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Early steps of awakening process

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Abstract

This paper summarizes the main aspects of sleep and waking development and shows results about awakening as a function of age. Awakenings come mainly from active sleep and their number decreases with age. Understanding the awakening process should take into account the development of sleep and waking states and of circadian rhythms and homeostatic processes.

Keywords: Awakening; Sleep; Preterm; Infants; Wakefulness; Arousal

1. Introduction

This paper deals with awakening. In the literature, the term arousal is often used synonymous to 'awakening': this has been discussed recently (see Ref. [1]). We believe that 'arousal' should be used to indicate a transient change of the activation level within a sleep episode, while 'awakening' corresponds to a transition between sleep and wakefulness, i.e. a clear discontinuity of an ongoing sleep episode, sometimes its end.

In the adult, spontaneous awakening depends on the combined effect of circadian (greater chance for sleep termination in the rising phase of body temperature) and homeostatic influences and on the phase of the ultradian non-rapid eye movement–rapid eye movement (NREM–REM) cycle with high probability to wake up out of REM sleep [2].

For a correct approach to developmental studies, one should acknowledge first that sleep and wakefulness progressively acquire distinct features. Thus, early steps of awakening are closely dependent on the development of both sleep and wakefulness and on the characteristics of the temporal distribution of several physiological activities.

In this paper, we will first shortly summarize the main aspects of sleep and wake development; second, we will examine the results about awakening as a function of age. Finally, we will discuss obscure and missing points and suggest further lines of investigation.

2. Development of sleep–wake cycle

Dreyfus-Brisac [3] named 'indefinite sleep' a pattern characterized by continuous motility, which can be found at 24–28 weeks of conceptional age (CA); she also showed that active sleep can be found only from 28–30 weeks of CA onwards. Curzi-Dascalova et al. [4], using electroencephalography (EEG) and REMs only, found 'active sleep, quiet sleep and indeterminate sleep' only from 27 to 30 weeks of gestational age onwards. Using behavioural variables (eyes open/closed; body movements), Parmelee and Stern [5] suggested that at 30 weeks active sleep, quiet sleep and indeterminate sleep could be identified.

Both humans and animals display large amount of indeterminate sleep (as it is called in the infants, or 'seismic sleep' in the animal), which represents poorly organized brain and behaviour patterns [6]. The selection of the behavioural and physiological variables is very critical to answer the basic questions, such as when sleep states first appear in human ontogenesis. The progressive coalescence of several physiological and behavioural activities contributing to the states was shown by Parmelee and Stern [5]. Body and eye movements are the first reliable indicators of states after 28 weeks, whereas respiration rate and EEG become reliable only after 32 weeks, followed by chin electromyogram (EMG).

After term birth, quiet sleep increases and active sleep decreases over the 24 h period [7]. Around the second month there is a clear change in some EEG activities, like

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trace alternant, which disappears, sleep spindles, which appear [8,9], and eye movements density, which reaches a plateau level [10]. After the third to fifth months, slow wave sleep (SWS) becomes easily detectable and it occurs in alternate quiet sleep (QS) phases, with a broad periodicity of about 100 min. [11]. At the end of the first year, sleep is somewhat different from the neonatal sleep.

The early development of the characteristics of waking state is a 'neglected topic' [12]. It is easier to distinguish sleep and wakefulness in term infants than in preterm infants at low gestational ages. Stefanski et al. [13] described wakeful behaviour at 30 weeks of postconceptional age as characterized by apparent non-reflex intermittent movements of limbs with prolonged startles and gross stretching and writhing; the infant is alert and in this condition he may be intermittently motionless. Facial activity is usually present and the eyes may be open or closed. Curzi-Dascalova and Mirmiran [8] detected wakefulness at 35 weeks of post-conceptional age distinguishing quiet wakefulness from active wakefulness.

Nijhuis et al. [14] reported that the foetus is awake for 7% of the recording time which lasts for 2 h. Preterm infants between 30 and 39 weeks of post-conceptional age spend in wakefulness about 8% of recording time which lasts 6 h [15]. Information about wakefulness distribution during 24 h in preterm infants is scarce. A recent study performed by Giganti et al. [16] reported that wakefulness distribution during 24 h is not uniform, showing a peak between 2:00 and 5:00 a.m.

More detailed qualitative and quantitative descriptions of wakefulness have been provided in infants after term age. Kleitman [17] distinguishes between wakefulness of necessity, a 'primitive' kind of wakefulness, and wakefulness of choice. Wolff [18] describes three types of wakefulness: 'waking activity', 'alert inactivity' and 'alert activity', which develop at different times. At 2 months, wakefulness is less dependent on both internal and external perturbations, and according to Hopkins [12] has become a real 'behavioural state'.

The developmental trend of wakefulness is to increase with age in the amount and duration of the longest episode which progressively allocates during the day [7,19].

3. Awakenings in preterm infants

The difficulty to identify behavioural states at early ages leads to the difficulty to identify sleep–wake transitions. There are very few studies about early ages. Most of them refer to 'arousal' [1]. Recently, Curzi-Dascalova et al. [20] reported the effect of prone vs. supine positions on awakenings in preterm infants: the number of awakenings was greater in supine position compared to prone position in both active sleep and quiet sleep.

Using motility we studied characteristics of awakening in a group of preterm infants [21]. Our results showed no changes between 34 and 40 weeks of post-conceptional age for both the number and the duration of awakenings, suggesting that this period of life is not really crucial for changes in the propension to wake up. Day–night differences were observed for both the number and the duration of awakenings: in preterm infants between 34 and 37 weeks postconceptional age awakenings are more frequent and with longer duration in the nocturnal period. This peculiar time distribution of awakenings tends to disappear near term, suggesting that this age could be a turning point towards the prevalence of awakening during the day found in older infants. The most frequent sleep state preceding awakenings is active sleep; awakenings with crying are less frequent than awakenings without crying.

4. Awakenings in the first year of life

In a nutshell, from the term onwards, up to the end of the first year of life, awakening is usually defined according to polygraphic and behavioural criteria.

All normative studies are consistent in showing a decreasing trend over the first year of life in the number of awakenings. From Fig. 4.1 of Salzarulo and Fagioli paper [22] it could be estimated that the number of awakening decreases in the first year of life and that the reduction is mostly accounted for by the decrease in the night-time. The latter result is in agreement with all those studies which took only the profile of nocturnal awakenings into account [23–26].

However, age does not remarkably affect the duration of awakenings. Both Louis et al. [25] and Ficca et al. [26] studies did not find any significant change over the first year of life, whereas Hoppenbrouwers et al. [24] reported only a slight increase.

Ficca et al. [26] highlighted that also the overnight distribution of the awakenings show age-related modifications. Infants younger than 4 months showed one main peak at the 5th hour and two minor peaks at the second and at the 7th hour, whereas infants after 6 months of age display a 'polymodal' distribution, with several alternating peaks and troughs.

The physiological events preceding the transition towards wakefulness may show remarkable differences with age. We found that the probability to wake up during the night is higher from REM sleep than from NREM sleep [27] across the whole first year of life, despite a decrease in the number of awakenings from REM sleep [26]. This decrease accounts for the above said reduction with age in the number of night-time awakenings [26]. Instead, the number of awakenings out of NREM sleep remains more or less unchanged.

5. Conclusions

Previous results provide some clear messages.

1. How often we awake in 24 h period is tightly related to

age: there is a trend to decrease which is obvious from the term onwards. Before term, when the number of awakenings is higher, states are shorter and, apparently, the circadian rhythm of temperature is not yet developed [28,29]. These two conditions could act together to facilitate a high number of awakenings. In particular, the absence of the circadian temperature rhythm could leave 'free' the awakening to take place mainly in relation to the ultradian cycle. To further establish the role of the emerging circadian rhythms on the frequency and time distribution of awakening, more and through investigations are necessary.
2. There is no change with age of the re-sleep time after night awakening. This suggests that frequency and duration of awakening at that time, could not be controlled by the same factors, or, at least that, if several factors control awakening features, they are not co-operating early in age.
3. The transition between sleep and wakefulness is greatly facilitated by REM sleep. This certainly supports the view that REM and wakefulness share some properties. Campbell [30] was proposing a similar concept when he said that REM sleep provides "optimal physiological conditions for the transition from sleep to waking".

Finally some suggestions for future research:

The reasons why 'gates' to awakening are open with a different frequency, or at a different time in the 24 h cycle remain an open question. The role of homeostatic and circadian components, as well as their interaction at each developmental step, should be explored.
Investigations concerning semiology of sleep–wake transitions are necessary, mainly at early ages. We suggest a fine grained analysis of the behavioural and physiological activities. Furthermore, it would be interesting to investigate if a 'leading variable' drags other behavioural and physiological variables toward the awakening.
The characteristics of autonomic variables as heart rate, respiratory rate and temperature preceding awakening, as well as motor aspects, should be fully explored as a function of age.

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