OP-07 RETINAL AND CORTICAL VASCULAR FUNCTION ACROSS THE MENSTRUAL CYCLE

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10.1136/bmjoo-2024-WVUK.7

Introduction Oestrogen has a protective effect against neurodegenerative conditions, including glaucoma and dementia. Animal models suggest that oestrogen has a vasodilatory effect, which is a possible mechanism for this. However, the full influence of oestrogen on specific cerebrovascular functions is unclear.

Aims This study aims to investigate the influence of hormonal fluctuations across a healthy menstrual cycle on measures of retinal and cortical vascular functioning.

Methods 27 menstruating participants (age mean[SD]=22.94 [3.52] years) completed a testing session during the early-follicular, late-follicular, and mid-luteal phase of their menstrual cycle. Bloods were taken to measure circulating hormones.

Retinal vasculature was assessed using a Swept-Source OCT (TOPCON healthcare), including:

- Choroidal thickness – 6mm^2 OCT scan
- Vessel density, radius, and resistance – 3mm^2 OCT Angiography

Cortical data were acquired on a Siemens MAGNETOM Prisma 3T MRI scanner and include:

- Grey matter Cerebral Blood Flow (CBF) and Arterial Arrival Time (AAT) – MPLD-pCASL scan
- Global Oxygen Extraction Fraction (OEF) – TRUST sequence

Linear models investigated the amount of variance explained by circulating oestradiol.

Results Oestradiol significantly decreased retinal resistance ($\chi^2(1)=6.1218$, $P=0.01335$), an effect which was greatest in the foveal vessels. Other retinal measures were stable across the menstrual cycle. No association was found with OEF, but oestradiol did significantly increase CBF ($\chi^2(1)=17.801$; $P=2.452e\text{-}5$) and AAT ($\chi^2(1)=9.5183$; $P=0.002034$), which was a global effect.

Conclusion Evidence for oestrogen's vasodilatory influence was demonstrated across a menstrual cycle and in multiple vascular beds. This provides information into how oestrogen influences the cerebrovascular system and highlights possible mechanisms by which oestrogen has a protective effect against neurodegenerative conditions.

Acknowledgements The Wellcome Trust (WT224267)

OP-08 ANALYSING THE TRANSCRIPTOME OF CHOROIDEREMIA PATIENT-DERIVED IPSC-RPE

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10.1136/bmjoo-2024-WVUK.8

Introduction Choroideremia is an X-linked recessive retinal dystrophy, marked by degeneration of the RPE, photoreceptors and choroid. Choroideremia is caused by loss-of-function variants in the *CHM* gene, with no genotype-phenotype correlation. The *CHM* gene encodes REP1 protein, which is involved in intracellular vesicle trafficking. Disruption to melanosome transport, photoreceptor outer segment digestion and phagolysosomal activation is reported in choroideremia models. The pathogenic mechanism of choroideremia is not yet fully characterised.

Aims There is no current animal model that fully recapitulates the choroideremia retinal phenotype. We aim to use patient-derived iPSC-RPE to identify novel disrupted pathways and therapeutic targets.

Methods We generated iPSC-RPE from a CHM^{S190X} patient-derived fibroblast line (n=3), and two wildtype control lines (n=3). Samples were sent off for paired-end RNAseq. Differential gene expression and enrichment analysis were performed (using threshold cut off for the adjusted p value of < 0.05, log2fold change > 2).

Results Significant disruption was seen in 4149 genes of CHM^{S190X} iPSC-RPE, compared to wildtype lines. Disrupted cytokine, cellular senescence, and oxidative stress pathways were seen in CHM^{S190X} iPSC-RPE, suggesting inflammatory pathomechanisms. Disruption of cell adhesion pathways was also highlighted, potentially causative of lymphocyte migration into the retina, as seen in choroideremia patients. Disruption of several ion transport mechanisms was observed, which could be associated with inflammation.

Conclusion To our knowledge, this is the first study to characterise the choroideremia iPSC-RPE transcriptome using RNA-seq. Disruption to inflammatory pathways were identified, which may draw parallels to underlying mechanisms in AMD.

OP-09 STRUCTURAL CORRELATIONS BETWEEN BRAIN MAGNETIC RESONANCE IMAGE-DERIVED PHENOTYPES AND RETINAL NEUROANATOMY

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10.1136/bmjoo-2024-WVUK.9

Introduction The eye is a well-established model of brain structure and function, yet region-specific structural correlations between the retina and the brain remain underexplored.

Aims To explore and describe the relationships between the retinal layer thicknesses and brain magnetic resonance image (MRI) derived phenotypes in UK Biobank.

Methods Participants with both quality-controlled optical coherence tomography (OCT) and brain magnetic resonance imaging (MRI) were eligible. Retinal sub-layer thicknesses and total macular thicknesses were derived from OCT scans. Brain image-derived phenotypes (IDPs) of 153 cortical and subcortical regions were processed from MRI scans. In this hypothesis-free study, we examined pairwise retinal-brain