DO THE EXTRAOCULAR MUSCLES CAUSE GLAUCOMA AND ANTERIOR ISCHEMIC OPTIC NEUROPATHY?

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Glaucoma is world’s second leading cause of blindness.
Most people with glaucoma do NOT have high intraocular pressure.
“Normal Tension Glaucoma”
Eye movements probably cause all this blindness.
If we understood the role of eye movements, could treat glaucoma more effectively.
... and maybe also non-arteritic anterior ischemic optic neuropathy.
Patient JH
With Primary
Open
Angle
Glaucoma

Take-Home Message
1. In everyone, the optic nerve sheath becomes taut in adduction and supraduction, consequently tethering the globe.

2. Modeling suggests that tethering concentrates medial rectus muscle reaction force at temporal peripapillary sclera, deforming the scleral canal and peripapillary region, and retracting the globe.

3. Medial rectus reaction force is dissipated differently in some people:
   A. Optic nerve and sheath elongation
   B. Globe translation

4. Reasons why peripapillary strain could be greater in normal tension glaucoma:
   A. Inner layer of optic nerve sheath stiffens with age.
   B. Peripapillary sclera is softer than elsewhere.

5. Repetitive strain in adduction may be a pressure-independent mechanism of optic neuropathy in glaucoma, and non-arteritic anterior ischemic optic neuropathy.


Eye Movements Incessant

People make more than 180,000 saccades daily, even during sleep.
Eye-head gaze shifts include eye movements averaging 30°.

Saccades of up to 40-45° occur during tabletop work.
Peak extraocular muscle tension is 40 gm-f for 20° saccade and 52 gm-f for 30° saccade.

Peripapillary phosphenes observed during ordinary saccades suggest deformation of the optic nerve head.
Adduction is even greater than normal in esotropic patients.

Optical Coherence Tomography
Adduction

Central Gaze

Big Effect of Adduction! Chang et al. AJO, 2016.

Tiny Effect of IOP!

**Multipositional Surface Coil MRI**

- Fiberoptic target fixation
- 312 micron resolution in plane
- 2 mm thick axial and quasi-coronal planes
- Digital image analysis
Subjects

POAG Low IOP: 19 patients
- Maximum IOP <20 mmHg
- Mean age 62 ± 10 (SD) years
- Mean deviation -8.2±1.2 dB

Controls: 35 normals verified by examination
- Mean age 37± 19 yrs
- Age-matched control subgroup: 14 normals
  - Mean age 63± 6 years (P = 0.71)
  - All 3 groups had mean axial length 25.6 mm by MRI

POAG High IOP: 2 patients

Esotropia: 31 patients

3-D Path of Optic Nerve

- 3-D tracking of optic nerve area centroid
- Temporal ON Sheath Straightest in Adduction

ON Length
- >>100% of Minimum

< Abduction

ON Length
~100% of Minimum

Adduction ->
Optic Nerve Straightening By Duction

- Adduction ~30°
- Central
- Abduction

ON Straight Only In Adduction

- P = 0.0005
- P = 0.022
- P = 0.003

Globe Retracts More In POAG

Not Due to Age or Axial Length

Effect of Adduction Still Significant After Accounting for Globe Diameter

No Significant Effect of Age

Anteroposterior Globe Translation

- Globe Retracts More In POAG
- P = 0.020
- P = 10^-7
- P = 0.212
- P = 10^-4
- P = 10^-5

Horizontal Globe Translation

- P = 0.006
- P < 0.0003
- P = 0.0003
- P < 0.0003
- P = 0.0003

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**Finite Element Modeling**

- Optic Nerve Head Tilts Temporal
- Temporal Scleral Stiffness Optic Nerve Stiffness
- Finite Element Modeling of Strain in Lamina Cribrosa During Adduction

**Finite Element Analysis of Strain in Adduction**

- IOP 15 mm Hg
- ICP 130 mm H2O
- Temporal → Nasal
- Temporal Peripapillary Atrophy Nearly Universal
- Andrew Shin, PhD
If optic nerve traction is pathologically significant, why do only some people get optic neuropathy from it? Presumably because of individual variations in anatomy and tissue biomechanical properties.

We need human tissue biomechanical data!

Mean of 18 normal orbits.
**Cadaveric Studies**

A 93 year old female

**Elastin in Optic Nerve Sheath**

Le et al. ARVO, 2017

H-7, Age 1.5

H-8, Age 57
Biomechanics

Optic Nerve Tension in Range of 10 - 60 gm

Shin and Park

30% Collagen

OCT Scanner

To Linear Motor

ON Sheath

To Force Sensor

Stress - Gram Force

Strain %

Movie by Alan Le
Conclusions and Speculations

1. In everyone, medial rectus counterforce is transmitted to the optic nerve head in adduction by the inner layer of the temporal optic nerve sheath, stretching the optic nerve by about the same ~3%.

2. The globe retracts abnormally in adduction in normal tension glaucoma, probably reflecting greater optic nerve sheath stiffness, maybe interacting with orbital connective tissues.

3. The elastin content of the optic nerve sheath variably increases with age, and maybe also with normal tension glaucoma. Greater force may be required to stretch the optic nerve sheath in normal tension glaucoma, and this force is applied to the soft, peripapillary sclera.

4. Age-related stiffening of the optic nerve sheath may be an intraocular pressure-independent mechanism of optic neuropathy.

5. Low tension glaucoma might therefore result from repetitive strain injury to the optic nerve head.

Possible Options For Therapy

1. Scleral or pulley posterior fixation of the medial rectus to reduce adduction range and force.

2. Combined medial and lateral rectus muscle recession to reduce adduction range and force.

3. Aggressive correction of esotropia in all adults.

4. Topical (glaucoma drops) or retrobulbar prostaglandin analog therapy to induce exophthalmos by orbital fat atrophy.

5. Orbital decompression by fat excision or orbital wall removal to induce enophthalmos.

6. Other ideas?