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Review article

Sleep, sleep deprivation, autonomic nervous system and cardiovascular diseases

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ABSTRACT

Sleep deprivation (SD) has become a relevant health problem in modern societies. We can be sleep deprived due to lifestyle habits or due to sleep disorders, such as insomnia, obstructive sleep apnea (OSA) and neurological disorders.

One of the common element of sleep disorders is the condition of chronic SD, which has complex biological consequences. SD is capable of inducing different biological effects, such as neural autonomic control changes, increased oxidative stress, altered inflammatory and coagulatory responses and accelerated atherosclerosis.

All these mechanisms links SD and cardiovascular and metabolic disorders. Epidemiological studies have shown that short sleep duration is associated with increased incidence of cardiovascular diseases, such as coronary artery disease, hypertension, arrhythmias, diabetes and obesity, after adjustment for socioeconomic and demographic risk factors and comorbidities.

Thus, an early assessment of a condition of SD and its treatment is clinically relevant to prevent the harmful consequences of a very common condition in adult population.

Contents

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1. Sleep physiology and autonomic nervous system (ANS)

Mammals spend around one-third of their lifetime sleeping. Although the biological meanings of sleep process is still debated, we know that sleep is a complex physiological event, which involves several different biological pathways, from neural cortical circuits to the heart (Saper et al., 2005; Tononi and Cirelli, 2006).

Most of the biological functions of the body changes during sleep compared to wake, such as heart rate (HR), arterial blood pressure (ABP), temperature, as well as hormonal secretion and immune function. Cardiovascular regulation is profoundly modified during sleep, and the interconnection between cardiovascular system and sleep processes must be considered as a bidirectional link. Cardiovascular diseases are associated with alterations of physiological sleep and vice versa sleep disorders can importantly alter the cardiovascular system, leading to an increased cardiovascular risk (Kendzerska et al., 2014; Gami et al., 2013).

In this context, autonomic nervous system (ANS) plays a pivotal role. In fact, during physiological sleep, HR and ABP lower during non-REM sleep, with marked increases during REM sleep (Trinder et al., 2001; Somers et al., 1993). These hemodynamic fluctuations are expression of the autonomic cardiovascular modulation of HR and ABP, due to sympathetic and parasympathetic oscillations of the sympatho-vagal balance. A predominant vagal modulation is observed during NREM sleep and a significant predominant sympathetic control during REM sleep, at levels higher than in wakefulness (Trinder et al., 2001; Somers et al., 1993). These data have been confirmed by the direct recordings of sympathetic fibers using microneurographic technicques (MSNA) (Somers et al., 1993) and using the analysis of heart rate variability (HRV), which is a non invasive tool able to detect the rhythmic oscillations embedded in heart period and blood pressure time series (Montano et al., 2009). HRV analysis identifies three main oscillatory components, very low frequency (VLF), marker of hormonal and circadian oscillations, low frequency component (LF), marker of sympathetic modulation, and high frequency component (HF), marker of vagal modulation and synchronous with respiration (Montano et al., 2009). HRV has been widely used for the assessment of cardiovascular autonomic control during sleep, showing a progressive decrease of LF component, marker of sympathetic modulation, and a predominant vagal control, as sleep becomes deeper (from wakefulness to deep NREM sleep). On the opposite, REM sleep is characterized by a predominant sympathetic modulation with surges of sympathetic activity at levels even higher than in wake (Brandenberger et al., 2003; Legramante et al., 2003; Trinder et al., 2001; Tobaldini et al., 2014).

2. Sleep deprivation: general aspects

In the last decades, several studies have investigated the effects of sleep deprivation (SD) on cardiovascular morbidity.

We know that we sleep less than in the past: in 1900 estimated adult average sleep in US was nine hours, in 1980 seven hours, in 2000 six and a half hours (Schoenborn and Adams, 2010). National Institutes of Health recommends at least 10 h of sleep for children, 9–10 h for teenagers, and 7–8 h for adults. It has been reported that in 2014 almost 1/3 of the adults slept less than 6 h per night (Schoenborn and Adams, 2010). Therefore, SD has become a huge health care problem in modern societies. Why are we sleep deprived? Several aspects must be taken into account. First, we can be sleep deprived for reasons related to our lifestyle, such as the use of electronic devices before going to sleep, which alter the physiological secretion of melatonin (Ackermann et al., 2013), hard work schedule, shift work etc. Second, we can be sleep deprived because of ageing process, because ageing is associated with a reduction of total sleep time and a disruption of physiological sleep. Third, we may suffer from a sleep disorders, namely a sleep disordered breathing (SDB), insomnia, periodic limb movements (PLM), and restless leg syndrome (RLS), to list just the more frequent.

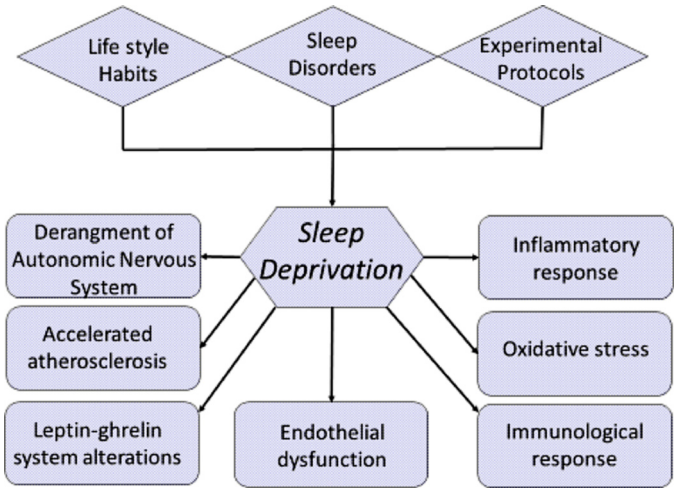

Fig. 1. Sleep deprivation (SD) can be due to lifestyle habits, sleep disorders and experimental sleep protocols. Despite the origine, SD activates several physiopathological pathways, such as autonomic nervous system dysfunction, endothelial dysfunction, increased inflammation, coagulation and oxidative stress resposnses, deregulation of hormones secretion. All these alterations are thought to be responsible for the link between SD and cardiovascular disorders.

It is important to underline that SD has important biological consequences, which can cause significant cardiometabolic and neurological sequelae. We will focus our review on the relationship between SD and cardiometabolic changes.

3. Experimental sleep deprivation

Several epidemiological evidences suggest a link between short sleep duration and an increased risk of developing cardiovascular diseases, i.e. coronary artery diseases, congestive heart failure and hypertension (Cappuccio et al., 2010), as well as infections (Patel et al., 2012) and metabolic diseases (Tasali et al., 2008a,b).

These clinical consequences are due to the activation of different biological pathways, such as a disregulation of the autonomic cardiovascular control (Tobaldini et al., 2013a,b, 2014), an altered inflammatory and immune response (Irwin et al., 2008; Meier-Ewert et al., 2004; Imeri and Opp, 2009) and a deregulation of leptin-ghrelin system and insulin sensitivity (Rafalson et al., 2010) [see Fig. 1].

Several experimental protocols have been carried out to assess the changes induced by both acute and chronic SD in healthy subjects. Except for the study by Kato et al. (2000), it has been reported that after a sleep loss of 24 h, ABP was significantly altered. Namely, after a sleep loss of 24 h, HR and BP were higher compared to baseline in healthy subjects (Sauvet et al., 2014; Sunbul et al., 2014; Zhong et al., 2005). One of the possible mechanism involved in these cardiovascular changes could be related to modification of the ANS activity. The role played by ANS has been widely investigated in this setting and almost all the data in literature report an increased sympathetic activity associated with acute SD. Zhong et al. reported a reduction of total variability, considered a marker of the capability of the cardiovascular system to respond to stressors (Zhong et al., 2005) as well as an important change of the sympatho-vagal balance towards a sympathetic predominance. In fact, the analysis of HRV showed that acute sleep loss was able to induce an enhanced sympathetic modulation, as shown by the increased of the LF component and the LF/HF ratio, and a reduction of vagal control, expressed by lower values of the HF component