Stress-induced sympathetic activity and the retinal vasculature: the SABPA prospective study
Malan L, Smith W, Malan NT
Central neural control

No oxygen & glucose storage

Brain up-/down-regulates activity (homeostasis) preventing pathology (Claude Bernard, 1878)

2170 invited
471 Teachers assessed for eligibility
Aged 20-65 years

Baseline
409 enrolled

200 Blacks

209 Whites

3 year follow-up
N=359

7 Deceased; 20 Losses
173 Blacks

Excluded:
65 unusable optical images and missing data;
1 stroke case;
15 HIV infected

2 Deceased; 21 Losses
186 Whites

N=342, 40-54 yrs

Exclusion criteria: Pregnancy, Lactation, Users of α and β-blockers, Psychotropic substance abuse, Blood donors / Vaccinated in previous 3 months, Tympanum temperature > 37.5°C
Cardiac injury and perfusion

BRAIN Metabolic demands Sympatho-adrenal responses

Defensiveness

• ↑Myocardial ischemia
• ↑Blood pressure

Homeostasis

Imbalance

*Social stress

Chronic Defensiveness:
• Downregulated HVR & NE
• Ischemic heart disease

Malan et al. 2017. Psychoneuroendocrinology
Retinal microvasculature?

Blood-Photoreceptor Barrier (BRB) similar to Blood-Brain Barrier (BBB)

Microvascular endothelial cells closely interact with glial cells & blood vessels forming a functional 'neurovascular unit'.

Vecino et al. 2016. Prog Retina Eye Res

Choi & Kim, 2008. BMB Reports
Mydriatic eye & Retinopathy signs
(Opthalmologist)
0.5-1.0 optic disc diameter
Endothelial dysfunction reflected in:

**Arteriolar narrowing**
Hypertension

**Venular widening**
Hyperglycaemia, *stroke risk marker*

Next challenge? Quantify stress hormone levels (Norepinephrine and Cortisol) - retina

Interaction term (stress hormones) fitted for NE:Cr tertiles (p ≤ 0.05)

NE:Cr 1 (44% Blacks; 64% Men)

...chronic 24h hypertension...

Malan et al. 2017. Psychoneuroendocrinology
The graph compares DOPP (mmHg), Arteriolar caliber (MU), and Venular caliber (MU) across different NE:Cr levels:

- **Low NE:Cr (n=93)**
- **Mid NE:Cr (n=91)**
- **High NE:Cr (n=91)**

Significance is indicated by:
- † for DOPP
- * for Arteriolar and Venular caliber

The data suggests a significant difference in Venular caliber between the High and Low NE:Cr groups.
Low NE:Cr (n=93)  Mid NE:Cr (n=91)  High NE:Cr (n=91)

-60 -40 -20 0 20 40 60

Δ3 yr NE:Cr (%)

Δ3 yr Serum Cortisol (%)

Δ3 yr ACTH (%)

HDL (mmol/L)

Saliva α-amylase (U/ml)

Saliva cortisol (nmol/L)
<table>
<thead>
<tr>
<th></th>
<th>Retinal Arterioles (MU)</th>
<th>Retinal Venules (MU)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adjusted $R^2$</strong></td>
<td>0.28</td>
<td>0.33</td>
</tr>
<tr>
<td><strong>Log-transformed $\beta$ (95% CI)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Saliva Cortisol (nmol/L)</strong></td>
<td>-</td>
<td>-0.23 (-0.1, -0.5)*</td>
</tr>
<tr>
<td><strong>Saliva $\alpha$-amylase (U/ml)</strong></td>
<td>-0.30 (-0.1, -0.5)*</td>
<td>-</td>
</tr>
<tr>
<td><strong>HDL (mmol/L)</strong></td>
<td>-</td>
<td>-0.19 (-0.1, -0.5)*</td>
</tr>
</tbody>
</table>

*P ≤ 0.05
Ferrier et al. 1992. Hypertension

NE: $\alpha_{2a} R$

$D_2 R$

Central control
Chronic depression (DMS-IV criteria) associated with:

- △ Stress hormones [OR 0.9-1.2; P ≤ 0.001]
- Wider venules [OR 1.7; P = 0.03]
- Low HDL [OR 4.8; P = 0.04]
Central neural control: Heart and Retina

BRAIN
Metabolic demands
Sympatho-adrenal responses

Blood-neural barrier
Chronic depression & Neuronal hyperactivity
*Risk*
- Disturbs neurovascular coupling and neuronal-membrane-integrity
- Ischemic stroke

*Social stress*

Chronic Defensiveness:
- Downregulated HVR & NE
- Hypertension
- Ischemic heart disease
Clinical implications?

- Social Support systems

- Screening - Perfusion deficits (Ischemic stroke risk):
  1. Heart - ECG (ST-segment depression)
  2. Retina – Diastolic Ocular Perfusion Pressure $( DBP – IOP \geq 50 \text{ mmHg} )$
  3. Signs of depression

Malan et al., 2016-2018
Gütterman, 2009. Circulation
Thank you