Alterations in Plasma Metabolites During Acute Sleep Deprivation

Ani Uyku Yoksunluğunda Plazma Metabolit Düzeylerindeki Değişimler

Mustafa Onur ULU

Istanbul University, Cerrahpasa Medical Faculty, Department of Neurosurgery, Istanbul, Turkey

Corresponding Author: Mustafa Onur ULU / E-mail: dronurulu@gmail.com

The battles with sleep are well known to neurosurgeons especially during the training years. The feeling of falling and quickly jerking awake, bumping your head to the assistant scope of the microscope may sometimes be inevitable especially while assisting a case if you are awake for 24 hours. Sleep deprivation, inadequate quality of sleep, and disruptions to the sleep-wake cycle have consequences on how we function in the daytime. A sleepy and fatigued person suffers from impaired judgment and decreased hand-to-eye coordination, and is more likely to make mistakes and bad decisions. Moreover, sleep restriction and circadian clock disruption are associated with metabolic disorders including obesity, insulin resistance, diabetes and cardiovascular disease (1). An interesting study by Davies et al. in the July 22 issue of the Proceedings of the National Academy of Sciences (PNAS) journal represents an important contribution to metabolic profiling during sleep and acute total sleep deprivation conditions in humans (2).

The investigators aimed to elicit plasma metabolite rhythms using untargeted and targeted liquid chromatography (LC)/MS metabolomics in healthy male participants during a 24-hour wake/sleep cycle followed by 24 hours of wakefulness. Fifteen males (mean age 24 ± 5 years, BMI 24.9 ± 2.6 kg/m2) were enrolled into the study and plasma samples from 12 were analysed (mean age 23 ± 5 years, BMI 24.5 ± 2.3 kg/m2). By using the untargeted LC/MS metabolomics method, the researchers extracted 367 metabolite features and quantified 171 metabolites for each sample. Among these 171 metabolites, 41 (25 glycerophospholipids, 9 acylcarnitines, 4 sphingolipids, 2 biogenic amines, 1 amino acid) exhibited significantly increased levels during sleep deprivation compared with during sleep.

Among these 41 increased metabolites, serotonin showed the largest percent change between the sleep and sleep deprivation states (44 ± 20%). Serotonin plays a major role in sleep cycles mainly by promoting wakefulness. Low levels or an imbalance of serotonin at the synaptic level has been closely related with major depressive disorders. First suggested as a therapy for "melancholia," by the German psychiatrist Johann Christian August Heinroth (1773-1843), sleep deprivation has been used as a treatment method for depression (3). The authors conclude that the raised levels of serotonin detected in the current study during sleep deprivation may provide a possible antidepressive mechanism for this intervention in humans.

Melatonin, taurine and tryptophan were found to vary significantly with sleep status and show increased levels during acute sleep deprivation. The authors suggest that high levels of tryptophan measured during sleep deprivation may also contribute to the antidepressive effect of sleep deprivation, directly or indirectly via serotonin synthesis. High melatonin levels could also be linked to high taurine levels that have been shown to increase melatonin by stimulating the activity of N-acetyltransferase, the enzyme that controls the rhythmic production of melatonin in the pineal gland.

Significantly high levels of 25 of the 86 glycerophospholipids (29%) and 4 of the 14 sphingolipids (29%) were also found during sleep deprivation. However, some of these glycerophospholipids (12 of 25) and 1 sphingolipid were found to have a steady increase across the study period. The authors suggest that inactivity and lack of exercise during the laboratory study protocol may explain this accumulation and diet should not be regarded as a factor since the food content at each set meal was identical. On the other hand, most of the glycerophospholipids and sphingolipids quantified in the study exhibited a significant fit to a cosine curve regardless of sleep status and meal pulses. The authors conclude that this finding is consistent with the results of previous human metabolomics and transcriptomic studies suggesting that the endogenous circadian system that controls lipid metabolism and the associated transcripts are robustly rhythmic, and are not affected by mistimed sleep. Nine acylcarnitines had significantly increased levels during sleep deprivation. The majority (8 of 9) was significantly increased only during sleep deprivation compared with sleep and not between the awake conditions; this finding has been regarded by the authors as the effect of high sleep pressure on acylcarnitine levels.

To sum up, the study by Davies et al. in my opinion is a valuable contribution to the accumulated data about the effects of acute sleep restriction and circadian clock misalignment on human

metabolism and the readers are strongly encouraged to read the full text of the article (2). Determining the full impact of exogenous factors such as sleep on the metabolome will be crucial for the future metabolic profiling-based identification of biomarkers of disease and drug effects.

REFERENCES

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