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EDITORIAL

Sleeping well and on time—a prevention and prescription for diabetes?

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In this issue of the journal, a study from Turkey shows that subjects with type 2 diabetes admitted in hospital had significant sleep disturbances as measured by Pittsburgh Sleep Quality Index. Depression was observed to be associated with sleep disorders in most of them [1].

For something that we spend a third of our life in, we knew very little about sleep for many years: how we do it, why is it needed, what it does and what happens when it is early or late, too little or too much, difficult to attain or disrupted. In the past few years, the bits of this complex puzzle are being unraveled piece by piece.

The brain lacks a lymphatic system and depends on the interstitial space and the CSF to remove waste and toxic metabolites. In an elegant study, Xie et al. demonstrated that the mouse brain shrinks allowing the interstitial space volume by 60 % allowing deeper penetration of CSF and consequent clearance of toxic brain metabolites [2]. This explains the restorative function of the brain. It is possible that a critical accumulation of these metabolites in the interstitial space is the switch that drives us to sleep.

Sleep and exposure to light appear to be intricately related to homeostasis at a fundamental level. Respiration, photosynthesis and feeding behaviour are linked to the light darkness cycle. "Clocks at the suprachiasmatic nucleus" in the brain and "clocks" in the periphery contribute together to long-term weight stability by maintaining a precise balance between energy intake and expenditure. These circadian clocks affect core metabolic functions including gluconeogenesis, adipocyte differentiation and possibly inflammation [3].

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Insufficient, excessive and decreased quality of sleep have all been linked to metabolic disorders including diabetes. A meta-analysis of seven longitudinal studies with 5–17 years of follow-up (total 107,756 participants) concluded that short sleep (<5–6 h/night) predicts the development of T2DM with a pooled relative risk (RR) of 1.28. In patients with established diabetes, sleep deficit may increase the HbA1C by a median of 1.1 % [4]. As regards to quality, self-reported difficulty in initiating sleep was associated with RR of developing diabetes of 1.56, while difficulty in maintaining sleep was associated with a RR of 1.84 making disordered sleep one of the strongest risks of diabetes (at par or higher with family history) [5]. Similarly, a five-point increase in the Pittsburgh Sleep Quality Index predicts a median increase of HbA1C by 1.9 % [6]. Needless to add, an extreme form of sleep disturbance such as obstructive sleep apnoea is associated with both increased risk of and poor control of diabetes.

While shortened and disturbed sleep are the bane of the modern world, there are two other dynamics that make this pie toxic: these are circadian disruption and circadian misalignment. When there is circadian disruption as occurs when the light dark cycle is reversed, there is evidence of altered pancreatic function with increase in apoptosis in rats prone to diabetes. In the Nurses' Health Study, those who worked in rotating night shifts had increased hazard ratios for diabetes between 1.03 and 1.24, after adjusting for traditional diabetes risk factors as well as body mass index (BMI), with higher risk in those who had a longer duration of shift work compared to those reporting no shift work [7].

When a person's natural circadian alignment (lark vs owl) is changed, there appears to be significant consequences. "Eveningness" itself seems to confer an increased risk of diabetes lending potency to the old adage "early to bed and early to rise". It appears that variations in some clock genes can

confer eveningness and consequently high BMI, insulin resistance and poor diabetes control [8, 9].

Combining these disturbances appears to be compounding. Chronic sleep restriction when combined with circadian disruption causes a 32 % reduction in insulin secretion and an 8 % reduction in resting metabolic rate translating into a 5.6-kg gain in weight [10].

But we are still scratching at the surface in our knowledge of the magnitude of the effects of sleep and circadian disturbance on diabetes. As a nation, this knowledge is important since so many of our young sacrifice sleep and darkness for the sake of our economy. Fundamental questions about balancing the health and progress await the outcome of research in this area. Yücel and colleagues have added some more information to this quest.

In the past 200 years, we have interfered with a natural order of things more than ever in the history of human kind. We eat more, more frequently, more processed and different kinds of food than our ancestors did. We work longer but less strenuously than our forefathers. We sleep less and less well and much different times than them. We have more light and less darkness but are exposed to less sunlight that our ancestors did. These rapid changes in a short span are bound to have consequences, and diabetes (and its poor control) appear to be one of them. It is important that we learn more about the effects of sleep and its disturbance and the light cycle and its disruption on human health. Our future as a species may depend on it.

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