Research on the correlation between insomnia and alcohol intake frequency: a Mendelian randomization study

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Abstract: This study is designed to explore the correlation between insomnia and alcohol intake frequency via a Mendelian randomization study. Data for Mendelian randomization analysis were obtained from the IEU Open GWAS project. GWAS datasets for insomnia and alcohol intake frequency were used to conduct the analysis. The random-effects inverse-variance weighted method was used in the main MR analyses and the weighted median method as complementary analyses. MR-Egger, weighted mode, and simple mode were also adopted to assess causal relationships between exposure and outcome variables. Sensitivity analysis proved the reliability of the analysis results. There was no positive relationship between insomnia and alcohol intake frequency.

1. Introduction

Sleep is one of the most basic physiological needs of the human body and an essential physiological requirement for restoring energy [1] [2]. Good sleep is essential for health, while poor sleep increases morbidity and mortality risk [3]. Adequate sleep duration, normal sleep rhythm, and good sleep quality are crucial for the recovery of human energy [3]. Moreover, sleep is also important for regulating many metabolism functions, with substantial evidence suggesting that sleep habits and disorders are related to diabetes [4]. However, sleep may be influenced by multiple factors. Insomnia is a common type of sleep disorder and may be a persistent condition [5, 6]. Insomnia is characterized by sleep loss due to problems initiating and maintaining sleep and/or early-morning awakening, with an inability to return to sleep, which can be influenced by many factors, such as emotion, psychology, personal preference, etc [7] [8]. Severe insomnia can lead to decreased work ability, cognitive impairment, and other related issues. Insomnia is also a common condition associated with marked impairment in function and quality of life, psychiatric and physical morbidity, accidents [8]. There are research reports that insomnia is related to unhealthy lifestyle habits and smoking and drinking[9] [10]. Alcohol-dependent patients may have a higher risk of insomnia and poor sleep quality [11]. However, there is currently no research to prove whether there is a correlation between insomnia and frequency of alcohol intake. This issue urgently needs to be determined.

Mendelian randomization is an epidemiological research method that can analyze the relationship between disease factors and disease outcomes from a genetic perspective. Mendelian random analysis can effectively reduce the influence of confounding factors. The present study is designed to explore the correlation between insomnia and alcohol intake frequency via Mendelian randomization study.

2. Materials and Methods

2.1 Study Design

Data for Mendelian randomization analysis were obtained from the IEU Open GWAS project (website: https://gwas.mrcieu.ac.uk/). GWAS datasets for insomnia (ebi-a-GCST90018869) and alcohol intake frequency (ukb-b-5779) were used to conduct the analysis. GWAS datasets for insomnia (ebi-a-GCST90018869) collectively involved 486,627 participants (1,402 cases and 485,225 controls) and the alcohol intake frequency (ukb-b-5779) collectively involved 462,346 participants. Single Nucleotide Polymorphisms (SNPs) associted with insomnia were identified from the GWAS datasets, using a significance threshold of $P < 5 \times 10^{-8}$. To ensure robustness, SNPs associated with the outcome were excluded. The SNPs with F-statistics (F = beta ^{2} se ^{2}) < 10 were removed.

2.2 Statistical analysis

The random-effects inverse-variance weighted (IVW) method was used in the main MR analyses and the weighted median method as complementary analyses. MR-Egger, weighted mode, and simple mode were adopt to assess causal relationships between exposure and outcome variables, too. Results were presented as odds ratios (ORs) with 95% confidence intervals (CIs). To evaluate the robustness of our findings, Cochran's Q test was used to identify heterogeneity ($P < 0.05$ indicating significant heterogeneity). The study followed the STROBE-MR guidelines.

3. Results

3.1 Causal relationship between insomnia and alcohol intake frequency

Detailed information of GWAS datasets included in the study was provided in Table 1. There was an association of genetic liability to insomnia with alcohol intake frequency (odds ratio, 0.969 [95% CI, 0.969 - 1.313], P= 0.838) (Figure 1). The forest plot and the scatter plot (Figure 2) showed that alcohol intake frequency did not increase the risk of insomnia.

Table 1 Detailed information of the GWAS datasets in the present study.

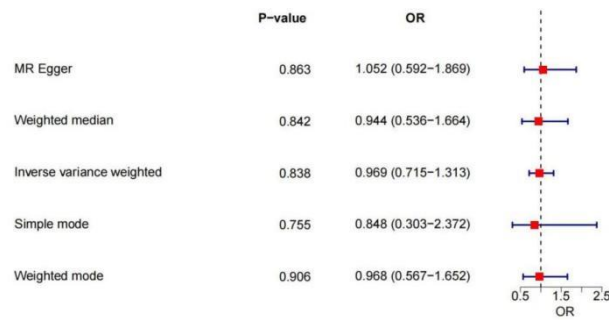| Dataset	Name	Sample size	Number of SNPs	Population
ebi-a-GCST90018869	insomnia	486,627	24,196,985	European
ukb-b-5779	alcohol intake frequency	462,346	9,851,867	European

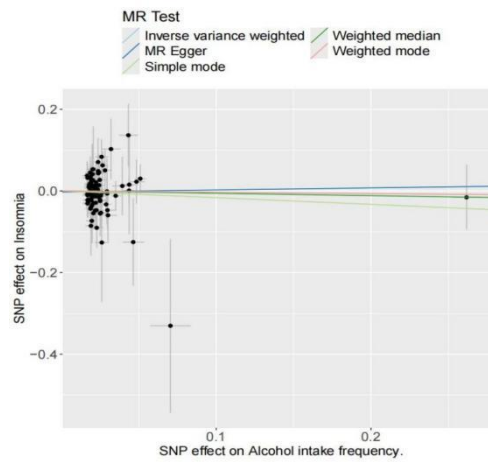Figure 1 Forest plot of insomnia and alcohol intake frequency.

Figure 2 Scatter plot of insomnia and alcohol intake frequency.

3.2 Sensitivity analysis

The IVW method was used to detect heterogeneity, and the results suggested that there was no heterogeneity. A funnel plot was drawn to show the heterogeneity results (Figure 3). The "leave-one-out" method used the IVW method by default, no single SNP had a large impact on the overall results after eliminating any SNP, indicating that the results were robust (Figure 4). Consequently, the estimated effects cannot be explicated by any single genetic instrument. Sensitivity analysis proved the reliability of the analysis results.
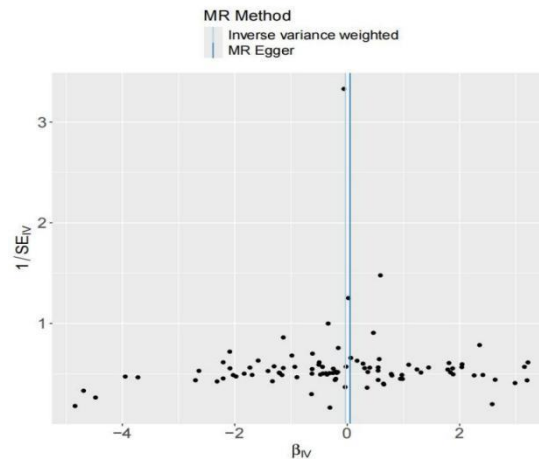

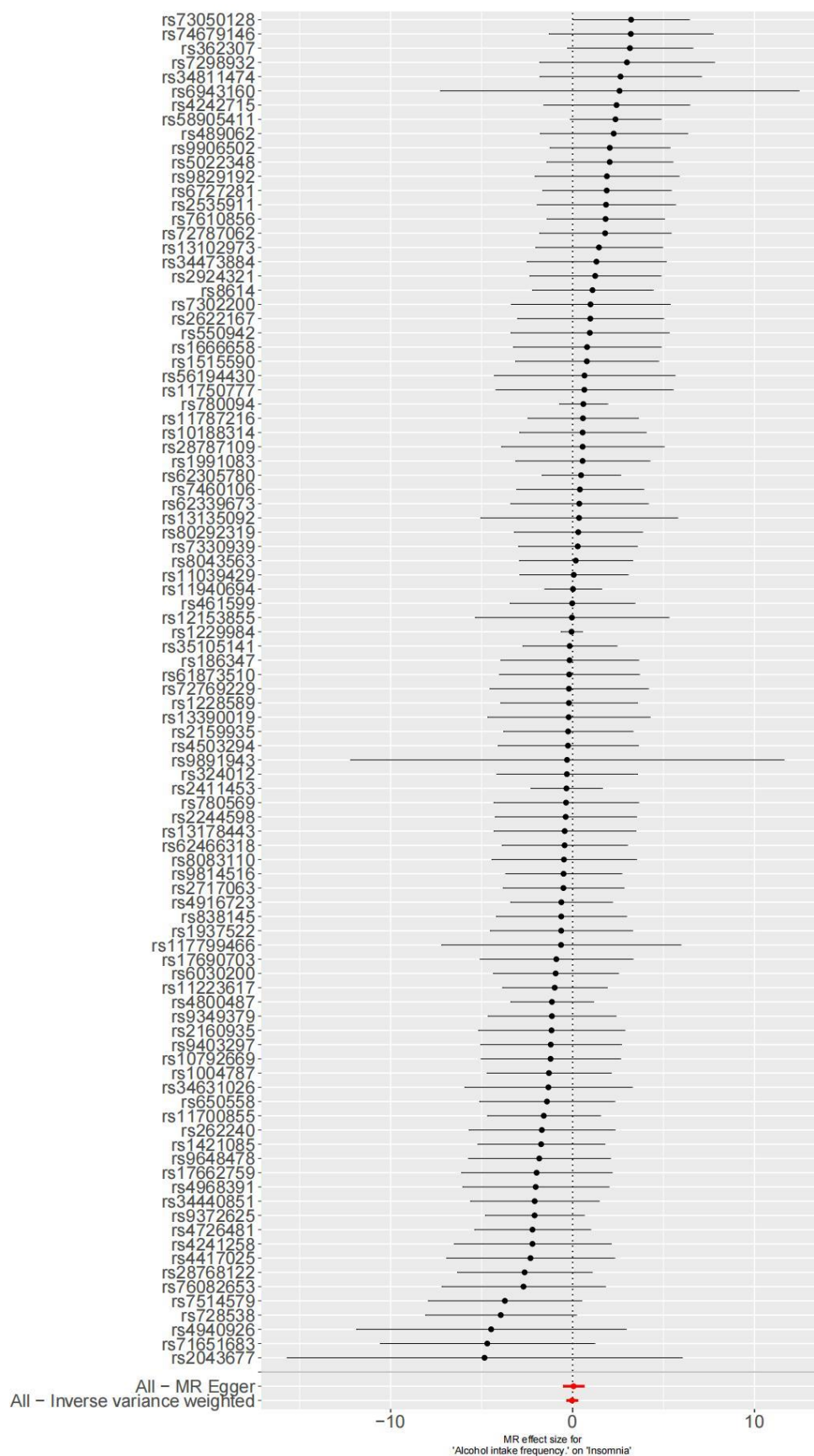Figure 3 Funnel plot of insomnia and alcohol intake frequency.

Figure 4 Single_snp_plot of insomnia and alcohol intake frequency.

4. Discussion

It is known that alcohol may be a potential risk factor for insomnia, but the causality of this association is still unclear [12]. The present study aimed to reveal the causal relationship between insomnia and alcohol intake frequency. The two-sample MR results showed no causal association between insomnia and alcohol intake frequency. Sleep is one of the most fundamental physiological functions of human beings and has garnered significant attention from researchers. Adequate sleep quality and quantity help the body maintain normal physiological and social functions [1]. There may be many risk factors that can affect insomnia, including personal preferences such as smoking and alcohol consumption. Previous studies have revealed that insomnia may be closely related to alcohol dependence [13].

Previous studies found that people with poor sleep may attempt to relieve anxiety for better quality, whether daily alcohol consumption was a factor that moderates and disturbance is not known [14]. The research covered eighty-four participants who reported poor sleep, aged 20 to 80 years, to detect the relationship between alcohol consumption and sleep quality, revealing that daily alcohol intake was related to moderating the relationship between anxiety and sleep quality [14]. Unfortunately, the sample size included in this study was relatively small. People with poor sleep quality should avoid misusing alcohol intake. A previous study found that sleep disruption was common in early alcohol recovery [15]. A study claimed that consuming alcohol on a daily basis and having anxiety were found to be predictors of poor sleep quality [14]. Studies have shown a close relationship between alcohol consumption and poor sleep quality. However, there was no positive causal relationship between insomnia and alcohol intake frequency determined by Mendelian randomization analysis in the present study. This suggested that there may be a close relationship between the amount of alcohol intake rather than just the frequency of alcohol intake and insomnia. Further research is urgently needed to explore the mechanisms involved.

In conclusion, our two-sample Mendelian randomization analysis recovered genetic support that there was no positive causal relationship between insomnia and alcohol intake frequency.

5. Limitation

GWAS datasets for Mendelian randomization analysis was from European population, not including all types of people in the world.

6. Conclusion

In conclusion, no positive causal relationship between insomnia and alcohol intake frequency was determined by Mendelian randomization analysis in the present study.

Conflicts of interest

There are no conflicts of interest.

Authors' contributions

Weilin Yang, Xianjie Zhang, Yanhua Peng, and Lei Deng carried out the experimental design work, participated in the data analysis, design of the study and drafted the manuscript; Weilin Yang and Lei Deng carried out the data collection; All authors helped conceive and coordinate the study. All authors participated in the patient recruitment. All authors gave final approval for publication.

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