# Leptin Alters Myometrial Contractility-Related Gene Expression in a Human Myometrial Cell Line

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## Background

- Obesity is associated with poor labor progression and higher rates of cesarean deliveries. The etiology remains unclear.
- Dysfunctional labor in the setting of obesity is hypothesized to result from reduced myometrial contractility.
- Leptin levels increase with obesity and are reported to have a cumulative inhibitory effect on spontaneous and oxytocin-induced myometrial contractility (Moynihan et al, 2006)
- However, the underlying biologic mechanisms by which leptin produces this effect is unknown.

## Objectives

To investigate the effects of leptin on the expression of genes associated with uterine contractility using a myometrial cell line treated ±oxytocin.

## Study Design

• Immortalized human myometrial (PHM1-41) cells were exposed to either vehicle or leptin(1μM) for 24hrs. Cytotoxicity assays confirmed this dose was non-cytotoxic

• The expression of mRNAs encoding oxytocin (*OXT*), oxytocin receptor (*OXTR*) and gap junction-related Debrin-1 (*DBN1*) were analyzed by real time qRT-PCR

• In addition, either vehicle or leptin(1μM) pretreated cells were then treated ±oxytocin for 2hrs and gene expression was assessed

•mRNA abundance calculated relative to GAPDH

•Vehicle vs. leptin data were analyzed using unpaired t tests with Welch's correction and combination treatment data were analyzed using non-parametric Kruskal-Wallis test, followed by Dunn's multiple comparisons

• P<0.05 was considered significant

## Results

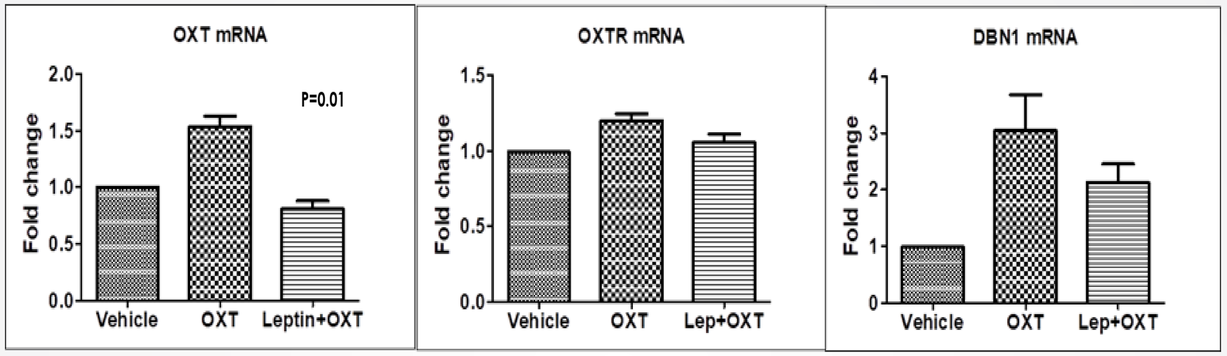


Figure 1: Leptin, when combined with oxytocin, suppresses the induction of oxytocin-induced genes (*OXT, OXTR, DBN1*) by human myometrial cells. Data are shown as mean fold change (±SD)

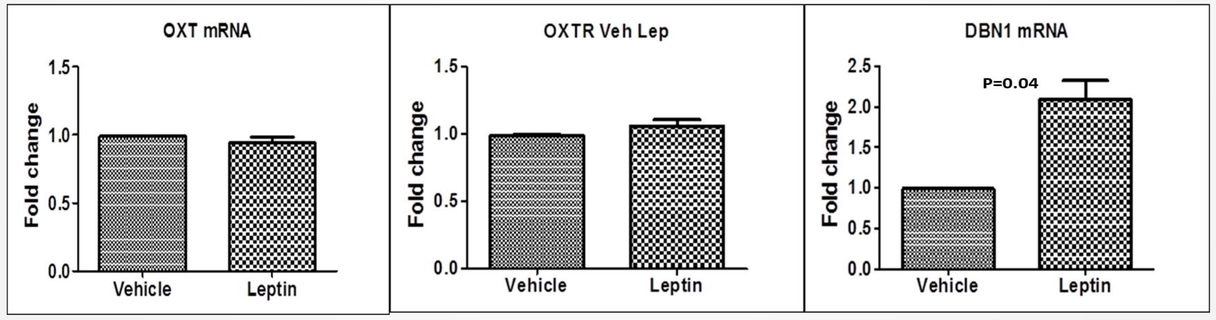


Figure 2: Leptin alone does not alter OXT, OXTR expression. Increases DBN1 expression in human myometrial cells. Data shown as mean fold change (±SD)

• Treatment of PHM1-41 myometrial cells with leptin alone did not affect *OXT* mRNA or *OXTR* mRNA expression by myometrial cells, but did significantly increase *DBN1* mRNA expression (p=0.04, Figure 2)

•As expected, oxytocin treatment increased *OXT*, *OXTR* and *DBN1* mRNA expression compared to vehicle-treatment

•Leptin significantly blocked oxytocin-induced *OXT* mRNA expression (p<0.01)

• Although not statistically significant, we observed a decrease in both oxytocin-induced *OXTR* and *DBN1* mRNA expression by leptin+oxytocin-treated cells compared to vehicle+oxytocin treated cells (Figure 1)

## Conclusion

• Our results suggest that although leptin alone did not alter *OXT* or *OXTR* mRNA expression by human myometrial cells, it suppressed oxytocin-induced contractility-related gene expression

•This novel finding supports that leptin modulates contractility-related gene expression by human myometrial cells and provides insight into possible pathways contributing towards reduced myometrial contractility in obese women.

## Translational Relevance

Understanding of the interaction between obesity-related adipokines and myometrial oxytocin signaling can help us better understand parturition dysfunction in laboring obese patients and obese patients undergoing labor induction. These results may guide us towards identifying pathways that reduce myometrial contractility in obese women that will assist in developing optimized labor management and labor induction protocols for this vulnerable sub-group, with the final goal of reducing high cesarean rates among obese women

## References

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• Moynihan AT, Hehir MP, Glavey SV, Smith TJ, Morrison JJ. Inhibitory effect of leptin on human uterine contractility in vitro. Am J Obstet Gynecol. 2006;195:504–509.