



Contents lists available at ScienceDirect

Journal of Physiology - Paris

journal homepage: www.elsevier.com/locate/jphysparis

Disruption of adolescents' circadian clock: The vicious circle of media use, exposure to light at night, sleep loss and risk behaviors

Yvan Touitou^{a,*}, David Touitou^b, Alain Reinberg^a

^a Unité de Chronobiologie, Fondation Ophtalmologique A. de Rothschild, 25 rue Manin, 75019 Paris, France

^b UHSA – Groupe Hospitalier Paul Guiraud, 54, avenue de la République, 94806 Villejuif, France

ARTICLE INFO

Article history:

Received 24 October 2016

Received in revised form 12 April 2017

Accepted 5 May 2017

Available online xxx

Keywords:

Electronic media use

Light at night

LEDs

Clock disruption

Melatonin

Adolescent sleep

Sleepiness

Fatigue

Chronotype

Internet use

Cellular phone

Rhythm desynchronization

Alcohol

Smoking

Binge drinking

Substance abuse

ABSTRACT

Although sleep is a key element in adolescent development, teens are spending increasing amounts of time online with health risks related to excessive use of electronic media (computers, smartphones, tablets, consoles...) negatively associated with daytime functioning and sleep outcomes. Adolescent sleep becomes irregular, shortened and delayed in relation with later sleep onset and early waking time due to early school starting times on weekdays which results in rhythm desynchronization and sleep loss. In addition, exposure of adolescents to the numerous electronic devices prior to bedtime has become a great concern because LEDs emit much more blue light than white incandescent bulbs and compact fluorescent bulbs and have therefore a greater impact on the biological clock. A large number of adolescents move to evening chronotype and experience a misalignment between biological and social rhythms which, added to sleep loss, results in e.g. fatigue, daytime sleepiness, behavioral problems and poor academic achievement. This paper on adolescent circadian disruption will review the sensitivity of adolescents to light including LEDs with the effects on the circadian system, the crosstalk between the clock and the pineal gland, the role of melatonin, and the behavior of some adolescents (media use, alcohol consumption, binge drinking, smoking habits, stimulant use...). Lastly, some practical recommendations and perspectives are put forward. The permanent social jet lag resulting in clock misalignment experienced by a number of adolescents should be considered as a matter of public health.

© 2017 Elsevier Ltd. All rights reserved.

The World Health Organization (WHO) defines adolescents as individuals in the 10–19 year age group, and youths as the 15–24 year age group. These two groups are considered to be young individuals, and they range from 10 to 24 years of age.

1. The circadian system

1.1. From the internal clock to circadian rhythms

Circadian rhythms are dependent on an internal clock, a central brain pacemaker, located in the suprachiasmatic nucleus (SCN) of the anterior hypothalamus. On the one hand, the SCN serves as a central clock, synchronizing other clocks in peripheral tissues

(e.g. liver, kidney, heart, retina, and others), and on the other hand it directly orchestrates circadian physiology (Richards and Gumz, 2012). The SCN generates circadian rhythms by means of a transcriptional-translational feedback loop. The molecular mechanism of the clock is present in every cell of the body. Clock genes (some examples in humans are *CLOCK*, *CRY*, *PER*, and *BMAL1*) comprise an autoregulatory transcriptional-translational feedback loop that cycles every 24 h (Hardin, 2000; Loros and Dunlap, 1991). The suprachiasmatic nucleus develops early in gestation, and circadian rhythms are present in the fetus and newborn (Kennaway et al., 1992; Serón-Ferré et al., 2001).

The SCN is connected to the retina on the one hand, and to the pineal gland which secretes melatonin on the other hand. Intrinsically photosensitive retinal ganglion cells (ipRGCs) in the eye contain melanopsin that is expressed in a small subset of cells representing 1–2% of all retinal ganglion cells. Melanopsin is an OPN4-photoreceptor that is sensitive to blue light (i.e. wavelengths ranging from 460 to 480 nm) and that is fundamental for the

* Corresponding author.

E-mail address: yvan.touitou@chronobiology.fr (Y. Touitou).

functioning of the circadian system and for SCN entrainment. This system is called the non-image-forming system (NIF), as opposed to the classical visual system (based on rods and cones) that is responsible for image formation (Berson et al., 2002; Lucas, 2013). The light signal received by the retina is transmitted to the SCN by a retino-hypothalamic pathway, and then to the superior cervical ganglion by multisynaptic complexes, so as to end up at the pineal gland which secretes melatonin (5-methoxy-N-acetyltryptamine) derived from its precursor tryptophan. Pineal melatonin production exhibits a high-amplitude circadian rhythm that is reflected in plasma levels, with low levels during the day and high levels at night. This circadian pattern is comparable in humans and in experimental animals, both diurnal and nocturnal, with daily dark phase plasma concentrations three to ten times higher than during the light phase. This is related to a neuronal message that is initiated in the SCN when the neurons are no longer subjected to the effect of light. This results in an activation of the release of noradrenalin (NA) by the terminal nerves of the sympathetic system that act at the level of the beta-adrenergic receptors, thus activating the adenylate cyclase system and the key melatonin synthesizing enzyme N-acetyltransferase.

1.2. From rhythm desynchronization to circadian disruption

Under normal environmental conditions light is the major synchronizer (also called entraining agent or Zeitgeber) of the circadian system. Daily exposure to light maintains the 24 h cycle (i.e. the 24 h period) of the biological clock. Light thus synchronizes (or entrains, or adjusts) the endogenous period of the circadian system which is which is not exactly 24 h but close to 24.2 h. When light is absent, such as in constant darkness as documented in experimental protocols, the circadian rhythm of melatonin free-runs. This means that as it is no longer synchronized with the environmental light-dark cycle, it becomes out of phase with this environmental cycle (Reinberg and Touitou, 1996; Touitou et al., 2011, 2017).

Desynchronization corresponds to a dissociation of the internal clock function from that of the local time and this results in a number of atypical symptoms such as, amongst others, persistent fatigue, poor appetite, sleep disorders that may lead to chronic insomnia, and mood disorders that can cause depression, although some desynchronized people do not experience any of these clinical signs (Reinberg and Ashkenazi, 2008; Reinberg et al., 2007, 2013; Touitou et al., 2011, 2017).

When the circadian desynchronization becomes chronic, as may be observed under various circumstances like, amongst others, blindness, shift- and night-work, transmeridian flights, alcohol consumption, ingestion of specific medications, and also aging (e.g. Danel et al., 2001; Danel and Touitou, 2004; Touitou et al., 1981, 2011; Reiter et al., 2012; Gooley et al., 2011), it is often referred to as disruption of the circadian system (or chronodisruption). A particularly long-term exposure to artificial light at night (ALAN) is experienced by shift- and night-workers, and several health issues, mainly documented in nurses, can arise as a result of this chronodisruption, such as breast cancer (review in Costa and Haus, 2010; Touitou et al., 2017), cardiometabolic risks and obesity (Fonken et al., 2010; Wong et al., 2015; Reiter et al., 2012) and cognitive impairments (Marquié et al., 2015). Inhibition of nocturnal secretion of melatonin, sleep deprivation, and clock disruption are three of the multiple mechanisms of action put forward to explain the deleterious effects of ALAN, and they are considered to be of primary importance (Touitou et al., 2017). Melatonin inhibition by ALAN results in the loss of the multiple biological effects of the hormone, such as free-radical scavenging activity, inhibition of aromatase activity, an anti-estrogenic effect by interaction with estrogen-receptors, inhibition of telomerase

activity, perturbation of DNA repair and of the immune system, and oncostatic action by regulation of the metabolism of linoleic acid (Reiter et al., 2014; Touitou et al., 2017).

Chronobiotics are substances that adjust the timing of internal biological rhythm and combat the circadian disruption. Amongst the substances potentially presenting chronobiotic properties, a consensus seems to be reached on the possible use of melatonin or its agonists to shift the phase of the human circadian clock, but optimizing the dose, formulation and especially the time of administration require further studies (Herxheimer and Petrie, 2002; Touitou and Bogdan, 2007).

1.3. Assessment of rhythm synchronization/desynchronization

Rhythm synchronization of an organism is assessed by marker rhythms. A marker rhythm is a physiological and rhythmic variable, for which the circadian pattern is highly reproducible on an individual basis and as a group phenomenon (Selmaoui and Touitou, 2003; Mailloux et al., 1999; Benstaali et al., 2001). A marker rhythm allows characterization of the timing of the endogenous rhythmic time structure, and it provides information on the synchronization (or desynchronization) of individuals (see Fig. 1).

Circadian patterns of plasma melatonin, plasma cortisol, core body temperature, and motor activity (i.e. actigraphy) are the most frequent markers of rhythms that are used to assess the circadian time structure both in humans and in laboratory animals (Selmaoui and Touitou, 2003; Mailloux et al., 1999; Benstaali et al., 2001). The choice of a marker rhythm varies according to the aims of the research, e.g. white blood cells in cancer research, core body temperature in sports research, melatonin and cortisol in research dealing with shift work, although most often more than one rhythm marker is used to assess the rhythm synchronization of the subjects being studied. Although melatonin is commonly used as a phase marker in human adults, relatively little data are available regarding chronobiological aspects in children and adolescents (Ehrenkranz et al., 1982; Attanasio et al., 1985; Ardura et al., 2003; Touitou et al., 2009). Saliva and urine collections provide a convenient, stress-free, non-invasive, and reliable technique for monitoring the biological rhythm of hormones. In prepubertal boys, we found a clear circadian rhythm for both salivary and urinary 6-sulphatoxy-melatonin (Fig. 2), with a higher level of secretion at night without any correlation with the body mass index (Touitou et al., 2009). For individuals of any age, the circadian pattern of melatonin is highly reproducible from day to day (Selmaoui and Touitou, 2003).

2. Physiology of melatonin from birth to adulthood

2.1. Fetus and infants

The fetus is exposed to the melatonin rhythm of its mother, i.e. low concentrations during the day and high concentrations at night. During a normal pregnancy, the maternal melatonin level increases progressively until term, and it is readily transferred to the fetus, in which it plays important roles in brain formation and differentiation. In this regard, we have to underline that animal studies have supported a fetal neuroprotective role for melatonin when administered to the mother during pregnancy. Whether melatonin administration to the mother in humans, can reduce the risk of neurosensory disabilities and death, associated with fetal brain injury, for the preterm or term compromised fetus is still unknown (Cochrane library Wilkinson et al., 2016).

The maternal melatonin provides the initial circadian signal to the fetus. Alteration of the maternal melatonin level has been

Download English Version:

<https://daneshyari.com/en/article/8649903>

Download Persian Version:

<https://daneshyari.com/article/8649903>

[Daneshyari.com](https://daneshyari.com)