



Systemic Metabolic Adaptations to Cold Acclimation in Humans Using Total Body Dynamic ^{18}F -FDG PET/CT

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INTRODUCTION

- Obesity and its associated cardiometabolic complications remain major health challenges. While most weight-loss strategies focus on reducing energy intake, increasing energy expenditure provides an alternative approach to improving metabolic health.
- Brown adipose tissue (BAT) is a unique thermogenic tissue in humans, and the presence of BAT is associated with improved risk factors such as insulin sensitivity, blood pressure and lipid profile, although the mechanisms mediating are unknown.
- Short-term cold acclimation increases BAT mass and activity, as measured by ^{18}F -fluorodeoxyglucose (FDG) positron emission tomography/ computed tomography (PET/CT), and improves dyslipidaemia, hyperglycaemia and blood pressure (Hanssen et al., 2016).
- However, the contribution of other organs to whole-body metabolic adaptation remains unclear.

Aims

- To determine whether 10 days of cold acclimation alters glucose uptake across multiple organs
- To investigate whether cold exposure changes inter-organ metabolic relationships

METHODS

Study Protocol

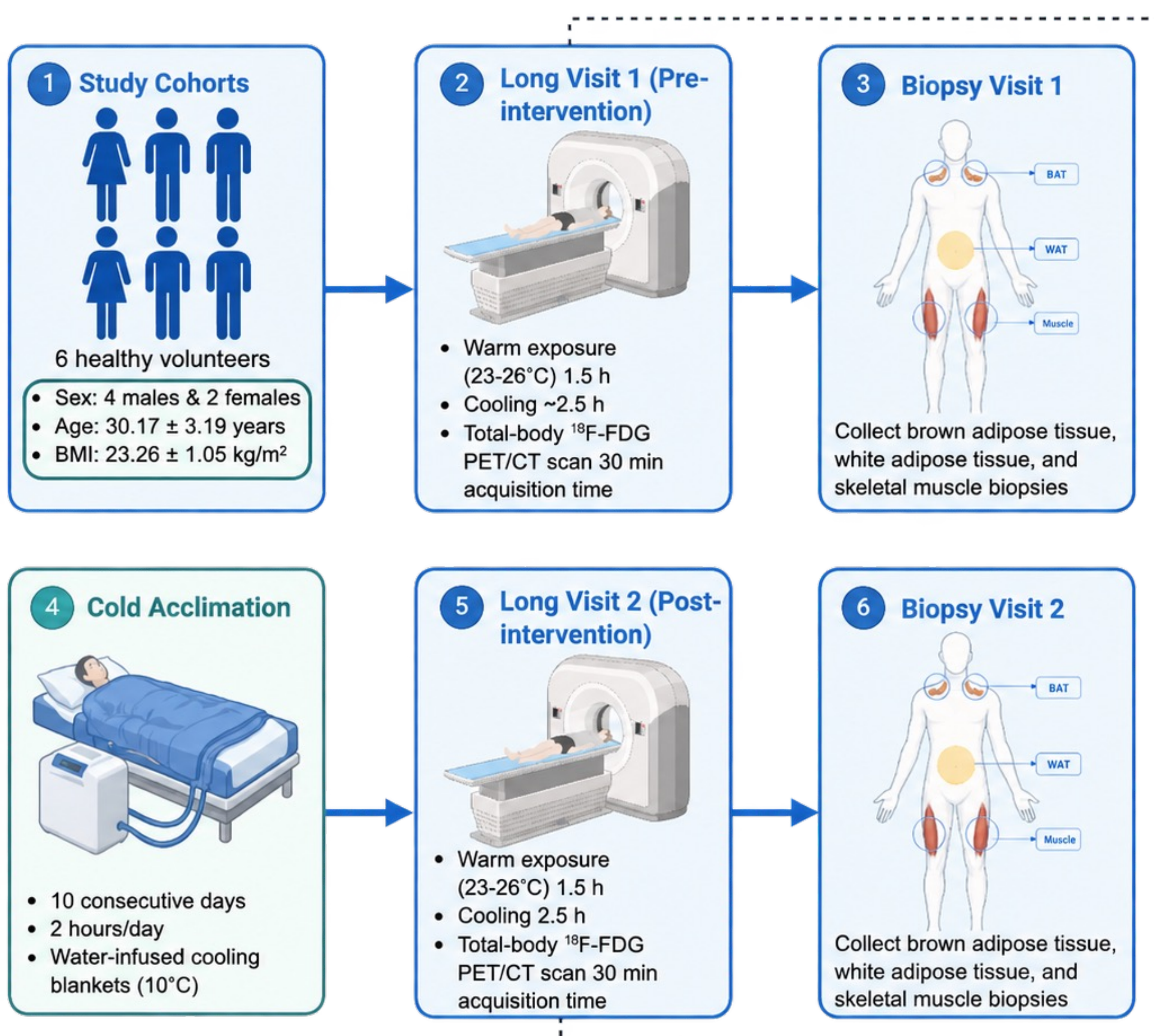


Image & Data Analysis

Image Processing (MOOSE & PMOD)
Multi-Organ Objective Segmentation Engine (MOOSE) AI-tool was used to segment > 140 tissues/organs from CT images. The segmentations were converted into volumes of interest (VOIs) in PMOD and then applied to averaged last frame of the PET scan for standardised uptake value (SUV) extraction. Brown adipose tissue (BAT) and skeletal muscle SUVs were manually extracted.

Statistical Analysis (R)
In R, pre- and post-acclimation SUVs were compared using paired t-test or Wilcoxon signed-rank tests depending on normality of the data, with false discovery rate (FDR) correction for multiple comparisons. PCA was performed to identify overall patterns of metabolic variation across organs.

Network Visualisation (Graphia)
Spearman correlation networks were visualised in Graphia to compare inter-organ metabolic connectivity before and after cold exposure.

RESULTS

i. Pre- vs Post-Acclimation Paired Analysis:

After FDR correction, no significant changes in organ glucose uptake were detected (all adjusted p values > 0.05; Figure 1). However, CT-derived BAT volume increased by 21%, while cholesterol, triglycerides, LDL cholesterol and diastolic blood pressure were reduced following cold acclimation.

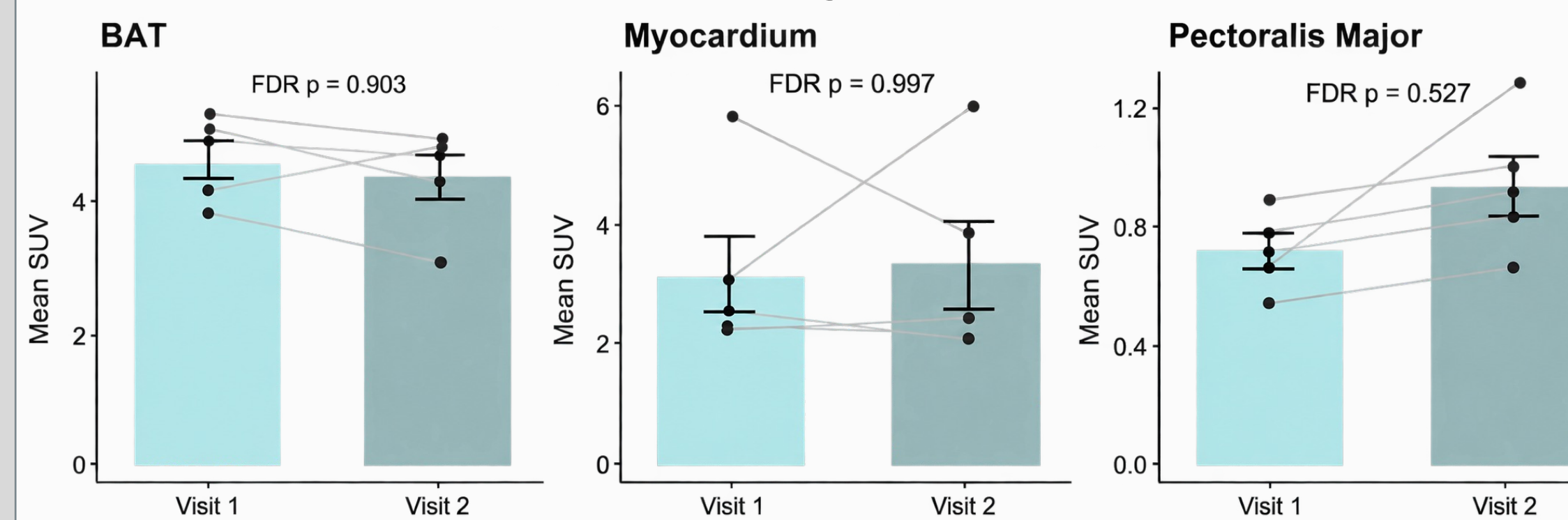


Figure 1. ^{18}F -FDG SUVs in representative tissues (BAT, myocardium and pectoralis major) before and after cold acclimation.

ii. Principal Component Analysis (PCA):

- PCA showed overlap between the pre- and post-acclimation sample distributions, indicating broadly similar uptake patterns, although individual response patterns varied (Figure 2).
- PC1 and PC2 explained 27.1% and 23.5% of the total variance in tissue glucose uptake, respectively.

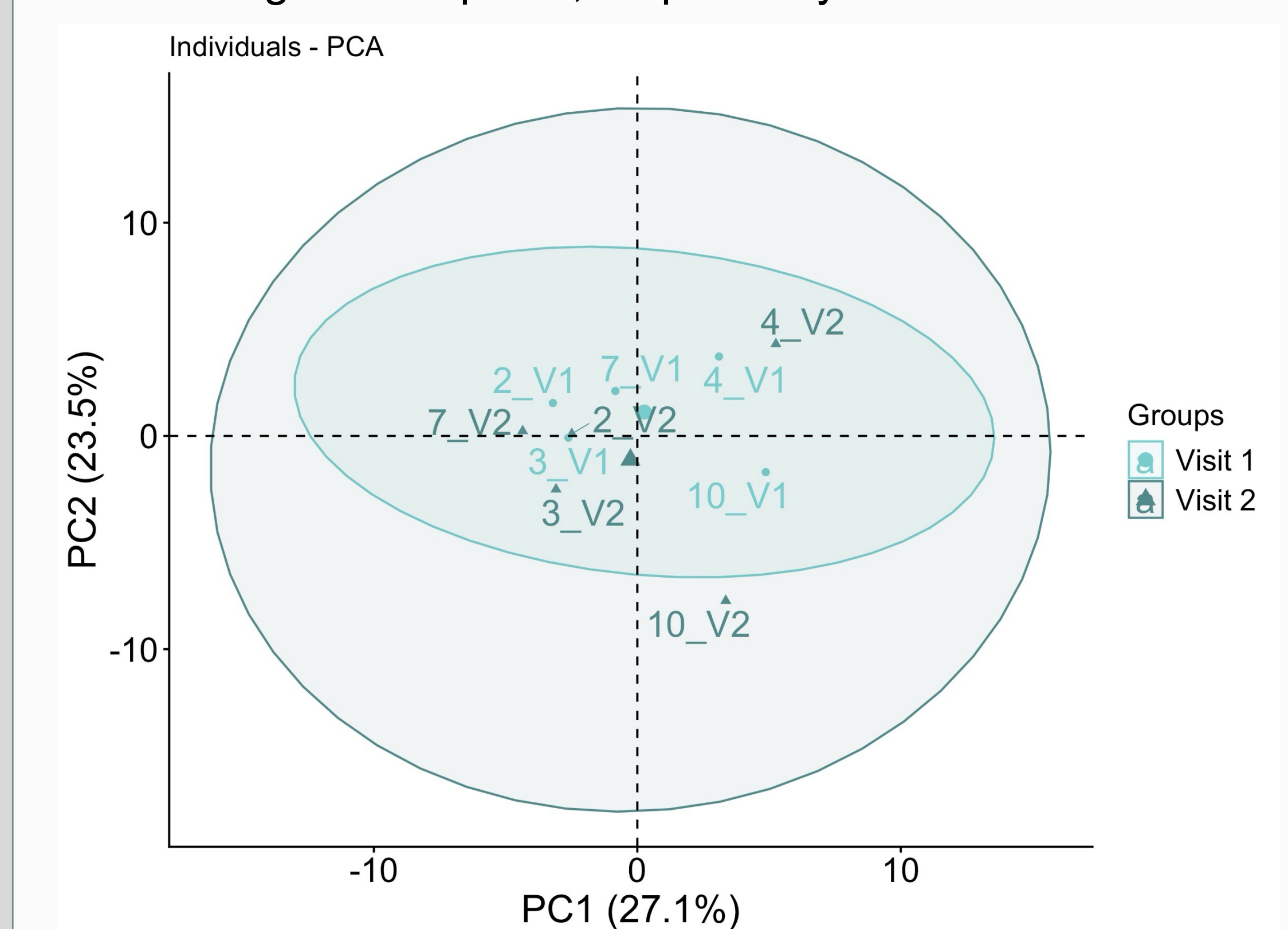


Figure 2. PCA of tissue ^{18}F -FDG SUVs before and after cold acclimation; ellipses indicate the dispersion of samples within each visit.

iii. Correlation Network Analysis:

The post-cold acclimation network appeared more interconnected, with more edges and fewer components than the pre-cold acclimation network (Figure 3). Its largest component included a broader range of metabolic, cardiovascular and musculoskeletal tissues.

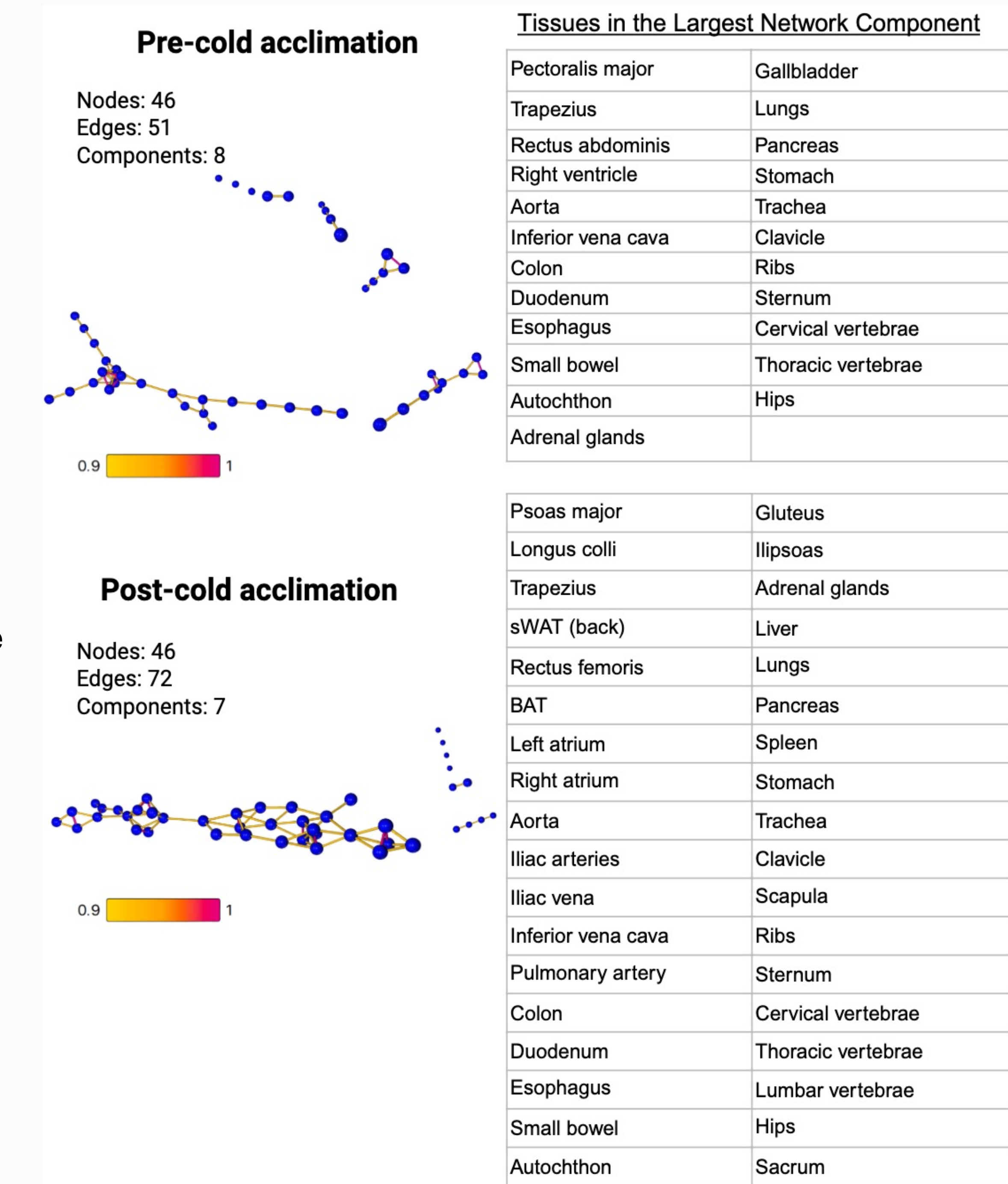


Figure 3. Tissue correlation networks before and after cold acclimation. Nodes represent tissues; edges represent Spearman correlations, with colours progressing from left to right on the scale indicating increasing correlation strength; components represent groups of interconnected tissues.

CONCLUSION

- Cold acclimation produced no statistically significant changes in individual organ glucose uptake or detectable overall uptake patterns, but was associated with greater connectivity post-intervention.
- These findings suggest that cold acclimation may influence the coordination of glucose metabolism across organ systems, without producing significant changes within individual organs.
- Given the short cold exposure period and small sample size, further studies with larger cohorts, longer interventions, and individuals with obesity and/or type 2 diabetes are needed.

REFERENCE & ACKNOWLEDGEMENT

- Hanssen, M.J.W., van der Lans, A.A.J.J., Brans, B., Hoeks, J., Jardon, K.M.C., Schaart, G., Mottaghy, F.M., Schrauwen, P. and van Marken Lichtenbelt, W.D. (2016) 'Short-term cold acclimation recruits brown adipose tissue in obese humans', *Diabetes*, 65(5), pp. 1179–1189. doi: 10.2337/db15-1372.

I would like to thank my supervisors, María Paula Huertas Caycedo and Prof Roland Stimson, for their patient guidance and support throughout the project, from which I have learned and grown greatly. I am also grateful to the BMTO for funding this Summer Vacation Scholarship.