Novel technique for diagnosis of retinal and optic nerve degeneration

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Incurable eye diseases cause vision loss and reduce quality of life

Age-related Macular Degeneration (AMD)

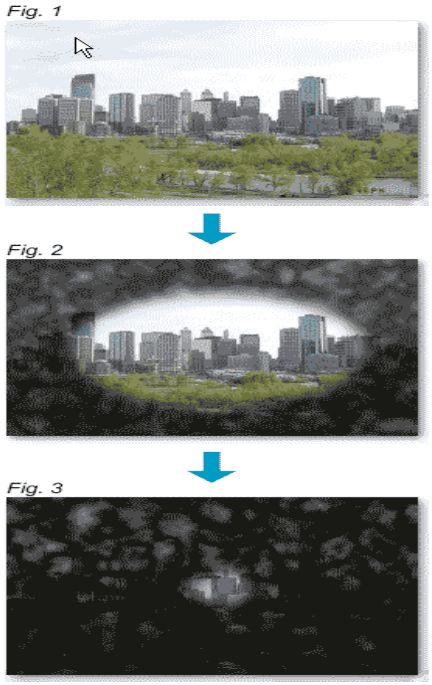
- ~30M patients

Diabetic Retinopathy

93M patients

Retinitis Pigmentosa (RP)

>1.5M patients

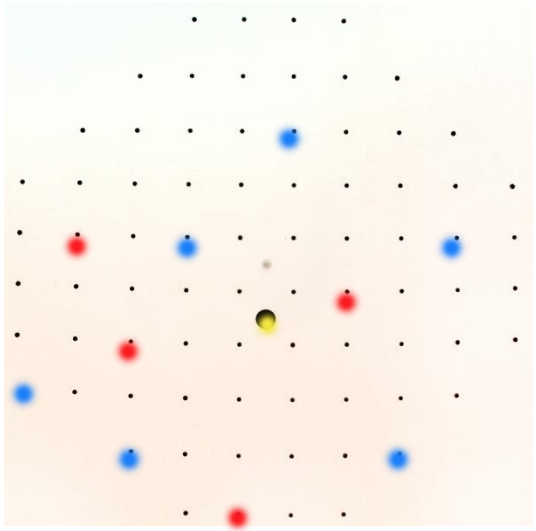


As an ophthalmologist and a researcher, my research is dedicated to the development of

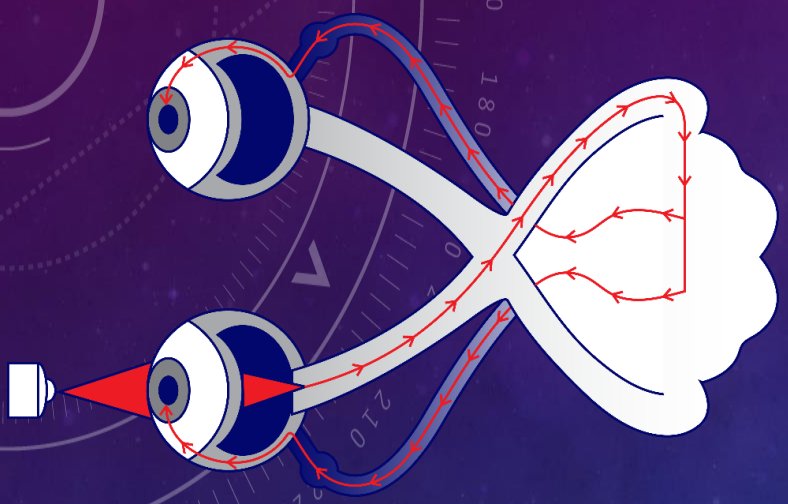
- ✓New treatments
- ✓Drug delivery systems
- ✓Objective clinical testing

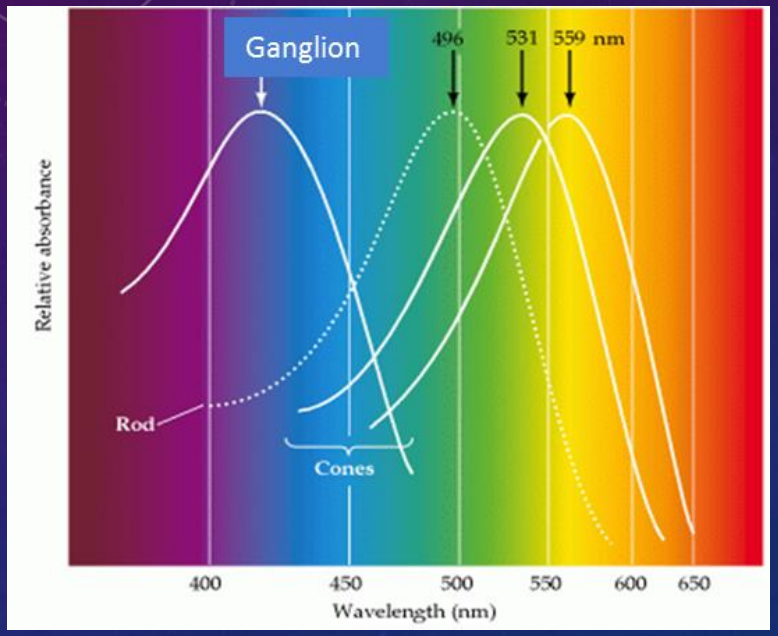
Moving from Subjective to Objective

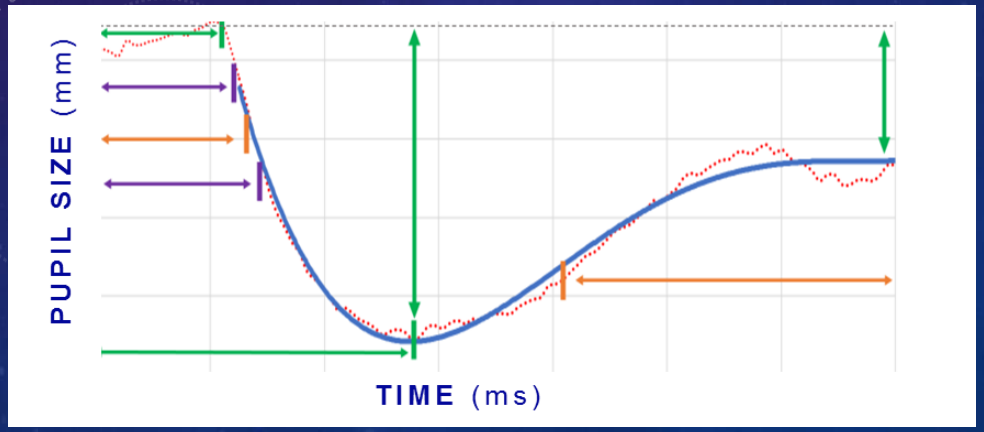
- 2009 - I realized that I need an objective VF test moreover children cannot be tested.
- In Fort Lauderdale, Miami - ARVO meeting is very busy
- I heard about blue and red light causing the pupil to constrict



The pupil light response to red and blue light – a new method for assessment of the visual pathways

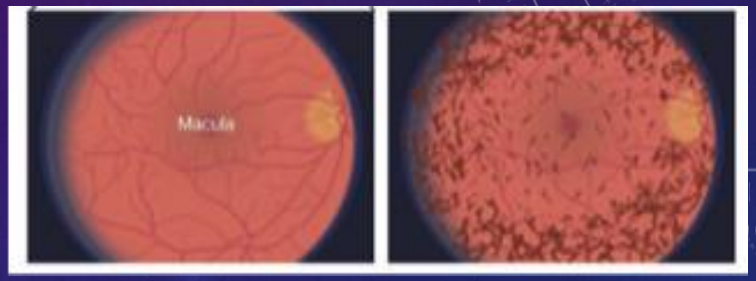






RETINITIS PIGMENTOSA (RP)

- An inherited progressive degenerative disease
- Rods degeneration
  - Night blindness
  - Tunnel vision
  - Fundus: bone spicules in the fundus



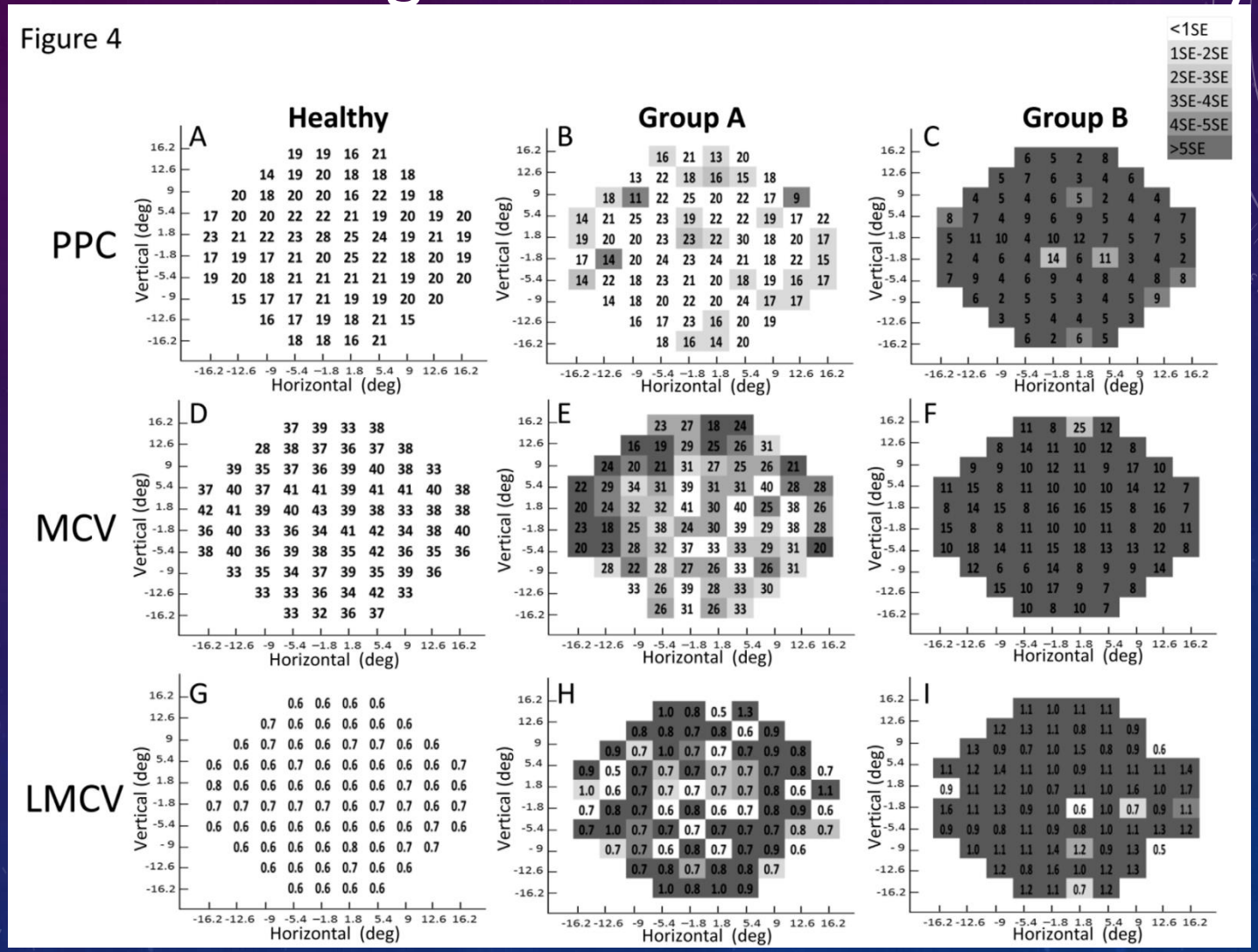
Study design

- 13 retinitis pigmentosa (RP) patients
- 17 healthy age-matched volunteers
- 16.2° Visual Field
- In RP patients, the chromatic pupillometer recordings were compared with their dark-adapted Chromatic Goldmann

TEST PROTOCOL

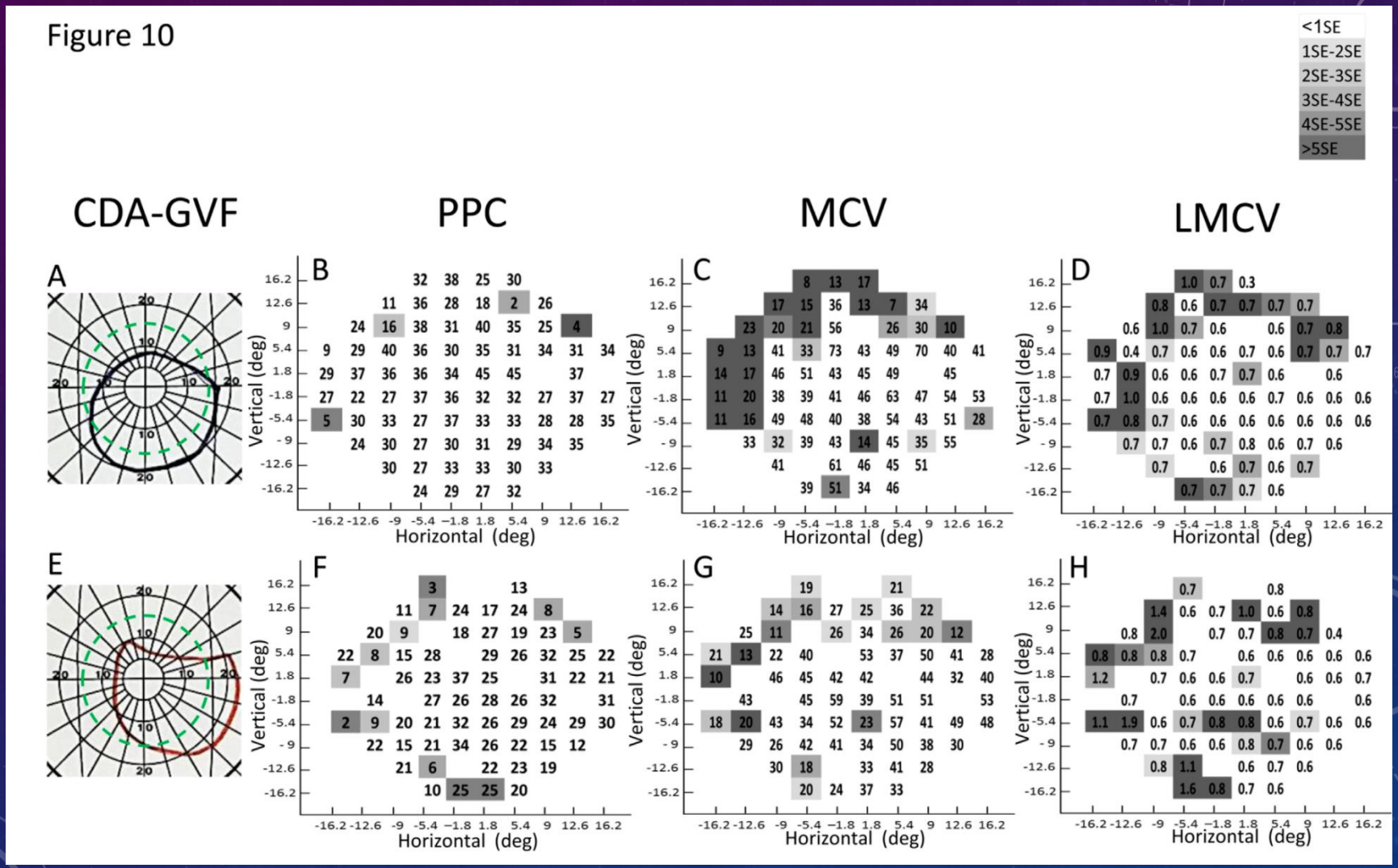
- Non-tested eye is covered by a patch
- Stimulus duration - 1 second
- Tracking of pupil size - 4 seconds
- Chromatic stimulus
  - Red (1000 cd/m², 625nm)
  - Blue (200 cd/m², 485nm)

1. RP patients: reduced response to blue light, correlating with VF restriction severity



Chibel *el at* Ophthalmology 2016

Case II – patient with VF restriction



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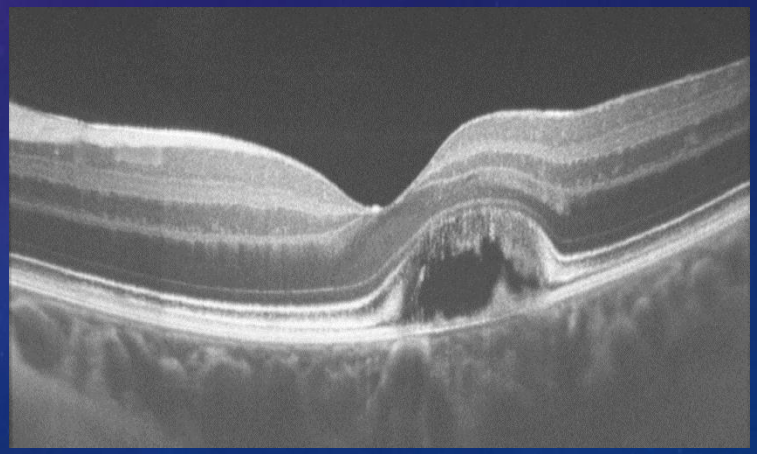
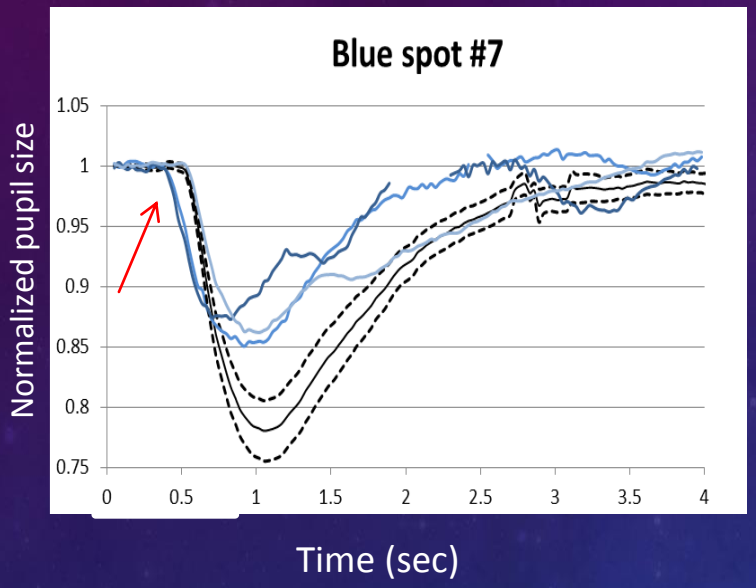
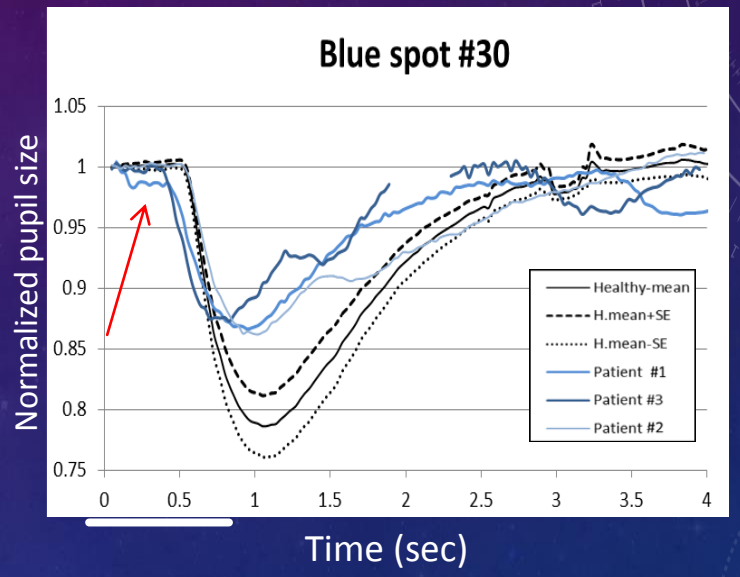
2. Best Vitelliform macular dystrophy (BVMD)

- Autosomal dominant disease that affects the retinal pigment epithelium (RPE) at a very young age.
- Characterized by lipofuscin accumulation in the RPE.
- Atrophic changes of the RPE or scarring cause loss of central visual acuity.

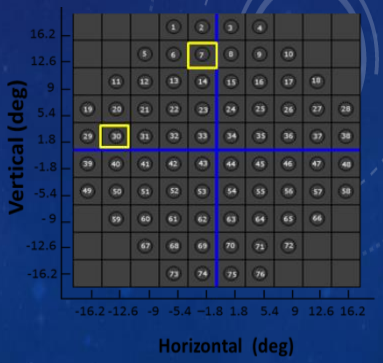


BVMD Patients demonstrated smaller PPC and shorter pupillary latency correlating with disease progression



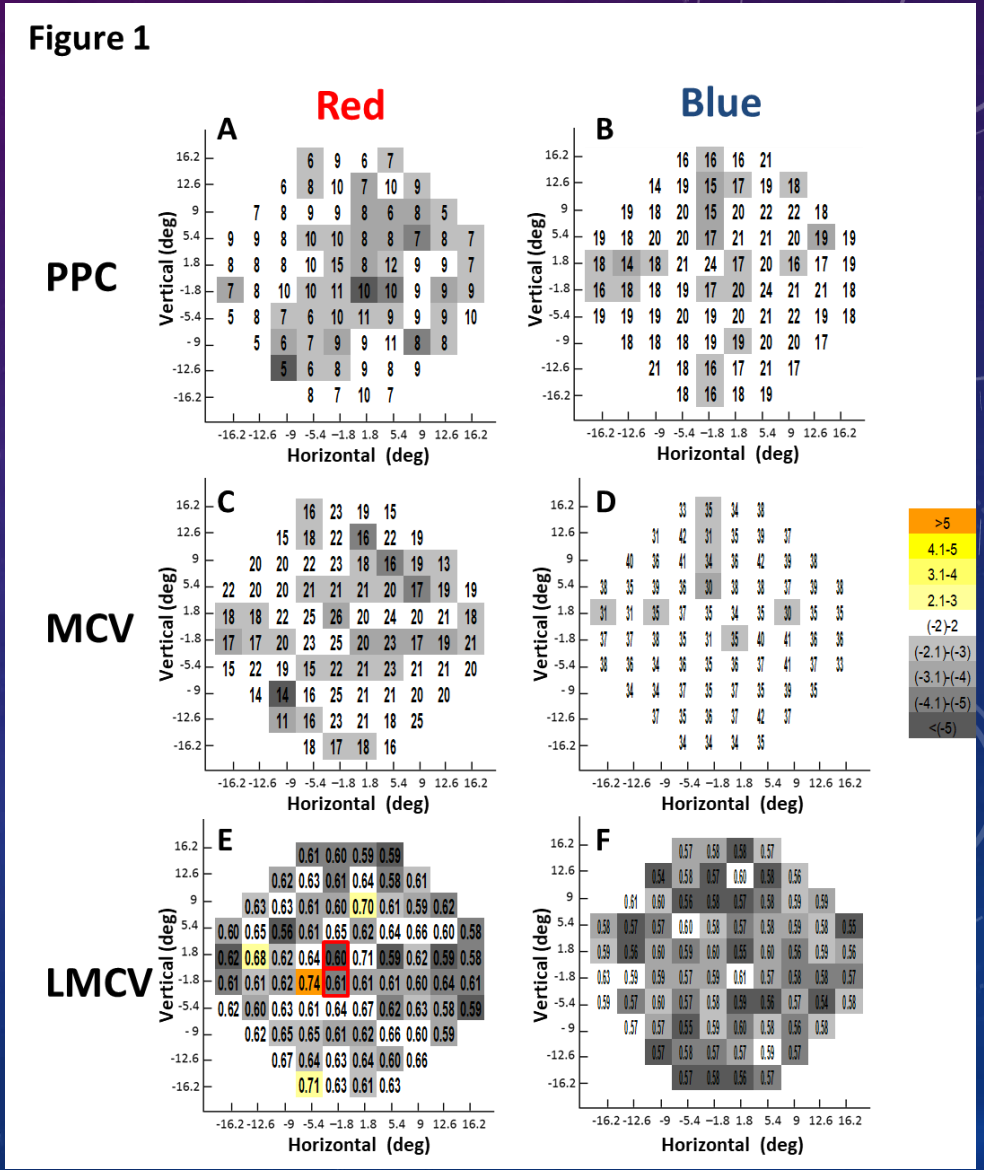


Subject	BCVA	Clinical Stage§
P#2	20/20	Vitelliform
p#3	20/50	Vitelliform
P#1	20/150	Vitelliruptive



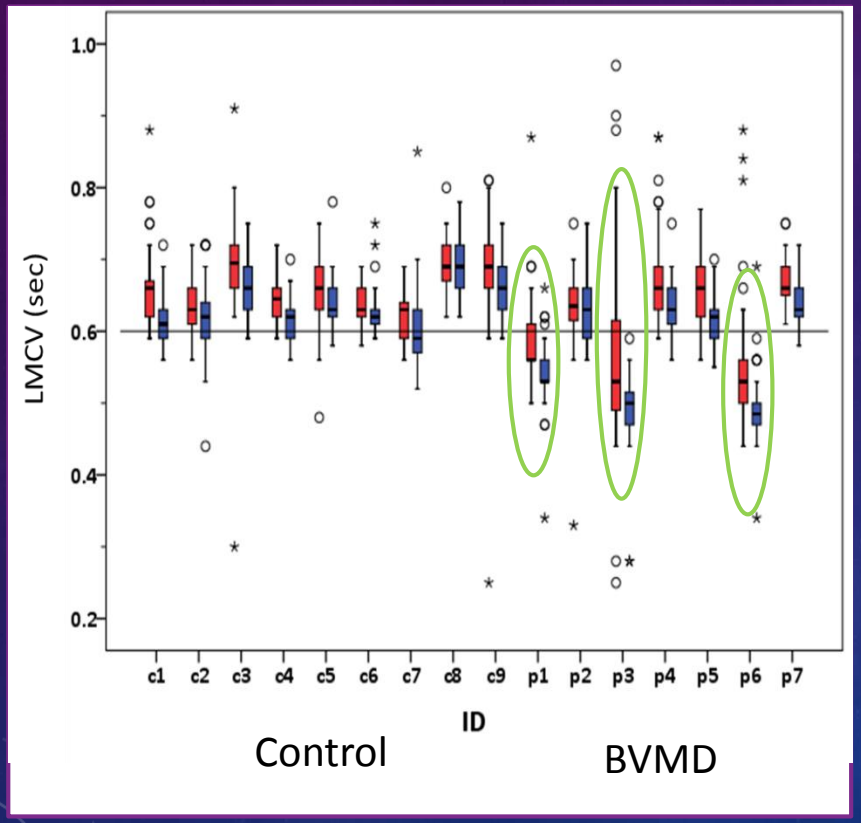
BVMD patients - diminished pupil responses with shorter latency

- Significantly smaller mean PPC, MCV and LMCV as compared with controls ($p<0.001$)
- The defect is more substantial in response to red light

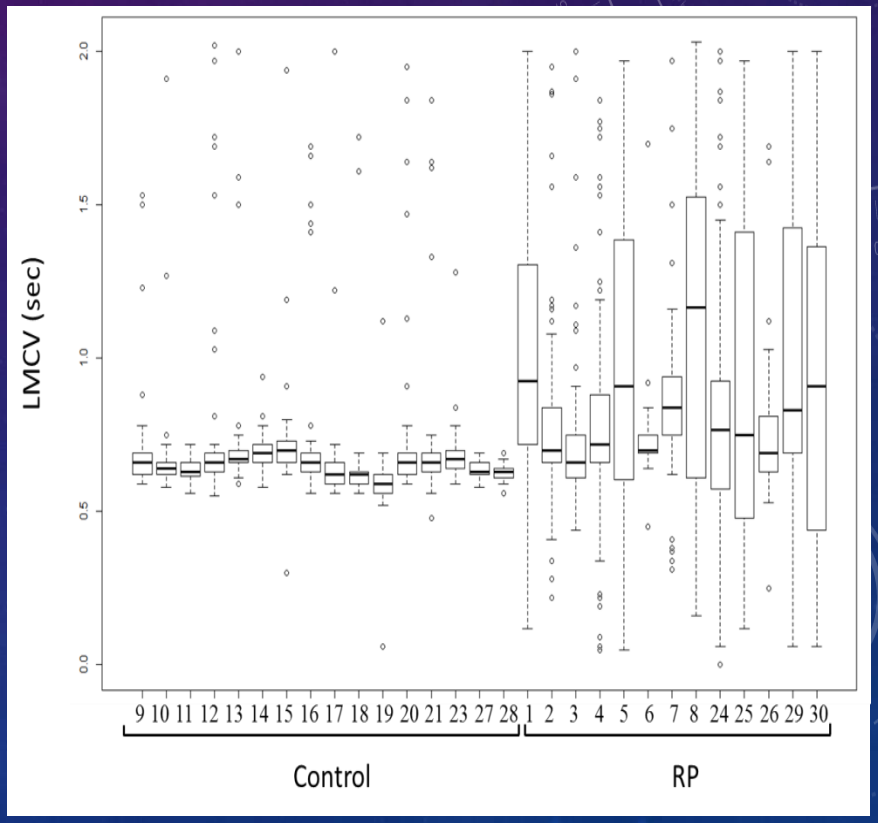


BVMD patients demonstrated substantially shorter LMCV with a narrow value range

BVMD



Retinitis pigmentosa

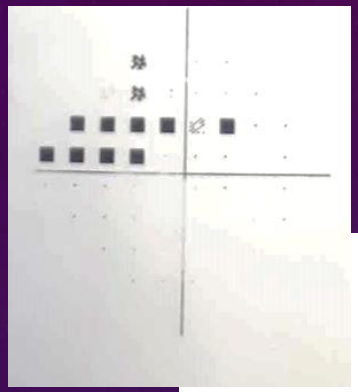


3. CHROMATIC PUPILLOMETRY FOR OBJECTIVE ASSESSMENT OF VF IN GLAUCOMA PATIENTS

Study design

- 11 Glaucoma patients
- 13 healthy age-matched volunteers
- 24-2 Visual Field
- The pupillary responses of patients were compared with the pupillary responses obtained from control subjects.
- Results of patients where also compared with their findings on Humphrey 24-2 perimetry and SD-OCT.

A6 (MD=-6.9, PSD = 10.38)



	BLUE	RED
PPC	2.5 8.9 7.3 7.3 3.9 6.9 7.5 9.8 10.2 6.0 1.7 2.4 8.4 9.4 10.8 11.6 8.6 8.1 3.7 2.0 6.5 9.8 8.6 9.1 9.6 3.1 4.3 1.5 0.9 2.8 8.8 10.4 13.6 8.0 4.6 1.9 7.5 7.8 9.0 6.9 6.5 3.6 3.0 7.8 3.4 5.2 4.2 4.6 10.3 5.7 3.4 1.4 10.5 4.7	3.5 3.1 8.0 10.7 5.6 9.2 9.1 6.5 9.9 9.3 1.8 6.1 1.9 7.1 7.9 9.2 9.1 8.7 1.2 1.5 1.0 8.0 11.4 10.6 4.7 4.7 5.5 1.8 1.1 4.1 4.8 4.4 11.4 8.5 11.2 10.2 2.4 3.9 3.4 11.5 6.3 9.7 6.5 7.3 1.5 2.1 3.7 10.4 6.3 10.7 3.6 3.0 7.3 6.4
MRV	4.6 9.3 5.6 6.0 4.0 7.0 6.1 9.0 7.4 4.8 2.6 0.4 13.0 10.6 7.1 9.1 6.7 7.4 2.8 3.0 5.3 8.3 8.8 7.1 7.9 5.1 3.4 1.8 0.0 5.1 8.1 7.7 10.3 5.2 4.2 4.1 8.5 6.0 7.1 6.9 4.4 3.5 4.9 4.0 2.8 8.3 4.4 4.2 7.1 5.3 4.2 2.0 6.2 4.6	2.7 5.8 6.4 8.6 5.3 7.4 10.3 5.6 7.0 7.1 0.9 3.0 1.3 7.5 5.1 6.8 7.4 8.1 1.0 3.3 0.8 6.5 6.4 7.3 3.7 6.7 5.8 2.3 3.5 8.7 3.6 6.3 9.6 5.8 9.3 9.0 2.3 3.5 2.9 9.2 5.3 7.5 6.0 7.6 1.5 3.1 4.5 8.5 4.6 6.7 4.6 4.8 7.6 4.7
LMCV	0.8 0.8 0.8 0.7 0.8 0.8 0.7 0.8 0.7 0.8 0.8 0.9 0.9 0.8 0.8 0.8 0.7 0.7 0.8 0.8 0.8 0.8 0.8 0.8 0.7 0.8 0.8 0.8 2.0 0.8 0.7 0.8 0.7 0.8 0.8 0.8 0.8 0.8 0.8 0.8 0.8 0.8 0.7 0.8 0.8 0.8 0.8 0.8 0.7 0.7 0.8 0.7 0.7 0.8	0.8 0.8 0.7 0.7 0.8 0.7 0.8 0.8 0.7 0.7 0.8 0.8 0.8 0.8 0.8 0.8 0.7 0.7 0.8 0.9 0.8 0.8 0.8 0.7 0.8 0.7 0.7 0.8 0.8 0.8 0.8 0.8 0.8 0.7 0.8 0.7 0.8 0.8 0.8 0.8 0.8 0.7 0.7 0.7 0.8 0.8 0.8 0.8 0.7 0.7 0.8 0.8 0.8 0.8

>5
4-5
3-4
2-3
1-2
(-1)-1
(-1)-(-2)
(-2)-(-3)
(-3)-(-4)
(-4)-(-5)
<(-5)

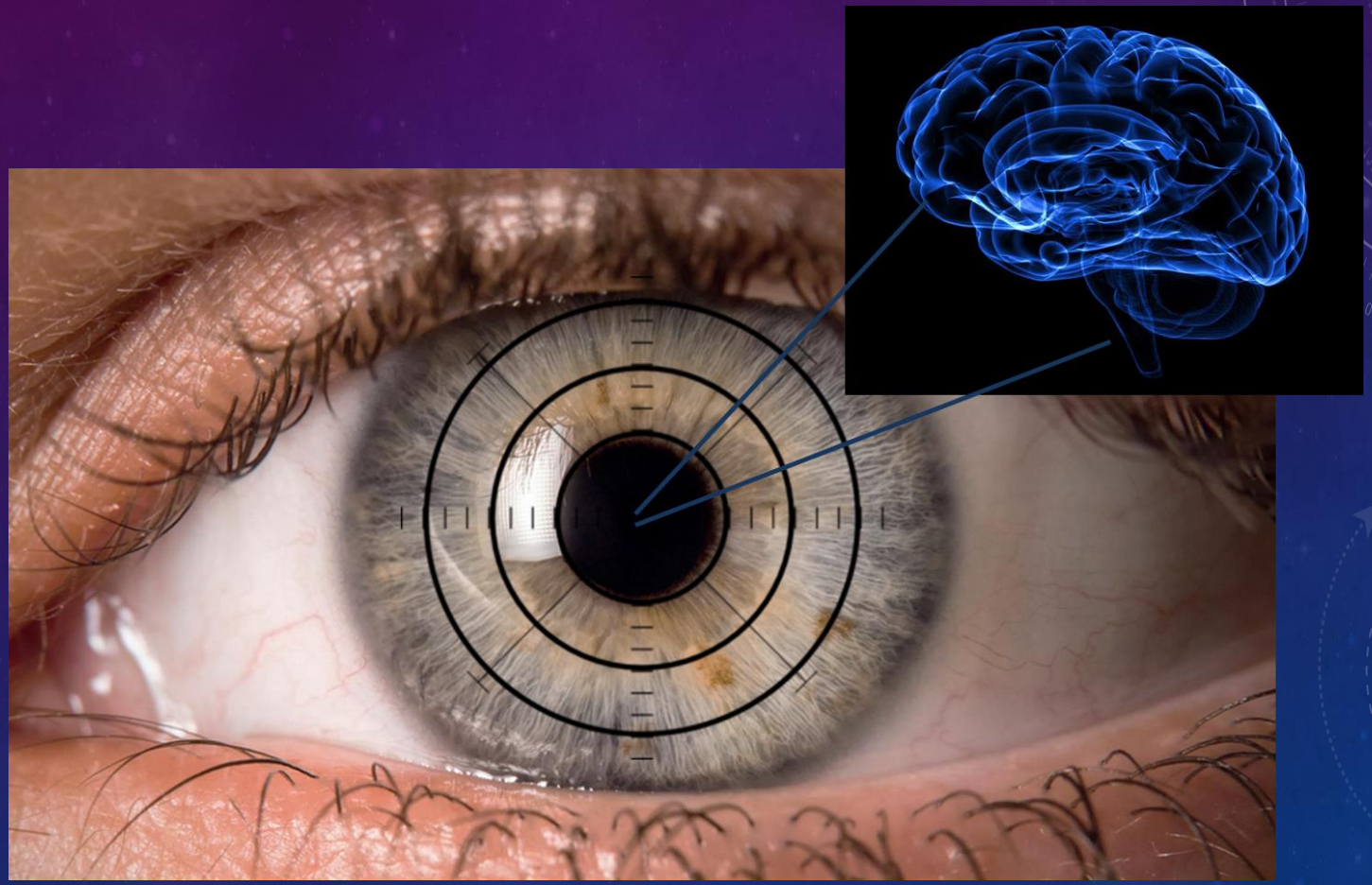
Conclusions

- The pupil multifocal response pathology - differs between retinal, macular and optic nerve diseases

	BVMD	RP	Glaucoma
Stimulus more affected	Red	Blue	Blue
Latency	Shorter	Longer	Normal
Latency variability	Normal	Large variability	Normal

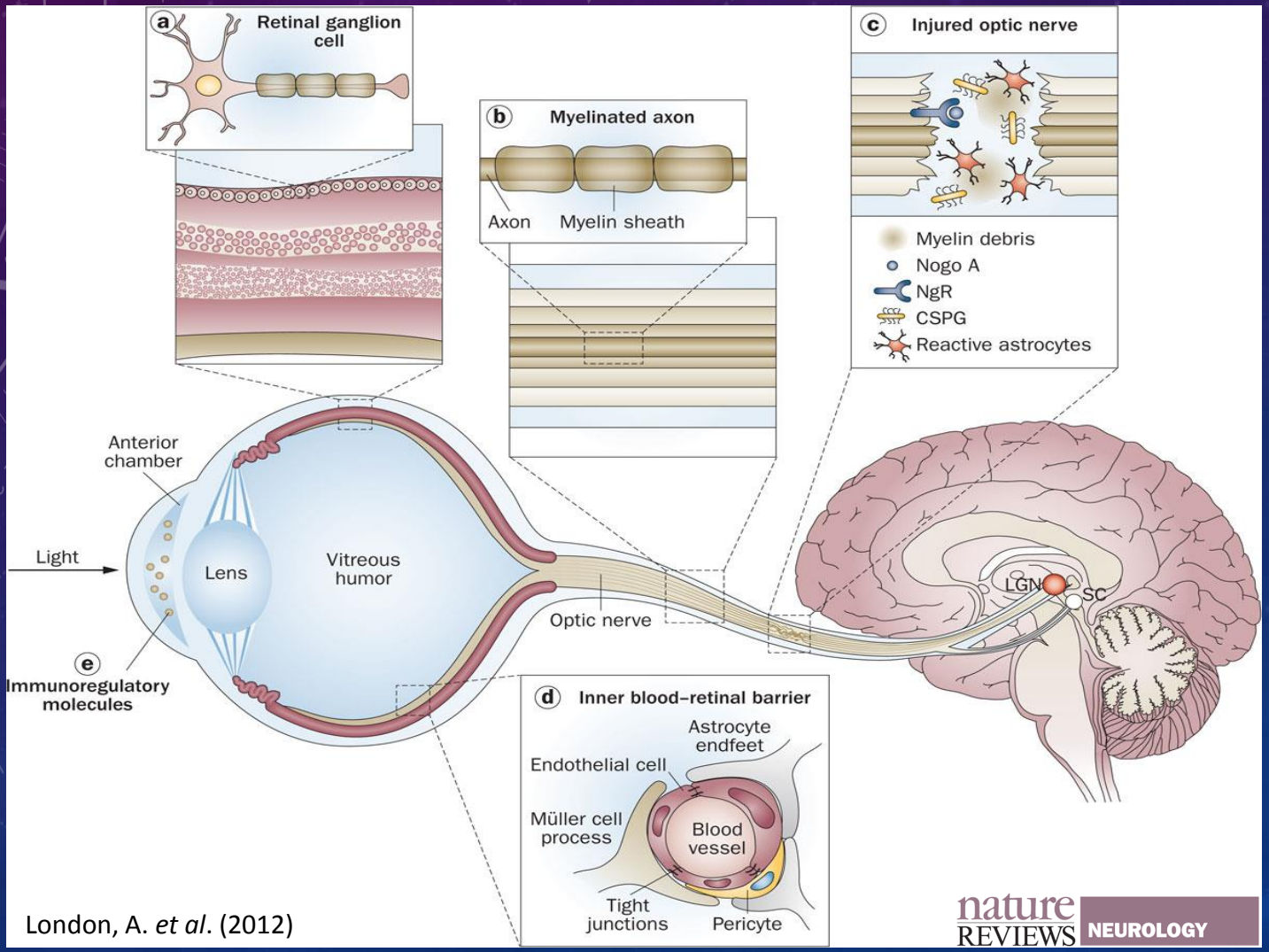
- The chromatic multifocal pupillometer may enable objective diagnosis of visual field defects and underlying pathology in retinal , macular and optic nerve degeneration .

The eye is a window to the brain



The EYE is an extension of the BRAIN:

- The neurons extend from the eye into the brain
- The eye has similar vasculature with similar barriers



London, A. *et al*. (2012)

nature REVIEWS NEUROLOGY

Alzheimer Disease - One of the Biggest Zunammy

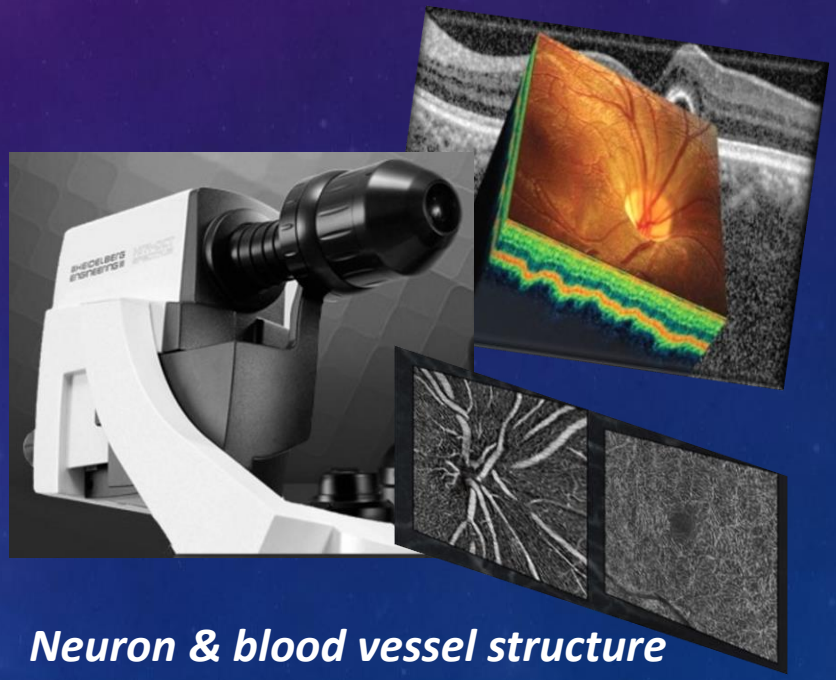
- Alzheimer's disease (AD)- the most common form of dementia
- Approved medications provide limited efficacy
- More than 450 new drugs failed in clinical trials

- Let’s think out of the box - no borders

NOVEL NEUROLOGICAL & IMAGING TESTING

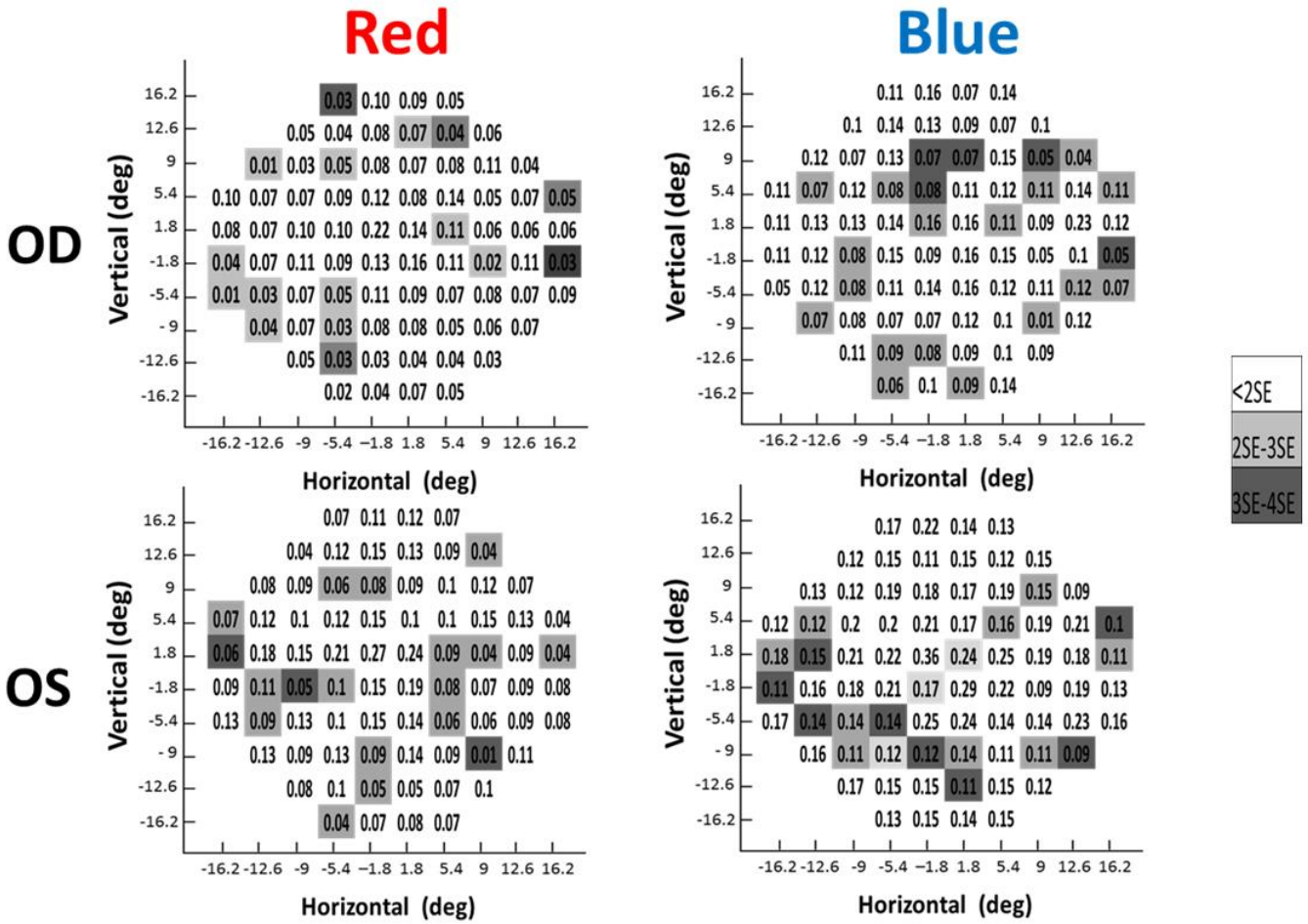
- Identify early non-invasive biomarkers to stop the degeneration before it is too late

Neuron function - Pupillometry



Neuron & blood vessel structure – Advanced imaging

Preliminary results – low pupil response to red and blue light in non demented elderly



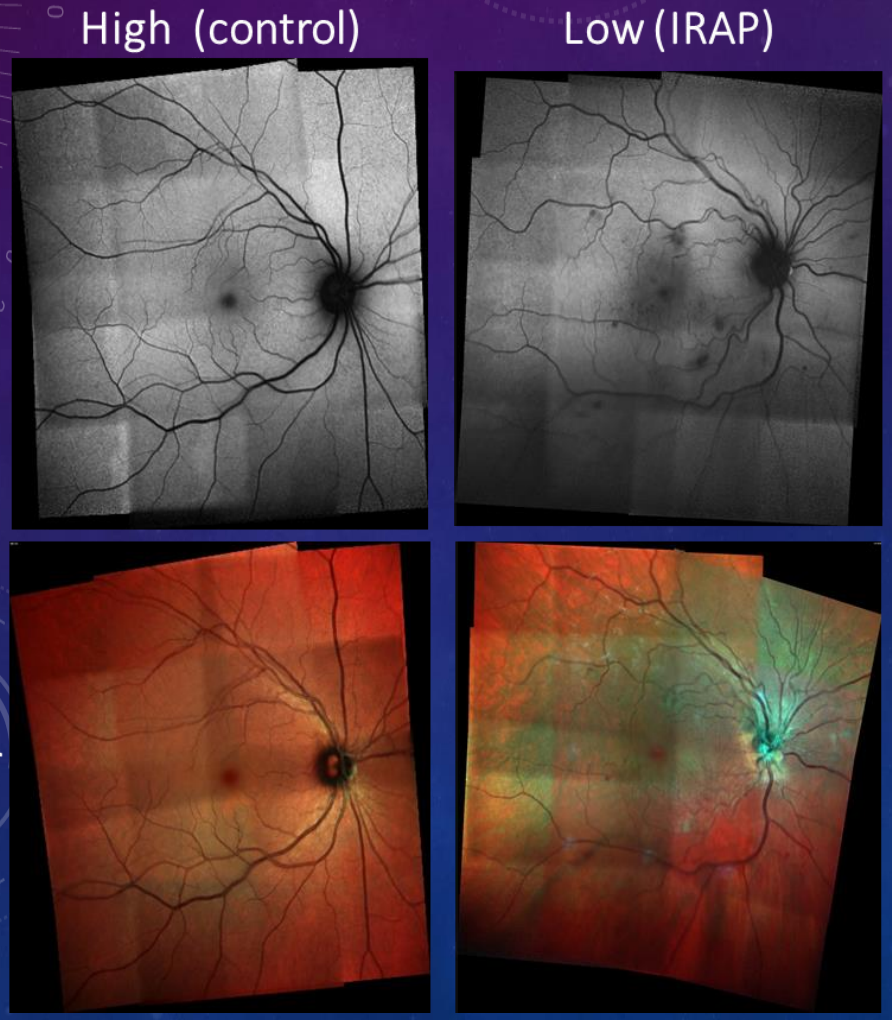
Study II- offspring of AD patients

Israel registry for Alzheimer's prevention (IRAP) –

a prospective longitudinal study

- Offspring (ages 40-65) of AD patients (n=430) and controls (n=100)
- Exquisite characterization
  - Cognitive
  - Brain imaging
  - Cerebrospinal fluid
  - Health-related
  - Life style
  - Genetics

Preliminary results: Sparser and more tortuous retinal vessels with in AD offspring with low cognition



Acknowledgements

Acknowledgements

Current Team

- Dr. Ifat Sher
- Inbal Sharvit-ginon
- Maya Gurevich
- Daniel Ben-ner
- Zachary Weinerman
- Biniaminov Luba
- Irina Kriaj
- Helena Solomon
- Reham Neserat
- Ettel Bubis
- Victoria Edelstein
- Zehavit Goldberg
- Lori Gueta

Past Team Members

- Ron Chibel
- Dr. Mohamad Mhajna
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- Dr. Asaf Achiron
- Dr. Kolker Andrew
- Dr. Kinori Michael
- Dr. Attar-Ferman Gili

Collaborations:

- Prof. Michal Beeri, Sheba Medical Center
- Dr. Ramit Ravona-Springer, Sheba Medical Center
- Dr. Ruth Huna-Baron, , Sheba Medical Center
- Dr. Alon Skaat, Sheba Medical Center
- Prof. Michael Belkin, Tel Aviv University

Funding: