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

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Disclosures

This work has been supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NIH K99/R00 1 K99 HD092606-01).



Down syndrome

Genotype and phenotype

- Trisomy 21
- Most common genetic syndrome
 - 1 in every 700 newborns
- Intellectual disability
- Co-occuring diseases, i.e. congenital heart disease, Alzheimer's disease, infections, hypothyroid disease, hearing problems, sleep apnea¹







Down syndrome

Cardiovascular risk

- More obesity²
- Lower physical activity³
- Lower fitness⁵
- 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*)





Governance gone wrong Subject of investigation

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





- 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.



- 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

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



- 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











Blood Flow

-Lower body negative pressure (LBNP)



- ≤60° probe insonation angle⁷
- 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: 0.6 40-§ Mean velocity (cm/sec) 30 Diameter (cm) 0.4-20 0.2-10-0.0 0 DS DS Control Control **Baseline** LBNP

§ = Effect DS vs Control (Group) + = 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

UIC

Down Syndrome

 During LBNP:
 ↓ velocity and FBF (potentially FVC)

As expected



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

Different from expected



- 1. Impaired vasoconstriction to redistribute blood flow in a nonexercise task
- 2. Smaller diameters in Down syndrome = structural difference
 → 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.



- Questions?
- <u>thessa@uic.edu</u>
- Many thanks to the entire IPL team, especially Sangouk Wee!



