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Master's Thesis

Understanding the Potential Causal Effects in Alzheimer's Disease

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Abstract

Alzheimer's disease is a progressive neurodegenerative disease that leads to cognitive decline, which includes impairment of memory, decision making, language, judgment, and physical surroundings. The disease was described for the first time in 1906 by Alois Alzheimer, and even though the disease has been continuously investigated since then, little is still known about the etiology of the disease. The lack of knowledge is also reflected in the opportunities for treatment, as only a few therapeutics are available with little to no effect. Currently, about 55 million people are globally suffering from dementia, of which Alzheimer's disease accounts for 60-70% of these cases. However, this amount is expected to triple by 2050, which highlights the importance of developing better treatment options for the disease. To do so, it is necessary to gain knowledge of Alzheimer's disease. In an attempt to do so, the focus of this study is to get a better understanding of potential causal effects in Alzheimer's disease. This is obtained by investigating the genetic correlation and the causal relationship between Alzheimer's disease and several relevant traits using LDSC and GSMR, respectively. The results from LDSC suggests that there is a genetic correlation between Alzheimer's disease and depression (rg = 0.1328, P = 0.0331), educational attainment (rg = -0.1505, P = 0.0365), height (rg = -0.1308, P = 0.0161), and sleep duration (rg = -0.1408, P = 0.0237). On the other hand, the results obtained from GSMR indicates that height (effect of -0.00122693 with P = 5.02034×10^{-5}) and migraine (effect of 0.00223245 with P = 0.0318533) seem to have a causal effect on Alzheimer's disease. However, in general the results seem very robust and some of them even seem ambiguous. This could be due to the fact that proxy cases and controls were included in the Alzheimer's disease GWAS data, as this might influence the statistical power in the analyses. For future studies of Alzheimer's disease, a more powerful Alzheimer's disease dataset might be necessary. This is obtained either by recruiting more clinically diagnosed Alzheimer's disease cases in order to increase the sample size, or if proxy cases are included, they need to be corrected for in the proper way to prevent the biases they might cause.

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