Could not win thee sleep: Metabolic cost of sleep debt

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Abstract

This presentation will discuss recent translational discoveries from our group that demonstrate metabolic profiling using cutting edge NMR spectroscopy and mass spectrometry are instrumental in understanding the biology of sleep and chronobiology. Sleep or sleep like behavior is conserved in almost all animal species across the evolutionary timescale. The physiological role of sleep to increased quality of life is known but not well understood. It is believed that sleep serves as a compensating mechanism for the systemic tax related to the activities during wakefulness. In spite of clear health benefits, sleep curtailment is an overwhelming and prevalent burden across the globe. Decreased sleep and sleep disorders are associated to life threatening diseases including cardiometabolic ailments and cancer. Using metabolomics technologies, we have shown in a rat model that sleep restriction imparts significant changes in hepatic metabolic profiles. Similar changes are also heavily manifested in circulatory peripheral metabolites and lipids. Together, these observations demonstrate a shift in oxidative metabolism. In humans, sleep restriction leads to global metabolic shift associated to alteration in energy metabolism. We have further demonstrated that metabolic changes are manifested in chronic diseases such as insomnia associated with decreased quality and quantity of sleep. These studies reveal that insomnia rewires the metabolic network to induce night-time catabolic activities and significantly affects the metabolic oscillation during the diurnal day. Some of the changes are associated to altered metabolic networks preceding type 2 diabetes hence reaffirming the notion that altered sleep leads to metabolic diseases. Finally, we posit that these types of studies will be critical in clinics for unraveling sleep deprivation related disorders and their treatment.

Sleep and its disorders are increasingly becoming important in our sleep deprived society. Sleep is intricately connected to various hormonal and metabolic processes in the body and is important in maintaining metabolic homeostasis. Research shows that sleep deprivation and sleep disorders may have profound metabolic and cardiovascular implications. Sleep deprivation, sleep disordered breathing, and circadian misalignment are believed to cause metabolic dysregulation through myriad pathways involving sympathetic overstimulation, hormonal imbalance, and subclinical inflammation. This paper reviews sleep and metabolism, and how sleep deprivation and sleep disorders may be altering human metabolism.

Consequences of sleep deprivation and fragmentation are being increasingly recognized. We are a sleep deprived society with evidence showing that we sleep on a mean 6.8 hours as against 9 hours a century ago. Around 30% of adults report sleeping but 6 hours per night [1–3]. The 24/7 economy and its subsequent impact on sleep patterns could also be testing the bodies limits to take care of metabolic and hormonal equilibrium. Prevalence of both diabetes and obesity has increased to accumulate pandemic proportions. Though other factors like diet and reduced physical activity have contributed to the obesity epidemic the impact of sleep dysregulation on causing metabolic derangements is being increasingly recognized. Considering only alittle percentage of individuals can maintain a healthy weight over an extended period on diet and exercise alone, the impact of sleep on weight has opened a new venue for potential intervention. Understanding this subject is vital as both sleep and metabolic dysregulation are common and growing problems. There are many unresolved issues including cause and effect, pathogenesis and potential implications to therapy.

Human sleep comprises of nonrapid eye movement sleep (NREM) and paradoxical sleep . NREM is further comprised of three stages (stages N1, N2, and N3). N3, also mentioned as slow wave sleep, is taken into account deep roll in the hay the body being least metabolically active during this era . REM sleep is characterized by vivid dreams, loss of muscular tonus , and rapid eye movements. The EEG pattern of paradoxical sleep closely mimics that of wakefulness marked by a high-frequency and low-voltage wave pattern. NREM and paradoxical sleep occur alternatively in cycles of around 90 minutes throughout the night [4]. The first half of the night is predominantly NREM, and the second half is predominantly REM sleep. Sleep architecture, though, is heavily influenced by genetic and environmental factors including sex, race, socioeconomic status and culture among others. Sleep

duration in mammals generally depends on the dimensions of the animal [5]. Elephants require only 3 hours of sleep while rats and cats can spend up to 18 hours in sleep. It is postulated that this might flow from to differences in metabolism. Smaller animals have higher rate and better body and brain temperatures compared to larger animals. Metabolism is defined because the whole range of biochemical processes that occur within a living organism. It constitutes the 2 processes of anabolism (build up) and catabolism (break down). In simpler terms, metabolism is that the amount of energy (calories) the body burns to take care of itself. Metabolism generally is related to cell injury thanks to the discharge of free radicals [6]. The lower rate and brain temperature occurring during non-REM sleep seem to supply a chance to affect the damage done during awake and metabolically active period. Siegel and his group from University of California at l. a. (UCLA) have shown brain damage in sleep-deprived rats [7]. Most data available and mentioned during this review deals with glucose utilization and energy expenditure. It is believed that in normal sleep the rate reduces by around 15% and reaches a minimum within the morning during a standard circadian pattern [8, 9]. Only a 15% reduction in rate appears counter-intuitive considering the prolonged state of physical inactivity. However, the basal rate constitutes 80% of the metabolism needed to take care of all cellular processes within the body. Glucose utilization in normal subjects is highest during wakeful state and lowest in orthodox sleep and intermediate in paradoxical sleep [10].

Biography :

Arjun Sengupta is a Chemist who has received his PhD training in the fields of Metabolomics of Infectious Diseases and NMR Spectroscopy. Currently, he is working in the Laboratory of Aalim M Weljie in University of Pennsylvania. His research interest involves deciphering the link between metabolism, sleep and circadian rhythm and how such links can be exploited for translational and clinical purpose. He uses high resolution NMR spectroscopy and mass spectrometry to profile tissues and biofluids from sleep restricted animals and human recruits to explore the connection between sleep, metabolism and other phenotypes related to disease and aging. His research in the field of Metabolomics of insomnia and sleep restriction unraveled crucial changes in metabolic pathways that may explain some of the clinical manifestation of sleep curtailment.This work is partly presented at International Conference on Metabolomics and Diabetology

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