Genetic architecture of open angle glaucoma and related determinants


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BACKGROUND: although the vertical cup-disc ratio (VCDR) and intraocular pressure (IOP) are important determinants of open angle glaucoma (OAG), it is unclear to what extent the genetic origin of these traits overlap with those of OAG. We evaluated whether the same genes that determine VCDR and IOP also predict OAG.

METHODS: genetic risk scores were constructed from single nucleotide polymorphisms (SNPs) using genome wide association data of 9326 participants from the Rotterdam Study cohorts (mean±SD age: 64.6±9.1 years). These risk scores were used to calculate the explained variance of VCDR and IOP in an independent cohort (Erasmus Rucphen Family study) consisting of 1646 participants (mean±SD age: 46.8±14.1 years) and the OAG risk in a subset of the Rotterdam Study cohorts. To evaluate false positive findings, we generated two new variables containing randomly sampled values to serve as a negative control.

RESULTS: The explained variance of VCDR increased when increasing the number of SNPs included in the risk score, suggesting a polygenic model. We found no clear evidence for a similar model for IOP, suggesting that a small number of SNPs determine the susceptibility to IOP. The SNPs related to IOP in terms of p values contributed little to VCDR. The risk scores associated with VCDR were also associated significantly with OAG. This suggests a common polygenic background for VCDR and OAG.

CONCLUSIONS: we found evidence for a polygenic model underlying one of the major traits of OAG, VCDR, and OAG itself. The IOP did not show any evidence for such a model.

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