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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