In vitro and in silico Retinal Models of Neurodevelopmental Disorders

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Early diagnosis of neurodevelopmental disorders (NDDs) such as Autism Spectrum Disorder (ASD) and Attention-Deficit/Hyperactivity Disorder (ADHD) enables early intervention and is crucial for improving lifelong patient prognosis. Current diagnoses entail multi-hour psychiatrist evaluations that expose the need for a more objective and efficient NDD screening tool. Motivated by past clinical studies that have suggested retinophysiological differences in NDD patients, this research explores the retina as a biomarker for ASD and ADHD. In this work, I developed an interpretable retinal image-based convolutional neural network model for ASD and ADHD diagnosis through post-hoc analysis. Latent feature space visualizations demonstrated that model-extracted retinal features effectively separate patient conditions. Important retinal regions were localized via generation of saliency heat maps that reveal the macula, optic disc, and blood vessels as diagnostically-relevant. To better understand these regions, I pursued further biological interpretability through the development and gene expression analysis of a novel in vitro retinal model of ASD. Murine and human retinal cell lines were treated with sodium valproate, a chemical used to generate widely-accepted induced mouse and brain cell models of ASD. The validity of the proposed model was supported by the observed disruption of gene expression in numerous high-confidence ASD risk genes. Several differentially expressed genes relating to retinal development were identified that this work newly implicates in ASD pathophysiology. Ultimately, this work developed novel in vitro and in silico models that support the retina as a viable biomarker for objective NDD screening.

Awards Won: