Ageing effects on the recovery of rat eyes from high intraocular pressure

Jeremiah Lim

Department of Optometry & Vision Sciences
University of Melbourne

Overview
Methods
Results
Conclusion

IOP alone cannot account for glaucomatous changes in the eye
- Normal tension glaucoma – not explained by mechanical stress theory
- Experimental evidence points to loss of ability to maintain blood supply
- OPP is a better indicator of metabolic stress (He et al, 2011)

Abnormal autoregulation is implicated in other eye diseases

Glaucoma

- Prevalence:
  - 4.5% above age 60
  - 8.6% above age 70
  - 9.7% above age 80

Ageing is a major risk factor for glaucoma
- Reduced blood supply to the eye (Embleton, Hosking, et al, 2002)
- Reduced ability to maintain blood supply (autoregulation) (Jeppeson et al, 2004)
Retinal metabolism

- What happens when we raise IOP in rats?
  - OPP and blood flow decreases
  - Function (ERG) decreases

Blood flow (OBF)

Function (ERG)

IOP (mmHg)

He et al, 2012

Bui et al, 2005

Aims

- What happens to blood flow, oxygen and ERG when we raise IOP in young rats?
  Aim 1a: What underlies IOP mediated functional loss?
  Aim 1b: Are middle-aged animals more susceptible to acute IOP stress?
  Aim 2a: What are the mechanisms underlying retinal recovery?
  Aim 2b: Does age affect the capacity for the retina to recover?

Blood flow and Oxygen

Electroretinography

- Measuring inner retinal function (b-wave)
  - Full field standard ERG

The b-wave is a sensitive marker for IOP stress

Electroretinography

Blood flow and Oxygen

IOP and OPP

Electroretinography

Blood flow and Oxygen

IOP and OPP

Electroretinography

Blood flow and Oxygen

IOP and OPP
IOP & OPP

• IOP determined by height of saline reservoir
  • Raised in 5 mmHg steps from 10 to 100 mmHg
  • Step increase from 100 mmHg to 120 mmHg

• MAP determined using tail cuff sphygmomanometry

Aim 1a: What underlies IOP mediated functional loss?

Conclusion: Oxygen changes explain functional loss better than blood flow during IOP elevation

Aim 1b: Are middle-aged animals more susceptible to acute IOP stress?

Conclusion: 2 and 14 month old rats show similar blood flow, oxygen levels and ERG responses to IOP elevation

Aim 2a: What are the mechanisms underlying retinal recovery (in young rats)?

1. ERG recovery has fast (5 min) and slow (<1 hr) phases
2. pO2 recovery also has two phases (fast and slow)
3. LDF recovery only shows 1 phase (<1 min to full recovery)

Conclusion: oxygen and function share similar recovery profiles (2 phases, prolonged recovery)
Aim 2b: Does age affect the capacity for the retina to recover?

**Blood Flow:** Faster recovery in older eyes (14mth: 120.8% vs 2mth: 104.5%, *p* < 0.05)

**Oxygen:** Recover to similar levels (14mth: 119.4% vs 2mth: 134.1%, *p* < 0.05)

**ERG:** Poorer recovery in older eyes (14mth: 80.9% vs 2mth: 105.3%, *p* < 0.05)

Conclusion: Middle-aged animals do not recover as well from IOP stress

Conclusions

- Opp is just as important as IOP in mediating retinal stress
- Oxygen tension is the most important metabolite in maintaining retinal function
- Middle-aged animals resist IOP as well as young animals during IOP
- Middle-aged animals do not recover as well from IOP
  - A greater reliance on continuous blood supply for oxygen means that older eyes are more susceptible to disruptions caused by high IOP (and OPP)

Supervisors:

Dr Bang Bui  
Dr Christine Nguyen  
Prof Algis Vingrys

Ocular physiology Laboratory  
Visual Functions Laboratory

Jason Chang  
Angel Duan  
Joe Paul  
Julia Jiao  
Selwyn Prea  
Flora Hui  
Darren Zhao  
Edward Liu  
Jia Jia Lek  
Bao Nguyen  
Rachael O’Connell Anna van Koeverden  
Dr Zheng He  
Dr Vickie Wong

Funded by:  
Melbourne International Research Scholarship (MIRS)  
National Health & Medical Research Council (NHMRC)