Peripheral blood flow regulation in response to sympathetic stimulation in individuals with Down syndrome

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Disclosures

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Down syndrome
Genotype and phenotype

• Trisomy 21
• Most common genetic syndrome – 1 in every 700 newborns
• Intellectual disability

• Co-occurring diseases, i.e. congenital heart disease, Alzheimer’s disease, infections, hypothyroid disease, hearing problems, sleep apnea¹

¹ Capone et al 2018
Down syndrome

Cardiovascular risk

• More obesity$^2$
• Lower physical activity$^3$
• Lower fitness$^5$

• But they struggle with exercise: fatigue, demotivated, ‘lazy’?

→ Has led to investigations into underlying causes of low work capacity

Down syndrome & ANS
Working model (Fernhall et al. 2013)

Altered Autonomic Function in Individuals with Down Syndrome

↓Parasympathetic Control
Baynard ‘04, Agiovlasitis ‘10

↓Vagal Withdrawal
Mendonca ‘11, Figueroa ‘05

↓Δ Heart Rate
Baynard ‘08

↓Work Capacity
Fernhall et al. 2013

↓Baroreceptor Sensitivity
Heffernan ‘05

↓Response To Adrenergic Stressors:
↓Catecholamines
↓Sympathetic Response
Fernhall ‘08

↓Sympathetic Control
Iellamo ‘05

Hemodynamic control?
Peripheral Blood Flow Regulation?
Cardiac Output?

Chronotropic Incompetence
Guerra ‘03
Governance gone wrong
Subject of investigation

Working hypothesis: Impaired ability to adequately shunt blood flow to working muscle

Cardiac output
- Stroke volume during exercise

Peripheral blood flow
- Vasoconstriction
- LBNP

Peripheral blood flow
- Vasodilation
- Hand grip exercise
- Combined with LBNP
• To investigate the effects of a mild sympathoexcitatory stimulus (-20 mmHg LBNP) on brachial blood flow in individuals with and without DS.

• We hypothesized:
  Individuals with DS would demonstrate less vasoconstriction and smaller reductions in brachial blood flow than the control group.
Participants

- Inclusion: 18-40 years of age, male, non-athletic, in general good health
- Exclusion: heart disease, high blood pressure, high fasting glucose, contra-indications exercise

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<tr>
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<th>DS (n=10)</th>
<th>Control (n=11)</th>
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<tr>
<td>Age (years)</td>
<td>24 ±3</td>
<td>24 ±3</td>
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<tr>
<td>BMI (kg/m²)</td>
<td>29.5 ± 4.0</td>
<td>25.1 ± 5.0 *</td>
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<tr>
<td>VO$_{2peak}$ (ml/kg/min)</td>
<td>28.2 ± 4.5</td>
<td>42.6 ± 6.0 **</td>
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<tr>
<td>HRpeak (bpm)</td>
<td>170 ± 13</td>
<td>195 ± 10 **</td>
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Study protocol

• Controlled: no caffeine, alcohol and exercise for at least 12 hours and a minimum 4 hour fast

• Continuous measurement of HR and BP
  – 3-lead electrocardiogram (ECG), finger plethysmography (Finometer)

• Doppler Ultrasound

• LBNP

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<th>Baseline</th>
<th>LBNP</th>
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<td>0</td>
<td>10</td>
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LBNP
Lower body negative pressure -20 mmHg
- Lower body negative pressure (LBNP)

- Forearm blood flow (FBF): velocity*πr²*60
- Forearm vascular conductance (FVC): FBF/MAP*100

7. Thijssen et al. 2011
Results

Mean arterial pressure

* = Effect LBNP response (Condition)
Results

Diameter and velocity

Significant interaction effect:

$\xi = \text{Effect DS vs Control (Group)}$  
$\dagger = \text{difference Baseline vs LBNP}$
Results: interaction effects

Blood flow and vascular conductance

Significant interaction effect

‡ = difference DS vs control

† = difference Baseline vs LBNP
Results

Controls

- During LBNP: ↓ velocity and FBF (potentially FVC)

As expected

Down Syndrome

- During LBNP: no changes, complete lack of, or opposite response

Different from expected
Discussion

1. Impaired vasoconstriction to redistribute blood flow in a non-exercise task

2. Smaller diameters in Down syndrome = structural difference
   \rightarrow suggests a chronic adaptation to:
   1. Less demand
   2. Less supply
Line of inquiry: potential causes

Less demand?

• Muscle mass

• Local mechanisms: ability to vasodilate
  – DS-specific oxidative stress $\rightarrow$ vascular dysfunction?
  – Dynamic hand grip without and with LBNP

• Muscle physiology: ability to use oxygen
  – Mitochondrial dysfunction $\rightarrow$ less oxygen uptake
  – Measuring microvasculature and oxygenation: NIRS

Less supply?

• Cardiac output during maximal exercise test
  – Ped-off ultrasound probe
Young males with DS exhibit **reduced peripheral regulation of blood flow**, indicating a **blunted sympathetic control** of blood flow.

First time: autonomic dysfunction in individuals with DS is **not only impacting systemic control** of heart rate and blood pressure, but also **peripheral blood flow**.

Further research into **underlying mechanisms to connect to the specific cardiovascular profile in DS** and extrapolate findings to other patient populations.
Thank you!

- Questions?
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- Many thanks to the entire IPL team, especially Sangouk Wee!