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Review

Growth and development of children with a special focus on sleep

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ABSTRACT

The first two decades of life are characterised complex biological processes involving growth and maturation as well as differentiation. The Central Nervous System (CNS) where among others internal and external stimuli are integrated and responses of the body are prepared starts to evolve quite early during ontogenesis. One of the complex behaviours, which are regulated by the brain, is the sleep-wake cycle.

The discussion of age-related changes in sleep comprises changes at the physiological level (e.g. changes in the frequency and amplitude of EEG signal, as well as development and distribution of sleep stages), changes in the corresponding behaviour (e.g. changes in the absolute amount of sleep and its distribution in 24 h perspective), and finally the subjective perception of sleep and sleep as a measure of well-being.

Studies on the impact of a specific factor on sleep during childhood and adolescence have to consider chronological and biological age as well as sex as relevant biological parameters. Even when these factors are controlled for large interindividual differences persist, that is why prospective instead of cross-sectional approaches should be used whenever possible. Furthermore, it has to be distinguished between sleep assessed at the level of brain functioning (i.e. by polysomnography), which gives information on effects at the physiological level and at the level of self-assessment, which focuses on behaviour. Both, sleep at the subjective as well as at the objective level, can to a considerable degree be affected by life style factors, which hence have to be considered as potential confounders.

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1. Introduction: sleep and brain

Sleep is a behaviour which is characterised e.g. by a recumbent posture, a raised threshold to sensory stimulation and a low level of motor output. This behaviour, which humans show approximately one fourth to one third of their lives, is regulated by the brain. However, the behaviour is not only regulated by the brain, it also occurs in the brain and it is the brain, which benefits most from it. Hobson (2005) phrased this to the point in a title of a Nature paper: *Sleep is of the brain, by the brain and for the brain*. Looking at the brain physiology sleep proves to be a quite active state. It can roughly be distinguished between NREM sleep and REM sleep and within NREM sleep according to the current standard (Iber et al., 2007) three different stages (N1, N2 and N3) are differentiated based on the amount of slow waves (<2 Hz) and their amplitude (>75 μV) as well as on the basis of special EEG patterns (e.g. spindles and K-complexes, which are characteristic for N2). For sleep (and wake) staging a whole night's recording of biosignals (the electroencephalogram - EEG, the electromyogram- EMG, and the electrooculogram – EOG) is divided into 30-second epochs and a stage (Wake, N1, N2, N3 or REM) is assigned to each epoch. For subjects without sleep disturbances the resulting sleep profile reflects that sleep proceeds in cycles, that slow wave sleep (N3) duration decreases,

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and that REM sleep duration increases during the course of the night.

It is important to note that the subjective perception of sleep is only a very rough proxy of sleep assessed by physiological or objective methods (polysomnography). The subjective perception of sleep – especially in sleep disturbed subjects – among others is influenced by own internal standards, expectations and psychological factors, placebo and nocebo effects are documented. Actigraphy, a method which basically records gross motor movement activity can be used to monitor rest/activity cycles, which sometimes is used as indicator of the sleep and wake state. A recent study by Spruyt et al. (2011), which analysed the concordance of polysomnographic and actigraphic recordings came to the conclusion that actigraphy provides reliable estimates for sleep quantity (sleep period time), but not for indicators of sleep quality like total sleep time and wake after sleep onset.

2. Growth and development

The first two decades of life are characterised by tremendous, complex biological processes, which induce and control all the changes, which are necessary that a highly differentiated organism with tissues, organs and organ systems evolves from a single cell. These processes involve growth and development. Growth is an increase in at least one measurable dimension, e.g. by an increase of cell number, cell size or increase of mass of non-cellular substances. Development is a progress from a simpler or lower to a more advanced or mature form or stage. Development comprises differentiation (cells aggregate into tissues, organs and organ systems) and maturation, a process leading to the attainment of full functional capacity.

One of these organ systems is the Central Nervous System (CNS) where among others internal and external stimuli are integrated, responses of the body are prepared and where communication with the second great control system of the human body, the endocrine system, takes place. One of the complex behaviours, which are regulated by the brain is the sleep-wake cycle (and within sleep the NREM-REM sleep cycle).

By birth the phase of growth and development is divided into a prenatal and a postnatal phase and the most tremendous changes already occur prenatally. The prenatal phase is subdivided into an embryonic (week 3 to 8 after conception) and a foetal (week 9 until birth) period. The Central Nervous system (CNS) including the brain starts to develop very early during embryogenesis and continuous during foetogenesis. During prenatal life embryogenesis is vulnerable for major morphological damages while foetogenesis is vulnerable to the development of functional and minor morphological abnormalities.

During normal prenatal development brain volume doubles during the third trimester of gestation and the volume of gray cortical matter shows a fourfold increase (Lodygensky et al., 2010). From the very beginning of life differences between males and females start to emerge. Head circumference at birth, which is a proxy of prenatal brain growth and development is 0.6 cm larger in boys (median: 34.5 cm) than in girls (median: 33.9 cm) (WHO Multicentre Growth Reference Study Group, 2007). The interindividual differences, however, are much larger. This is for example evident from the distance in head circumference between the 97th and the 3rd percentile, which is 4.4 cm in boys and 4.6 cm in girls.

After birth growth and maturational processes continue and this is specific for different structures of the body. The often reproduced systematic growth curve published by Scammon (1930) shows the growth of four different structures expressed as a percentage of total gain between birth and the age of 20 years illustrates that the growth of neural components is far ahead of the general growth (as represented for example by the height growth curve) and even more of the growth of genital organs. The lymphoid component shows its maximum in size well before adulthood and declines in the second decade, which is mainly due to the decrease in size of the thymus.

The increase in head circumference as a proxy of brain growth is most marked for the first year of life. Out of 16 cm postnatal increase in head circumference during the first five years of life more than 50% is completed by the age of six months and more than 80% by the age of two years (WHO Multicentre Growth Reference Study Group, 2007).

After birth the morphological sexual dimorphism continues to evolve as well as sex differences in maturational processes. For head circumference as a proxy of brain growth the difference increases from 0.6 at birth to 1.0 cm at 6 months of age and to 1.2 cm at the age of 12 months (WHO Multicentre Growth Reference Study Group, 2007) which according to data from the Fels Longitudinal Study is the same as the sex difference in 18 years old boys and girls (Roche et al., 1987).

Head circumference is an easy applicable somatometric approach to measure brain growth. It can be applied in large series of subjects, leading to detailed information about individual and group differences. Besides head circumference there are other measures or proxies of brain growth (e.g. brain volume and brain weight) and morphological changes (relation of cortical grey and white matter), which require more specific methods, e.g. magnetic resonance imaging (MRI) techniques. Usually the sample sizes on which results are based are much smaller than in somatometric studies. According to MRI data, brain weight shows the fastest growth in the first three years of life. At the age of five years 90% of adult brain weight is attained and between 10 and 12 years of age adult values are reached (Paus et al., 2001). In adults, cerebral volume (defined as sum of grey and white matter in the cerebrum) is approximately 11% larger in males (Giedd et al., 1999). Data from a large longitudinal MRI data set ($n = 145$ children and adolescents) show that the changes across the second decade of life show a peak of the cerebral volume at the age of 10.5 years in girls and at 14.5 years in boys with a decrease thereafter, with a greater decline in girls (Lenroot et al., 2007). The u-shaped age related changes can be seen both for cortical and for subcortical gray matter with sex and structure related difference in the ages of the peak volumes (Lenroot et al., 2007). The total white matter volume on the other hand shows an increase for the covered age range from 7 to 19 years. At the age of seven sex differences are present. Boys show a higher white matter volume. This differences increases steadily due to a steeper increase of the white matter in boys (Lenroot et al., 2007).

Besides morphological aspects there are indicators of the functional maturation of the brain like the degree of myelination (Deoni et al., 2011) and brain activity as measured by the electroencephalogram (EEG).

2.1. Sleep related indicators of brain maturation

Sleep EEG and EEG show age related changes during the first 2 decades of life. The frequency of the resting waking EEG increases from birth until young adulthood while the amplitude increases after birth to a maximum during adolescence and decreases thereafter (Fig. 1). The qualitative changes in sleep EEG, which are obvious from Figs. 2–4 (Scholle and Feldmann-Ulrich, 2007), are also reflected in quantitative data.

The analysis of longitudinal polysomnographic sleep data collected over a period of five years from two age cohorts (one started at the age of 9 years and one at the age of 12 years) covering the age range 9 to 17 years with initially 70 subjects (35 girls) showed that delta power (1–4 Hz) and theta power (4–8 Hz) declined with increasing age. While theta showed the decreasing trend already from age 9 years onwards, delta starts to decline from