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Estrogen and Satiety in the Paraventricular Nucleus

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INTRODUCTION

Menopause has been associated with physiological shifts such as decreased subjective satiety and energy expenditure[1]. The combination of changes following menopause have been shown to result in weight gain and body composition alterations[2]. Increased fat mass, coupled with decreased skeletal muscle mass, elevate risk for osteoporosis and metabolic disorders in post-menopausal women[3]. Estrogen is a key regulator of satiety and bone mass [4,5], and decreased levels following menopause are thought to play a major role in body composition alterations in the post-menopausal population [2]. However, the mechanisms of central satiety and energy expenditure signaling due to estrogen have not been well established. The purpose of this poster was to explore the influence of estrogen signaling in the paraventricular nucleus (PVN) of the hypothalamus on the thyroid and cortisol pathways as a possible mechanism in central satiety and energy expenditure.

METHODS

Animals: In this study, adult female Sprague-Dawley rats (n=6) underwent bilateral ovariectomy. After a recovery period of 7 days, the rats were divided into 2 equal groups. The first group received injections of an oil vehicle (0.1 mL), while the second group received injections of estrogen (10 µg, 0.1 mL) on days 8 and 9. On day 11, the rats were sacrificed for further analysis. Rats' body weights were recorded pre-operatively, days 3-5, and days 8-11.

Tissue Preparation: Brain punches (1 x 3mm) were collected from the ARC, PVN, and NTS during sacrifice for analysis.

RNA Isolation: RNA was extracted from the ARC, PVN, and NTS, using a Biorad Aurum Total RNA Mini kit following the manufacturer's instructions. The isolated RNA samples were subsequently sent to ThermoFisher Scientific's Microarray Research Service Lab for microarray analysis using the Rat ClariomS Assay. Results were analyzed using the Transcriptome Analysis Console (TAC) software version 4.0.

RESULTS

Table 1: Differences Between Estrogen vs Oil Treated Mice in the PVN

	Estrogen Fold Change	P Value
TRH	2.97	0.22
TRH Receptor	-1.09	0.30
TSH	-1.01	0.80
TSH Receptor	-1.24	0.041*
CRH	3.66	0.10
CRH Receptor	-2.18	0.01*

Figure 2: Weight Changes Between Estrogen and Oil Treated Mice

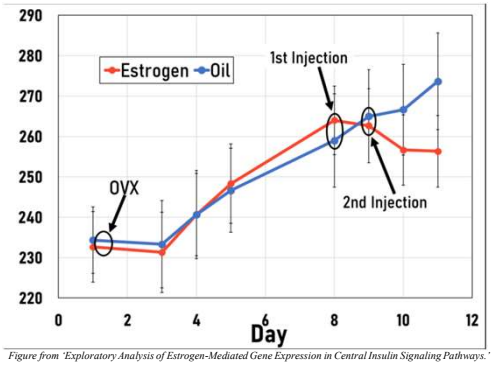


Figure from 'Exploratory Analysis of Estrogen-Mediated Gene Expression in Central Insulin Signaling Pathways.'

Figure 1: Negative Feedback Loops Within the Thyroid and Cortisol Pathways

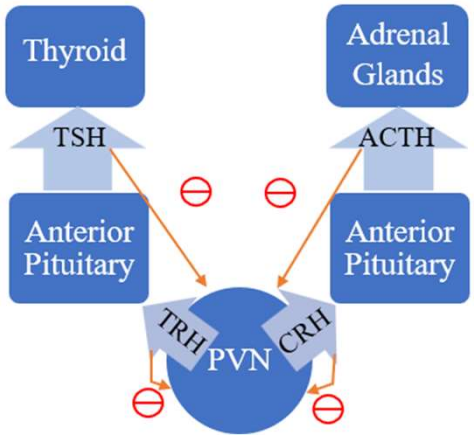
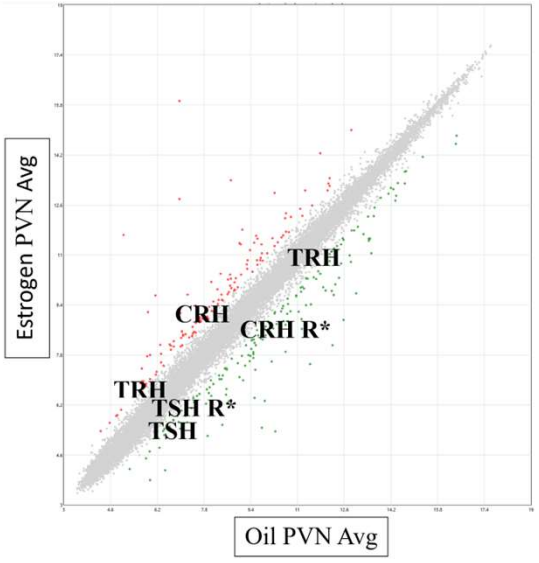


Figure 3: Fold Change in Estrogen PVN Avg (Log2) vs Oil PVN Avg (log2)



CONCLUSION

Body weight changes demonstrate oil treated rats at a higher weight following injections, suggesting estrogen decreased weight. Results indicate TRH and CRH signaling may modulate estrogens effects on satiety and energy expenditure. The non-significant increase in CRH, coupled with the decrease in CRH receptors, in the PVN, suggest estrogen may increase satiety and energy expenditure via direct mechanisms of CRH [6], and through inhibition of CRH negative feedback in the PVN [7]. To our knowledge, the roles of TSH and TRH in the PVN are unknown, but lower TSH receptors, and possibly TRH receptors, in the PVN may act in a similar manner to CRH receptors, inhibiting via a short negative feedback loop, although research is needed to confirm this hypothesis. Increased TRH acting on the anterior pituitary could lead to upregulated thyroid signaling, increasing energy expenditure and skeletal muscle mass [8,9].

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