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22 UNDERGRADUATE RESEARCH CRITIQUE

Research Critique on "Assessment of MTNR1B Type 2 Diabetes Genetic Risk Modification by Shift Work and Morningness-Eveningness Preference in the UK Biobank"

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ABSTRACT

Introduction: Rotating night shifts has been correlated with increased T2D risk via circadian misalignment between endogenous circadian cycle and behavioral cycles, potentially affecting worse glucose regulation. The MTNR1B single nucleotide polymorphism has been associated with T2D as it relates to melatonin rhythms and food intake. Despite the possible linkage between genetic mutation on MTNR1B and consequences of night shift work, there is lack of scientific evidence on their relationships so that it is unknown whether MTNR1B risk allele could potentially exacerbate T2D risk via the mechanisms linking circadian misalignment.

Purpose: Dashti et al. aimed to test (a) the independent association of MTNR1B risk allele, night shift work, and chronotype on the prevalence of T2D and HbA_{1c} levels, and (b) its interactive effects of MTNR1B risk allele in a large population from the UK Biobank, investigating the respective contributions of genetic predisposition and environmental exposure to the development of chronic disease.

Methods: The present study included 189,488 participants from the UK Biobank as being employed or self-employed and of European decent. The participants self-reported their work schedule and morningness-eveningness preference for chronotype and a genotype containing MTNR1B risk allele and HbA_{1c} levels was obtained. The association between work and morningness-eveningness preference when compared to the prevalence of T2D and HbA_{1c} were evaluated utilizing crude and adjusted linear regression models.

Results: In comparison to day workers, shift working participants had a higher prevalence of T2D (odds ratio [OR] 1.26 [95% CI 1.15-1.39]). The participants who self-reported definite eveningness and those who were classified as definite eveningness from the accelerometer had a significant increase in the prevalence of T2D (OR 1.29 [95% CI 1.13–1.47]). Together with increased OR of T2D, higher HbA_{1c} was observed with shift worker and morningness-eveningness preference. Participants self-reporting

definite morningness preference saw an increase in prevalence of the MTNR1B risk allele (OR 1.17 [95% CI 1.07–1.28]). With each additional G allele (risk allele) in MTNR1B gene, a 10 % increase in T2D risk was observed. However, there was no interaction between shift work and the MTNR1B risk allele.

Conclusion: Comprehensive examination of T2D risk stemmed from genetics and/or environment is essential for better understanding of etiology and optimal identification of early intervention and treatment. In this study, current and night shift work and definite morningness-eveningness has been shown to elevate the prevalence of T2D and HbA_{1c} levels, although there was no association between shift work and MTNR1B risk allele. The data suggest that night shift work and misalignment of endogenous circadian rhythm with behavior cycles may put an individual at increased risk of T2D; however, there should be small effects of MTNR1B genetic variation interacting with environmental factor (i.e., night shift) on T2D risk.

Critique: With a growing number of individuals needed to work night shifts, it's especially important to understand the potential increased risk for T2D together with genetic predisposition. However, some limitations in this study hinder the definitive conclusions on the relationship between MTNR1B variants, night shift and T2D risk. First, there was a lack of available data on physical activity, education level and socioeconomic components that should be accounted when examining potential interaction between MTNR1B and environment on T2D risk. Additionally, common night shift jobs include security guard, taxi driver, and emergency room doctors. The health literacy of a security guard may be different than that of an emergency room doctor, thereby skewing the associations with T2D. Patients with low literacy skills may not be able to make good judgements in everyday life concerning eating habits and exercise leading to an increased risk of T2D. Lastly, their cross-sectional design does not allow the investigation of causal relationship. Although the odds of T2D was a primary outcome, not having prospective observation could hinder proper interpretation. In this case, the study may use continuous/sensitive variables of fasting and 2-hr glucose concentrations which are the classical risk biomarkers as their outcome. It is also noted that fasting and 2-hr glucose will provide more accurate risk information than HbA1c (which the current study used). In closing, MTNR1B has a potential to be investigated as an interactive factor with environment on T2D risk so that further comprehensive examination of T2D pathophysiological components along with its genetic mutation is warranted.

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