Thomas Sydenham

Father of English Medicine

A man is as old as his arteries.

Vascular Aging

(1624-1689)

Franklin SS. J Hypertens 2002; 20:1693–1696
The vasculatures in the eye and cerebral cortex have the same main blood supply, which is the internal carotid artery (ICA).
Eye is the Window of the Brain

- Retina is the extension of brain.
- Eye and brain are in similar constricted environment.
- Retinal and cerebral small vessels share similar:
  - embryological origin
  - Anatomical features
  - Blood-retinal barrier
- The transparent ocular media enables noninvasive visualization and analysis in vivo:
  - Neurodegeneration
  - Microvascular dysfunction
Retinal Microvascular Abnormalities
large scale epidemiologic study

- **Atherosclerosis Risk in Communities Study (ARIC)**
  - Strong link between the presence of retinal vascular abnormalities and both clinical (stroke) and subclinical (white matter lesions) detected on MRI
  - With and without diabetes and hypertension

- **The Rotterdam Study**
  - Larger venular calibers associated with an increased risk of vascular dementia
  - After adjustment of stroke and cardiovascular risk factors

- **Cardiovascular Health Study**
  - Total number of retinal signs reversely correlated with the executive function and gait speed
  - After adjustment of vascular risk factors

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Yatsuya H. et al., Stroke 2010; 41: 1349–1355
Wong TY et al., Lancet 2001; 358: 1134–1140
Kawasaki R. et al., Stroke. 2010; 41: 1826–1828
De Jong FJ et al., Neurology, 2011. 76 . 816–821
Dae Hyun Kim et al. Stroke. 2011;42:1589-1595
Observable retinal microvessels in the eye
Advanced Ophthalmic Imaging Lab

- Extended infrastructure of McKnight Brain Institute
- Novel non-invasive imaging modalities
  - Retinal Function Imager (RFI)
    - quantitative analysis of microcirculation (pre-capillary arteriole, post-capillary venule)
  - Optic coherence tomography angiography (OCTA)
    - depth resolved microvascular network
  - Ultrahigh resolution optic coherence tomography (UHR-OCT)
    - tomographic intraretinal thickness analysis
  - Polarization sensitive optic coherence tomography (PS-OCT)
    - Micro-structural integrity of retinal nerve fiber layer
A retinal function imager (RFI, Optical Imaging Ltd, Rehovot, Israel) was used to capture reflectance changes as a function of time under stroboscopic illumination.

Hemoglobin in red blood cells was used as an intrinsic motion-contrast agent in the generation of:
- Blood flow velocity maps
- Microvascular network

Jiang et al. Microvasc Res. 2013 Epub ahead of print
RFI blood flow measurement

Blood flow-velocity visualization

Movie from a series of 8 mages
Field of view: 20 degree

Automatic Quantification (mm/sec)

Image size 4.6 x 4.6 mm²
1024 x 1024 pixels
Aging of Retinal Microcirculation

Retinal Blood Flow Velocity in Arterioles

- Normal
- MCI
- Linear (Normal)
- Linear (MCI)

$r = -0.34$

$r = 0.51$

Retinal Blood Flow Velocity in Venules

- Normal
- MCI
- Linear (Normal)
- Linear (MCI)

$R^2 = 0.0062$

$R^2 = 0.004$

N = 28 (Normal = 14, MCI = 13)
Optic Coherence Tomography Angiography (OCTA)

OCTA for Quantitative Analysis of Microvascular Network in Intra-retinal Layers

Aging of Retinal Microvessels

Retinal Superficial Capillary Plexus

- Normal
- MCI

Linear (Normal): $R^2 = 0.2547$
Linear (MCI): $R^2 = 0.0097$

Retinal Deep Capillary Plexus

- Normal
- MCI

Linear (Normal): $r = -0.41$
Linear (MCI): $r = -0.36$

$N = 31$ (Normal = 18, MCI = 13)
Aging of Retinal Microvessels

Superficial

A

Dbox = 1.768

B

Dbox = 1.762

Deep

C

Dbox = 1.741

D

Dbox = 1.760

Normal

MCI
Optic Coherence Tomography (OCT) of the Human Retina

Retinal segmentation on SD-OCT

Correlation of anatomy with OCT for the human retina
RNFL thickness in patients with MCI, mild, moderate, severe AD and control subjects

Ultrahigh Resolution OCT (UHR-OCT)

Axial resolution = ~ 3 µm, automated segmentation of 6 intraretinal layers
Cross-Sectional Retinal Segmented Tomographic Thickness Maps of Intraretinal Layers

RNFL: retinal nerve fiber layer;
GCIPL: ganglion cell layer + inner plexiform layer;
INL: inner nuclear layer;
OPL: outer plexiform layer;
ONL: outer nuclear layer;
PR: retinal photoreceptor layer

Ultrahigh resolution OCT (UHR-OCT, axial resolution = ~3 µm)
Fully-automated 3D segmentation software
Aging of Retinal Neurons

Retinal Nerve Fiber Layer (RNFL)

- Normal: $R^2 = 0.1049$
- MCI: $R^2 = 0.2418$

Retinal Ganglion Cells (GCL)

- Normal: $R^2 = 0.0585$
- MCI: $R^2 = 0.1754$

N = 28 (Normal = 18, MCI = 10)
Summary

- **Vascular aging** is evident in retinal microcirculation and capillary network.
- More profound **vascular aging** in MCI patients is apparent.
- **Non-invasive** novel ophthalmic imaging is promising in studying the role of vascular aging in cognitive decline.
- Future longitudinal studies with large sample size are needed.
Our main hypothesis predicts that impairment initially occurs with the microvessel network and microcirculation, followed by cognitive aging and the loss of RNFL/GCL structure.
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