjects fall asleep, whereas when the decreasing S process (expressed by the decreasing trend of slow wave activity during sleep) meets the increasing C process subjects awake.

It is difficult to evaluate whether this model can be applied also to the early stages of life. We know that some circadian rhythms as that of hearth rate, of temperature and of melatonin secretion become established during the first months of post-natal life and their amplitude progressively increases (FAGIOLI and SALZARULO 1985, GULLEMINAULT et al. 1996, SADEH 2007). As far as the homeostatic component is concerned, a sketch of the decreasing trend of slow activity was found already from the first weeks of post-natal age (BES et al. 1994). In addition, in the first months of post-natal age several sleep and waking episodes alternate across the 24 hour period (KLEITMAN 1963, COONS 1987).

An adaptation of BORBELY'S model to the first steps of development was proposed by FAGIOLI and colleagues (2002). These authors suggest that the numerous awakenings during night sleep and the numerous naps during the daytime could be understood in the framework of the two –process model by BORBELY. Namely, the "rise rate" of the S Process during waking and its "decay rate" during sleep would be faster in infants than in adults; the maximum amount of S process (sleep pressure) sustainable during waking would be lower in infants than in adults; the C process fluctuation would be less ample in infants than in adults taking into account the lower amplitude of the circadian rhythms. Only when homeostatic and circadian components are fully developed, awakenings could be reduced in number and delimited in time.

As previously mentioned, in the elderly awakening often increases in number; the morning awakening is anticipated and, in addition, is much closer to the temperature nadir than in young adults (DIJK and DUFFY, 1999). Difficulties in maintaining sleep could explain the last result.

Polygraphic studies showed some differences between age groups concerning the sleep pattern preceding the awakening Figure 2.

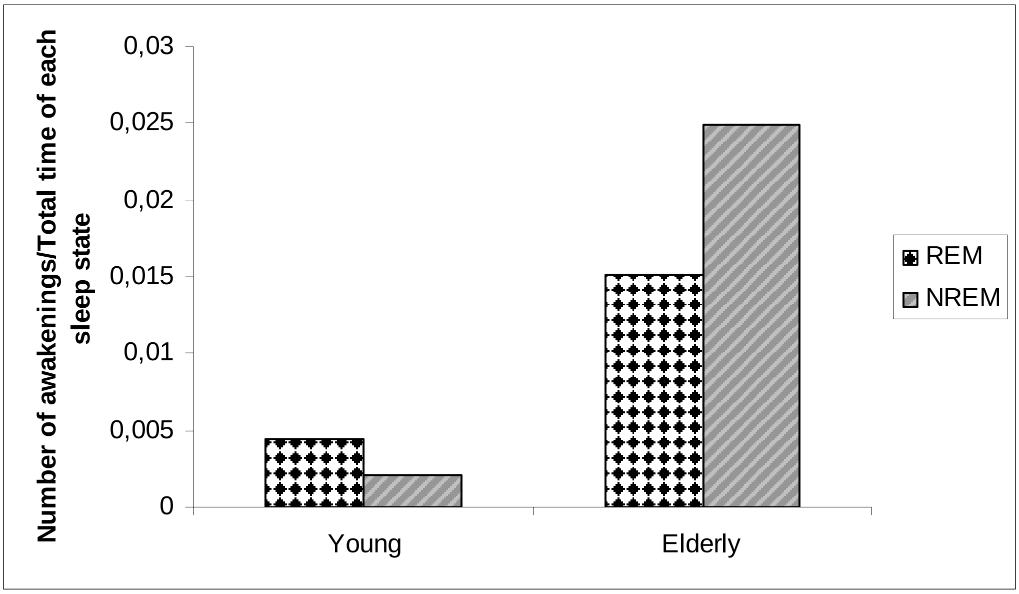

Figure 2: Number of awakenings/total time of each sleep state in young and old subjects.

REM sleep is the prevalent pattern in both babies (SCHULZ et al. 1985) and young adults (SCHULZ and ZULLEY 1980), while NREM sleep, mainly stage 2, is often preceding awakening in the elderly (SALZARULO et al. 1999).

It is interesting to remark that old subjects with sleep efficiency above the median awake more likely from REM sleep than old subjects with lower sleep efficiency (MURPHY et al. 2000). This result confirms differences across age in state preceding the awakening and led to hypothesize that sleep efficiency can be among the factors modulating the relationship between awakening and the sleep state preceding it.

The time course of individual physiological activities before awakening which could give information of the progressive versus abrupt change from sleep to wake, has been scarcely investigated. In babies Zampi et al. (2002) showed that the level of EEG activation before the awakening is high along all the minutes preceding the awakening from REM sleep, whereas it increases before the awakening in the last minutes of NREM sleep. These results suggest that a high level of EEG activity is necessary for the spontaneous awakening whatever the sleep state preceding it, while it does not lead necessarily to the awakening since in REM it is already high several minutes before awakening.

In the adult a decrease of delta and theta EEG power and an increase of alpha EEG power were reported in the transition from sleep to waking, that is “a loss of hypersynchronization, which begins rapidly at the point of waking and continues beyond it” (Ogilvie and Simons 1992, p.85).

The night-time course of adrenocorticotropin (ACTH) has been investigated (Born et al. 1999). The authors evaluated the ACTH’s time course under three experimental conditions: a) an early planned awakening, b) a late planned awakening and c) an induced awakening performed by the experimenter earlier than expected by the subject. Results showed that ACTH increases at the time of awakening in a) condition, within an hour before early awakening in b) condition and only after sleep ending when the early awakening is unexpected (c) condition). The raise of ACTH before awakening can be a significant internal mechanism in order to prepare the individual to awake.

In the elderly, studies investigating body movements during the nocturnal sleep (Gori et al. 2004, Giganti et al. 2008) showed that the number of movements is reduced compared to young adults; the probability to awake after a body movement is higher in old subjects than in the young ones, thus confirming the fragility of sleep at advanced ages.

In young adults the REM density in those REM phases which are followed by an awakening (REM-W) is higher than in those followed by NREM sleep (REM-N) (Barbato et al. 1994). A recent study (Ficca et al. 2004), investigating rapid eye movements activity before spontaneous awakening in old and very old subjects reported no significant differences between REM density of REM-W and that of REM-N.

Behaviour after the awakening

The final awakening in humans is usually accompanied by behavioural events, subjective feelings, mood changes and mental processes.

Among behaviours, the yawning is a frequent event after the awakening, often accompanied by stretching (PROVINE 2005). Whereas many authors proposed yawning as a way to enhance the vigilance level (BAENNINGER 1997, DAQUIN et al. 2001, WALUSINSKI and DEPUTTE 2004, PROVINE 2005), the role of stretching has been less investigated. Yawning occurs also before sleep onset (in this case frequency of stretching is low): this suggests that it is a behaviour involved in the sleep- wake transitions and vice-versa rather than just in awakening.

Bad or good mood can accompany the final awakening; the characteristics of sleep could be among the factors which contribute to modulate the quality of mood. KRAMER et al., (1976) reported happiness feeling at the awakening when the beginning of sleep is delayed and the sleep-wake rhythm is desynchronized with respect to the temperature rhythm. The role of sleep state preceding the awakening on mood is not clear by now. KRAMER and colleagues (1976) investigated the role of NREM sleep and more recently DINGES (1989) took into account the effect of afternoon naps. Qualities changes of mood after afternoon awakenings has been previously mentioned by KLEITMAN (1963) and considered an aspect of the “sleep inertia” (see below), possibly linked to the amount of slow wave sleep preceding the awakening.

Cognitive processes and performances after awakening were widely examined (for a review see TASSI and MUZET 2000). After the awakening there is a period named *sleep inertia* (LUBIN et al. 1976): at that time cognitive performances are reduced and the vigilance level is very low. The duration of sleep inertia rarely exceeds 30 minutes (DINGES et al. 1987); it can be longer after sleep deprivation (NAITOH 1981, HASLAM 1985). The characteristics of sleep inertia differ as a function of several factors such as prior sleep duration, sleep stage preceding the awakening, time of day and type of task. Surprisingly, sleep inertia is more pronounced after shorter naps (20 min) than longer ones (50 min) (STAMPI et al. 1990), but this difference is modulated by the sleep stage preceding the awakening. Sleep inertia was the most intense when awakening is preceded by slow wave sleep (WEBB and AGNEW 1964, FELTIN and BROUGHTON 1968, BONNET 1985) and when awakening is abrupt. In addition sleep inertia is more pronounced when subjects awake near the nadir of the core body temperature (DINGES et al. 1985, LAVIE and WELER 1989). However, many features previously mentioned are modulated by the type of the task. In general, in normal sleep-wake schedules, sleep inertia seems to affect the speed at which the subjects perform the task, rather than its accuracy (TASSI and MUZET 2000).

Awakenings changes and pathology

In an old study (SALZARULO et al. 1968), conducted in small group of Parkinson patients submitted to polygraphic recording of nocturnal sleep, we showed that they did not awake more frequently during the night than healthy subjects, except patients who complained for sleep disturbances as insomnia. In a more recent study (MERLINI et al. 1998) investigating sleep features throughout a sleep diary, Parkinson patients showed a number of night awakenings higher than in healthy subjects. A community based survey evaluating sleep disorders in Parkinson patients (Tandberg et al. 1998) showed that the percentage of patients showing sleep fragmentation is approximately three times more than that of healthy control subjects (39.9% versus 12%). A further research (Wetter et al. 2000) investigating sleep in 10 drug-free Parkinson patients throughout polysomnographic recordings, found more frequent awakenings and greater overall wake time in patients than in controls. It is important to remark that dopaminergic treatment is shown to produce negative effects on sleep, with an increase in the number of awakenings (Brunner et al. 2002).

Patients with Alzheimer's disease (AD) were known to awake frequently during the night, however the morning awakening time does not differ from that of control subjects of the same age (Wahbeh et al. 2008). The effect of pathology seems to concern more the frequency of the awakenings (i.e. those interrupting sleep) than its circadian distribution (i.e. the final morning awakening). Saltin and cowerkers (1995) recorded locomotor activity in AD and control healthy subjects through a portable piezoelectric activity monitor, and reported a greater amount of nocturnal activity (corresponding to a fragmented night sleep) in AD than in control subjects; they suggest that the difference may be partially due to the circadian rhythm dysfunction of AD (Bliwise 1993, Van Gool and Mirmiran 1986, Van Someren et al. 1993).

Self- planned awakening

The ability to self awaken at a predetermined time has been investigated for long using subjects' reports: 10 to 50% of subjects (depending among other causes by the criteria) show this ability. Lavie (1979) investigated through polygraphic recordings subjects selected for their ability to awake at a predetermined time and reported 66% of success. These results agree with previous ones (49 % of success) obtained among unselected subjects (OMWAKE and LORANZ 1933). The accuracy of awakening varies according to the studies: 10% of awakening exactly at time (OMWAKE and LORANZ 1933), 31% of awakenings within 10 minutes of the target among unselected subjects (ZUNG and WILSON 1971) and 50 % of awakenings within 7 minutes of the target among selected subjects (MOORECROFT et al. 1997).

What is helping to wake-up at a predetermined time? Mechanism involved are not much clear: psychological disposition and mental process (for ex. pre-sleep visual representation of time to awake; sub-vocally repetitions; dream inclusion of the time to wake up) have been suggested, while the physiological mechanisms (kinds of sleep features, motility level, chemical substances secretion during sleep) remain to be further explored. Some factors related to the experimental setting, as to leave the subjects to choose their own target time or as sleeping in a familiar setting (MOORECROFT et al. 1997) seem to be useful to achieve the task successfully. Also the age can contribute: among young adult older subjects were found to be more successful than younger ones (MOORECROFT et al. 1997).

A recent study comparing the time-course of motility in subjects who successfully performed the task of awakening at a pre-determined time in advance compared to the habitual one and subjects who did not, found a linear increase of motility throughout both baseline (ABOUDAN et al. 2008) and experimental night (unpublished data) only in successful subjects. The increasing motility during sleep could express a well organized sleep which could facilitate the awakening at a desired time.

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