Alpha Retinal Ganglion Cell Dysfunction Precedes Vascular Dysfunction in a Mouse Model of Type 1 Diabetes

Introduction

Diabetic retinopathy (DR), a complication of diabetes, is the leading cause of blindness among working-age adults (CDC)

DR is diagnosed by changes to retinal blood vessels, but changes to retinal neurons may occur first

- Thinning of retinal layers, changes in function (van Dijk, 2011) (Adams, 2012)

Retinal ganglion cells (RGCs) are the most likely neuron to show signs of damage

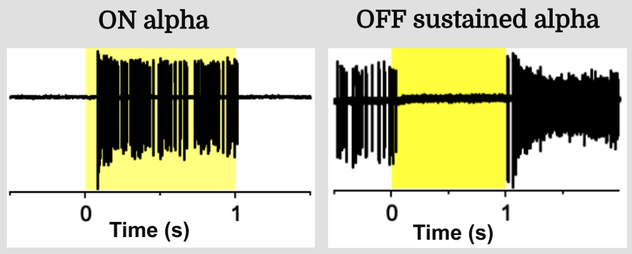
- Output neurons, indicate health of visual pathway
- Communicate visual features by firing spike trains in response to light stimuli (Goetz *et al*, 2021)

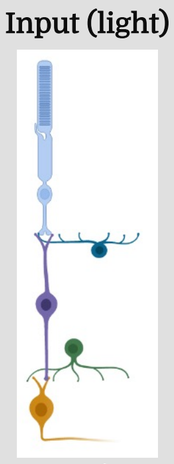
Specifically, alpha RGCs

- Affected by other retinal diseases (Della, 2017)
- Weakened baseline firing and contrast responses in preliminary experiments (Schwartz, 2022)

Example light response traces. Yellow indicates duration of stimulus.

(Credit: Retinal Ganglion Cell Typology Project)



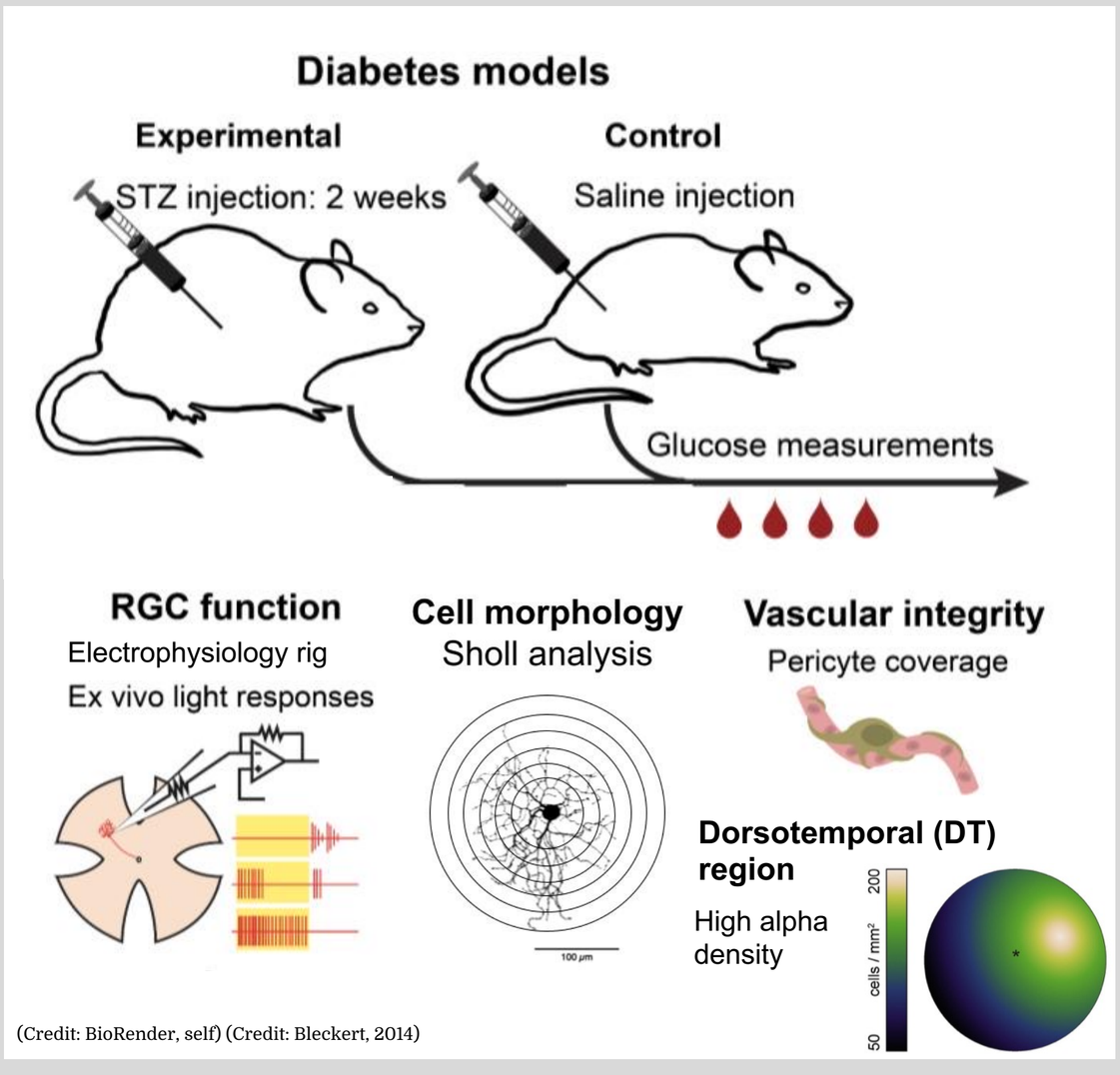


(Credit: BioRender)

Purpose

To identify the earliest detectable effects of diabetic retinopathy in the STZ mouse model by testing the function and morphology of ON and OFF sustained alpha RGCs.

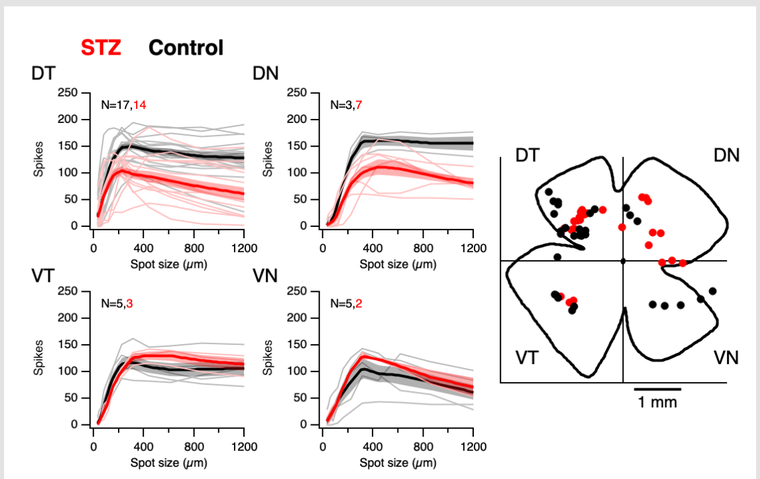
Methodology



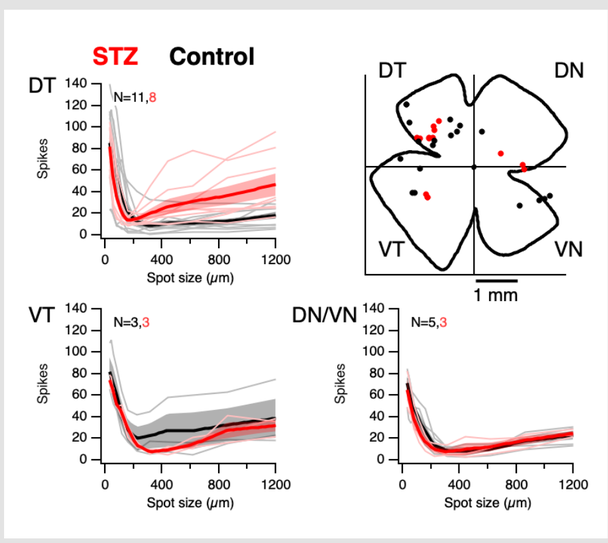
(Credit: BioRender, self) (Credit: Bleckert, 2014)

Results

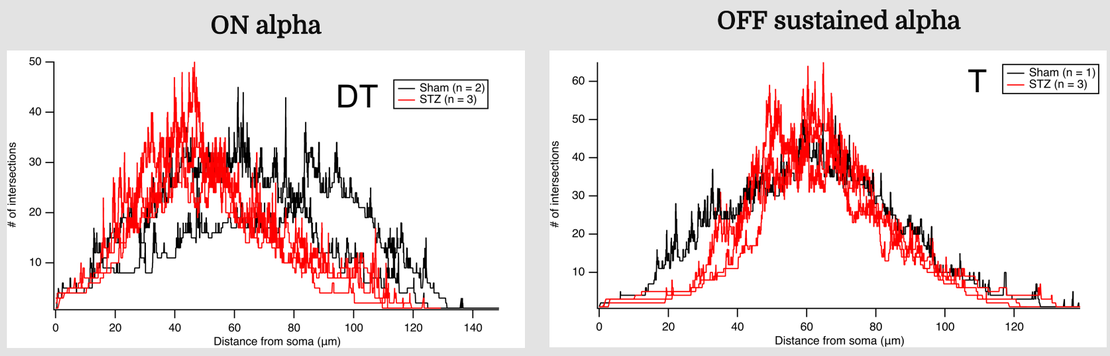
Diabetic DT and DN **ON alphas** have lower peak and avg. firing rates.



Diabetic DT **OFF sustained alphas** have higher baseline firing rates and less surround suppression.



Diabetic DT **ON alphas** have smaller cell diameters. Diabetic **OFF sustained alphas** do not display changes in cell size.



Conclusions

- Earliest evidence of neurodegeneration in DR
- Changes in firing rate and cell size
- May affect contrast vision
- Damage precedes vascular changes
- 2 weeks post-diabetes induction, vessels remain healthy

Future Research

- Determine if the cell itself is affected or if the input it receives is affected by DR
- Test other mouse models of diabetes
- Identify pharmacological targets for treatment

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