Genetic correlations between intraocular pressure, blood pressure and primary open-angle glaucoma: a multi-cohort analysis


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Primary open-angle glaucoma (POAG) is the most common chronic optic neuropathy worldwide. Epidemiological studies show a robust positive relation between intraocular pressure (IOP) and POAG and modest positive association between IOP and blood pressure (BP), while the relation between BP and POAG is controversial. The International Glaucoma Genetics Consortium (n=27,558), the International Consortium on Blood Pressure (n=69,395), and the National Eye Institute Glaucoma Human Genetics Collaboration Heritable Overall Operational Database (n=37,333), represent genome-wide data sets for IOP, BP traits and POAG, respectively. We formed genome-wide significant variant panels for IOP and diastolic BP and found a strong relation with POAG (odds ratio and 95% confidence interval: 1.18 (1.14-1.21), P=1.8 × 10−27) for the former trait but no association for the latter (P=0.93). Next, we used linkage disequilibrium (LD) score regression, to provide genome-wide estimates of correlation between traits without the need for additional phenotyping. We also compared our genome-wide estimate of heritability between IOP and BP to an estimate based solely on direct measures of these traits in the Erasmus Rucphen Family (ERF; n=2519) study using Sequential Oligogenic Linkage Analysis Routines (SOLAR). LD score regression revealed high genetic correlation between IOP and POAG (48.5%, P=2.1 × 10−5); however, genetic correlation between IOP and diastolic BP (P=0.86) and between diastolic BP and POAG (P=0.42) were negligible. Using SOLAR in the ERF study, we confirmed the minimal heritability between IOP and diastolic BP (P=0.63). Overall, IOP shares genetic basis with POAG, whereas BP has limited shared genetic correlation with IOP or POAG.


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