

COVID-19 and Retinal Layer Thickness: A bidirectional Mendelian Randomization Study

lili Lang¹, Kun Zhao¹, Xiqiao Xiang¹, Wang Wenwen¹, QingWei Zhang², Bingxin Gu³, Yanyan Zhang⁴, xingxing zhang¹, Zhen Tang¹, Meixiang Guo¹, Wei YuanHao⁵, Lin Yuan¹, and Shaoling Yang¹

¹Shanghai 6th Peoples Hospital Affiliated to Shanghai Jiao Tong University

²Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital

³Fudan University Shanghai Cancer Center Radiation Oncology Research Center

⁴Fudan University Institute of Radiation Medicine

⁵Harbin Medical University School of Public Health

February 11, 2023

Abstract

Observational studies have reported that COVID-19 is associated with alterations in retinal layer thickness, including changes in the ganglion cell inner plexiform layer (GCIPL) and retinal nerve fiber layer (RNFL). However, observational studies are susceptible to confounding factors and reverse causality. Therefore, we assessed the direction and strength of the causal relationship between COVID-19 patient phenotypes (susceptibility, hospitalization, and severity) and GCIPL and RNFL thicknesses using a bidirectional two-sample Mendelian randomization (MR) design. The inverse-variance weighted (IVW) method is the primary approach used to estimate causal effects. MR Egger, weighted median, weighted mode, MR Egger (bootstrap), and penalized weighted median methods were applied. In addition, we performed sensitivity analyses using RadialMR, MRPRESSO, MR Egger regression, Cochran's Q statistic, and Leave-one-out analysis. Forward MR analysis revealed that genetically identified COVID-19 susceptibility significantly increased the risk of GCIPL thickness (OR: 2.428, 95% confidence interval[CI]:1.493-3.947, $P_{IVW}=3.579 \times 10^{-4}$) and RNFL thickness (OR: 1.735, 95%CI:1.198-2.513, $P_{IVW}=3.580 \times 10^{-3}$). The results after excluding MRPRESSO and RadialMR to identify outliers and SNPs associated with confounding factors showed RNFL thickness(OR:1.800, 95%CI: 1.192-2.717, $P_{IVW}=5.147 \times 10^{-3}$). Reverse MR analysis did not indicate a significant causal association between GCIPL and RNFL thicknesses and COVID-19 phenotypes. In conclusion, the host genetic liability to COVID-19 susceptibility was causally associated with increased GCIPL and RNFL thicknesses. Documenting this association increases our understanding of the pathophysiological mechanisms underlying COVID-19 susceptibility in retinopathy.

Hosted file

Manuscript.doc available at <https://authorea.com/users/585096/articles/623958-covid-19-and-retinal-layer-thickness-a-bidirectional-mendelian-randomization-study>