Browning of White Adipose Tissue: Role of β-adrenergic Receptor Signaling

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INTRODUCTION

- Obesity has become an epidemic in both the human and animal population affecting 36% of adults in America and 25-40% of dogs and cats.
- This increase in obesity is of a growing concern because of the associated health risk including but not limited to type 2 diabetes, metabolic disorders, coronary heart disease, stroke, respiratory problems and high blood pressure.
- As white adipose tissue grows in size, it will eventually become hypoxic due to lack of perfusion. This causes the up regulation of the HIF-1 transcription factor, leading to the transcription of genes such as GLUT1, LEP, and VEGF to try and rescue the cell, but will eventually lead to the expression of genes that cause inflammation and apoptosis.
- The death of the cell will cause recruitment of macrophages and CD8+ T cells causing an inflammatory response and the release of cytokines into circulation, leading to systemic inflammation causing metabolic dysfunction.
- Brown adipose tissue is more metabolically active and does not contribute to the inflammatory response as much as does white adipose tissue.
- There is some preliminary evidence that beta adrenergic receptor agonist may impart a more brown-like adipose tissue appearance and metabolism to the existing white adipose tissue.
- We therefore conducted an experiment to determine whether chronic systemic treatment with isoproterenol, a beta adrenergic receptor agonist, would result in a more brown-like phenotype in white adipose tissue.

METHODS

- Minipumps containing either saline (vehicle control; n = 6) or isoproterenol (n = 6) were surgically implanted into the mice at 10 weeks of age.
- At 12 weeks the mice were then sacrificed and the retroperitoneal, subcutaneous, and brown adipose tissue were harvested.
- RNA was then extracted from the samples and converted to cDNA.
- Real time polymerase chain reaction was used to determine the relative quantities of 8 genes MCP1, UCP1, PGC1a, TNF, Adiponectin, CIDEA, LEPTIN, and PRDM.
- The relative quantities of each gene was then compared to the relative quantity of 18S, a gene with a stable expression.

SUMMARY & CONCLUSIONS

- The data shows a trend in the conversion of white adipose tissue into a more brown like tissue when chronically administered a Beta 2 agonist
- Genes involved in the inflammatory process showed an overall decrease in the treated group, an expected observation in a more brown like tissue, being a less inflammatory tissue than white adipose tissue.
- Overall in the treatment group the genes involved in metabolism trended toward an increase, which would be expected in a more brown like adipose tissue, being a more metabolically active tissue.
- Interestingly, retroperitoneal adipose tissue responded differently to systemic treatment then the subcutaneous adipose tissue, in the expression of Adiponectin, PGC1a, and PRDM.
- Implications: If a safe and effective treatment is found to convert white adipose tissue into a more brown like tissue, it could have beneficial effects in the fight against obesity, its comorbidities, and on the quality of life of both pets and human beings.

RESULTS

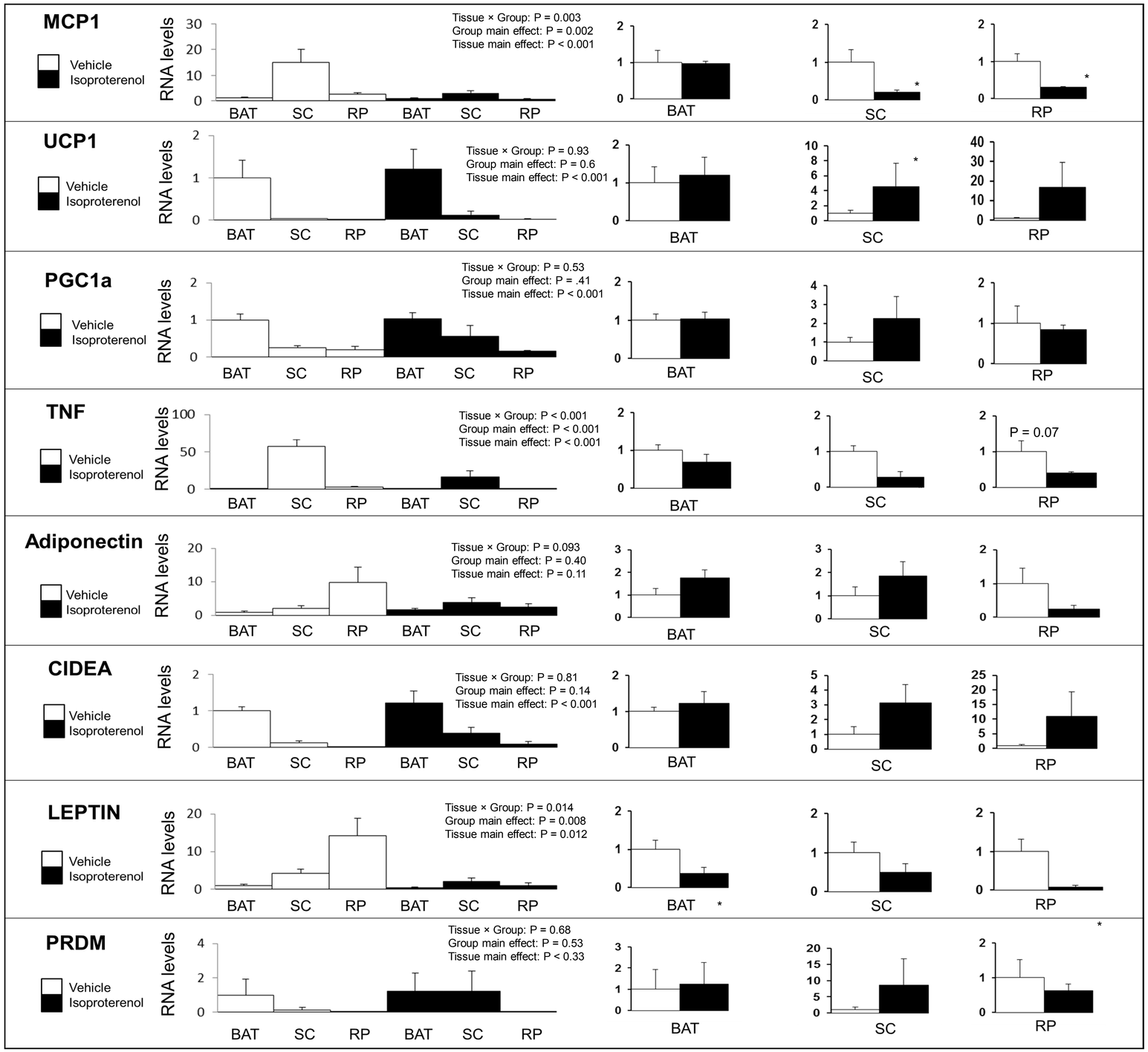

Figure 1: MCP1, monocyte chemotactic protein-1; UCP1, uncoupling protein-1; PGC1 -α, peroxisome proliferator-activated receptor γ coactivator-1 α; TNF α, tumor necrosis factor α; CIDEA, cell death-inducing DFFA-like effector A; PRDM, PR domain containing.

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