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From Total Sleep Deprivation to Cardiovascular Disease: A Key Role for the Immune System?

Commentary on Ackermann et al. Diurnal rhythms in blood cell populations and the effects of acute sleep deprivation in healthy young men. SLEEP 2012;35:933-940.

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In our 24 h, 7-days a week society, more men and women become sleep deprived due to professional constraints, family obligations, greater work pressure with extended working hours, and shift schedules. Furthermore, beside these professional obligations, 24-h access to media, leisure activities, and sport induce situations in which many individuals will choose to remain awake at the detriment to obtaining adequate sleep. This creates a situation of voluntary sleep deprivation with seeming disregard for the impact of this behavior on their health. According to the 2009 National sleep Foundation Survey, 20% of the US population is sleeping less than 6 h per night on weekdays.[1]

Epidemiological data as well as sleep deprivation experiments indicate that lack of sleep impairs several health aspects such as metabolism, cardiovascular system, and immunity.[2,3]

Using a carefully controlled design, the study of Ackermann and colleagues[4] reported in this issue of *SLEEP* very precisely describes the diurnal rhythms in circulating levels of different blood leukocytes subsets, their intercorrelations, and the impact of one night of total sleep deprivation, in young healthy men. They report for the first time that total sleep deprivation induces a loss in granulocyte rhythmicity with increased levels and lower amplitude.

Several studies have investigated the effect of sleep deprivation on blood cell counts but using a limited number of time points. These studies have consistently shown an increase in granulocytes and neutrophil counts after either total sleep deprivation[5] or severe sleep restriction.[6] Thus these studies as well as the study of Ackermann et al.[4] indicate that granulocytes and neutrophil are reacting immediately to the stress induced by sleep loss. The health significance of these changes need further study in order to understand their possible role in the development of long term-health conditions, such as cardiovascular disease. Cardiovascular diseases are the main cause of death in our modern societies, and there is now growing evidence suggesting a relationship between short sleep duration and these diseases.[7]

Increased leukocyte and neutrophil counts have been shown to be an independent risk factor for cardiovascular mortality. Furthermore, leukocytes are involved in atherogenesis and in the plaque destabilization through proteolytic and oxidative actions. In this process, neutrophils are well known to release proteolytic proteases inducing a desquamation of endothelium,[8] as well as chemotactic agents such as leukotrienes B4 in patients with stable angina[9] and large amounts of inflammatory mediators.[10] Neutrophils also produce superoxide anions in hyperlipidemic patients.[11]

Now that the circadian fluctuations of the leukocyte subsets and the effects of sleep deprivation on leukocyte subsets are well characterized,[4] the next step should be the study of the activation status of leukocytes. Indeed, the monocyte-derived macrophage plays an important role in the development of macrovascular disease, by initiating and supporting the atheromatous lesions in the subendothelial space. The adhesion of the monocytes to the endothelium and their extravasation into the intima are key steps in the atherogenesis. The essential role of L-selectin (CD62-L) expressed by monocytes has been demonstrated.[12] Platelets are also involved in this process by forming complex with monocytes,[12] and these complexes are correlated with the lipidic profile.[13] In this context, the observation of circadian variations in cell adhesion molecule expression by normal human leukocytes[14] should be taken into account in future sleep deprivation experiments.

Last but not least, the extrapolation of sleep deprivation experiments to the effects of chronic sleep loss in everyday life remains debatable. Indeed, the accumulation of sleep debt without sufficient recovery could have deleterious effects. However, it is also possible that long term compensating immune response could occur in some subjects, as observed in shift workers.[15]

In conclusion, despite the fact that several epidemiological data suggest that sleep loss has cardiovascular effects, sleep deprivation experiments dedicated to this topic remain scarce. Further studies are needed to help to understand how sleep, sleep loss and circadian disruption are affecting the cardiovascular system and how to prevent these effects.

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