**Supplementary Table 1.** Genomic-SEM models to evaluate the association between POAG and neurodegenerative disorders (AD, ALS and PD); models are in lavaan syntax.

**Supplementary Table 2.** Genetic correlation between four neurodegenerative conditions, Alzheimer's disease (AD), frontotemporal dementia (FTD), Amyotrophic lateral sclerosis (ALS), Parkinson's disease (PD), and primary open-angle glaucoma (POAG) related phenotypes; high tension glaucoma (HTG), normal tension glaucoma (NTG), vertical cup-to-disk ratio (VCDR), macular thickness (MT), intraocular pressure (IOP), retinal nerve fibre layer (RNFL), ganglion cell-inner plexiform layer (GCIPL).

**Supplementary Table 3.** Genomic SEM model fit and correlation values.

**Supplementary Table 4.**  Shared regions between neurodegenerative disorders and POAG or POAG-related phenotypes, based on the GWAS-PW posterior probability of a shared region with a common causal variant (PPA) and local correlation using LAVA.

**Supplementary Table 5.** Causal association of thegene expression on POAG-related phenotypes, Alzheimer’s (AD) and Parkinson’s disease (PD) based on the SMR of peripheral blood eQTL data.

**Supplementary Table 6.**  Significant causal associations between glaucoma endophenotypes and T1 volume of brain regions based on GSMR. beta shows the effect of one SD unit change of the exposure on the outcome.

**Supplementary Table 7.** Significant causal associations between glaucoma endophenotypes and freesurfer ASEG volume of brain regions based on GSMR. beta shows the effect of one SD unit change of the exposure on the outcome.

**Supplementary Table 8.** Significant causal association between glaucoma endophenotypes and freesurfer parcellation based in the Desikan-Killiany brain atlas on GSMR. beta shows the effect of one SD unit change of the exposure on the outcome.

**Supplementary Table 9.** Causal association between glaucoma endophenotypes and MRI structural brain measurements based on different MR methods.

**Supplementary Table 10.** Multivariate MR association between glaucoma endophenotypes, intraocular pressure (IOP), Retinal Nerve Fiber Layer (RNFL), Ganglion Cell-Inner Plexiform Layer (GCIPL) and MRI structural brain measurements and mediated by cerebrospinal fluid (CSF) and systolic blood pressure(SBP).

**Supplementary Table 11.** GSMR results for the causal effect of Alzheimer's (AD) on glaucoma and related phenotypes. None of these results reached the statistical significance threshold after correcting for multiple testing (p < 2.4e-5).

**Supplementary Table 12.** Phenotypic association between glaucoma-related phenotypes and brain structure.

**Supplementary Table 13.** Effect estimate of instrumental variants used in the IVW MR analysis.