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REVIEW

The Effect of Sleep Deprivation on Coronary Heart Disease△

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Abstract Sleep deprivation (SD) has been associated with an increased morbidity and mortality of coronary heart disease (CHD). SD could induce autonomic nervous dysfunction, hypertension, arrhythmia, hormonal dysregulation, oxidative stress, endothelial dysfunction, inflammation and metabolic disorder in CHD patients. This paper reviewed the study results of SD in clinical trials and animal experiments and concluded that SD was associated with cardiovascular risk factors, which aggravated CHD in pathogenesis and outcomes.

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SLEEP deprivation (SD) represents loss of sleep and short of sleep duration. It can be divided into partial sleep deprivation (PSD), total sleep deprivation (TSD), acute sleep deprivation (ASD) and chronic sleep deprivation (CSD) according to time and duration. In addition, according to sleeping state, it is divided into rapid eye movement sleep deprivation (REMSD) and non-rapid eye movement sleep deprivation (NREMSD). SD has been associated with increased cardiovascular morbidity and mortality in epidemiologic and case-control studies.[1] It has been suggested that sleep duration is an independent predictor for morbidity and mortality of cardiovascular disease.[2] Many studies have indicated that the incidence of coronary heart disease (CHD) appears an obvious negative correlation with sleep duration, and SD has been related to a great risk of myocardial infarction and heart failure.[3-7] Results of Coronary Artery Risk Development in Young Adults (CARDIA) study showed that short sleeping time is associated with coronary artery calcification, a precursor of CHD,[8] and SD has been regarded as a marker of subclinical heart disease.[9]

Therefore, it is important to understand the effects of SD on pathogenesis, progress and prognosis of CHD. This paper summarized the effects of SD on CHD in terms of autonomic nervous dysfunction, hypertension, arrhythmia, hormonal dysregulation, oxidative stress, endothelial dysfunction, inflammation and metabolic disorders.

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AUTONOMIC NERVOUS DYSFUNCTION

Autonomic nervous system was significantly modulated by age, environmental conditions, and activities undertaken. Studies have shown that SD can increase the sympathetic outflow to the heart or periphery through increasing catecholamine, coronary vasomotor tone, blood pressure and heart rate, thus alter the balance between demand and supply of oxygen.[1,10] Autonomic nervous dysfunction and activation of the sympathetic nervous system are primary contributors to cardiovascular disease, which can lead to excessive vasoconstriction, fibrosis, and cardiac remodeling.[11]

Large quantities of researches have suggested that SD has important effects on sympathetic nervous system of the heart. Zhong *et al*[12] studied 18 healthy adult and found that, heart rate, low-frequency components of heart rate variability and blood pressure variability were all increased after 39 hours of SD, while baroreflex sensitivity was decreased. Another study with 12 healthy males showed that, heart rate, systolic blood pressure and the low-frequency components of heart rate variability were increased significantly within 32 hours of TSD.[13] Furthermore, Dettoni JL *et al*[14] investigated 5 nights of PSD (<5 hours per night) in 13 healthy male volunteers, found that high-frequency components of heart rate variability decreased in percentage, low-frequency components of heart rate variability increased in percentage, low-frequency band of blood pressure variability and serum norepinephrine also increased as well. Recently, Tobaldini E *et al*[15] measured heart rate variability, blood pressure variability and baroreflex sensitivity in 15 healthy residents of Internal Medicine Department and found a sympathetic activation and a parasympathetic withdrawal after one night of ASD. It was reported that ASD blunted cardiovascular autonomic response and impacted autonomic regulation of cardiac function.[16] It was also reported that 40 hours of TSD had a worse deleterious effect on the autonomic nervous system in older women than in young women.[17]

HYPERTENSION

More and more evidences have suggested the close relationship between short sleeping time and hypertension.[18] SD can increase sympathetic nerve activation with a high catecholamine level, leading to hypertension under the synergistic effects of norepinephrine, renin-angiotensin system and endothelin.[1,19] Hypertension elevates afterload pressure and exacerbates cell death, which aggravates myocardial ischemic and increases the risk of cardiovascular events.[18,20]

Many studies have shown a strong association between SD and the development of hypertension. Irwin MR *et al* [9] found that PSD induced great increase of heart rate, norepinephrine and epinephrine levels in the alcohol-dependent men. Robillard R and colleagues observed the effect of SD on blood pressure and its response, found that half of the subjects, both young and elderly, showed hypertensive responses instead of systolic blood pressure dropping when transitioning from semi-recumbent to standing. In the semi-recumbent position, blood pressure showed a notable increase in the elderly group but not in the young group, and 25% of normotensive elderly subjects had remarkable systolic hypertension of >140 mmHg after one night of SD.[21] Carter JR et al investigated the heart rate, blood pressure and muscle sympathetic nerve activity in 30 healthy subjects. The results showed both male and female presented increases of systolic, diastolic and mean blood pressure after 24 hours of TSD, while reduced muscle sympathetic nerve activity was only observed in males. Another study had similar results showing that TSD-induced hypertension occurred in both male and female, but only men had sympathetic baroreflex dysfunction.[22] As a result, the effects of SD on hypertension might be dependent on age, gender, alcohol-dependence, measurement postures and deprived time.

ARRHYTHMIA

It has been shown that SD can increase the incidence of arrhythmia by damaging the inherent biological rhythms and causing physical stress,[23] and arrhythmia is the main cause of CHD mortality. The ventricular tachycardia, ventricular fibrillation and atrioventricular block are fatal arrhythmia in CHD, and heart rate variability has high predictive value in malignant arrhythmia.

Studies have revealed that cardiac arrhythmia has close relationship with SD. Walker AD *et al*[24] discovered that respiratory sinus arrhythmia was increased after 28 hours of SD. Joukar S *et al*[25] found that blood pressure levels and the QT interval of the electrocardiogram increased significantly after 72 hours of REMSD, the latency times of premature ventricular contraction and ventricular tachycardia increased significantly as well, which indicates the increased risk for CHD. In addition, Chen WR *et al*[26] studied 60 young healthy subjects who had 24 hours of SD, and found that the ratio of low frequency to high frequency of heart rate variability was increased compared with the normal sleeping controls. Some subjects