

Vacation Scholarship 2021

Investigation of associations between maternal BMI and fetal adrenal development.

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Objective:

The objective of my scholarship research was to investigate associations between maternal BMI and fetal adrenal development, as the rising incidence of obesity has led to ever more high maternal body mass index (BMI) pregnancies. This increases the risk of adverse outcomes for offspring in later life, including altered adrenal function in adulthood. The human fetal adrenal contains a unique fetal zone that produces precursors to steroid hormones.

Methods:

We combined whole organ RNA-seq (n= 40, gestational weeks 12-19) and pathway review with targeted analysis of genes of interest in first and second trimester fetal adrenals. The genes investigated included those associated with body weight, adrenal development, and the insulin and leptin pathways. We also measured AGRP in fetal plasma (n=60 by multiplex assay). In the analyses we include male and female fetuses categorised into high (>25), or control (<25) maternal BMI groups. RT-qPCR (n=40 fetuses) was done on first trimester adrenals for LEPR, IRS1 and POMC, which were identified from the RNA-seq findings.

Results:

Adrenal RNA-seq showed 588 genes altered with fetal age in females and 1,262 in males. In terms of maternal BMI, 1 gene was altered in females and 0 in males. Accounting for interactions between maternal BMI and fetal age, 0 genes were altered in the female and 7 in the male, including structural and extracellular matrix genes. Fetal plasma AGRP concentrations did not alter with maternal BMI. The statistical analysis of the results of the qPCR showed that there is no significant effect of BMI group on the gene expression unless fetal age is considered. When age is added as a covariate, BMI group was shown to have a significant effect on the expression of LEPR, and age had a significant effect on IRS1 and POMC.

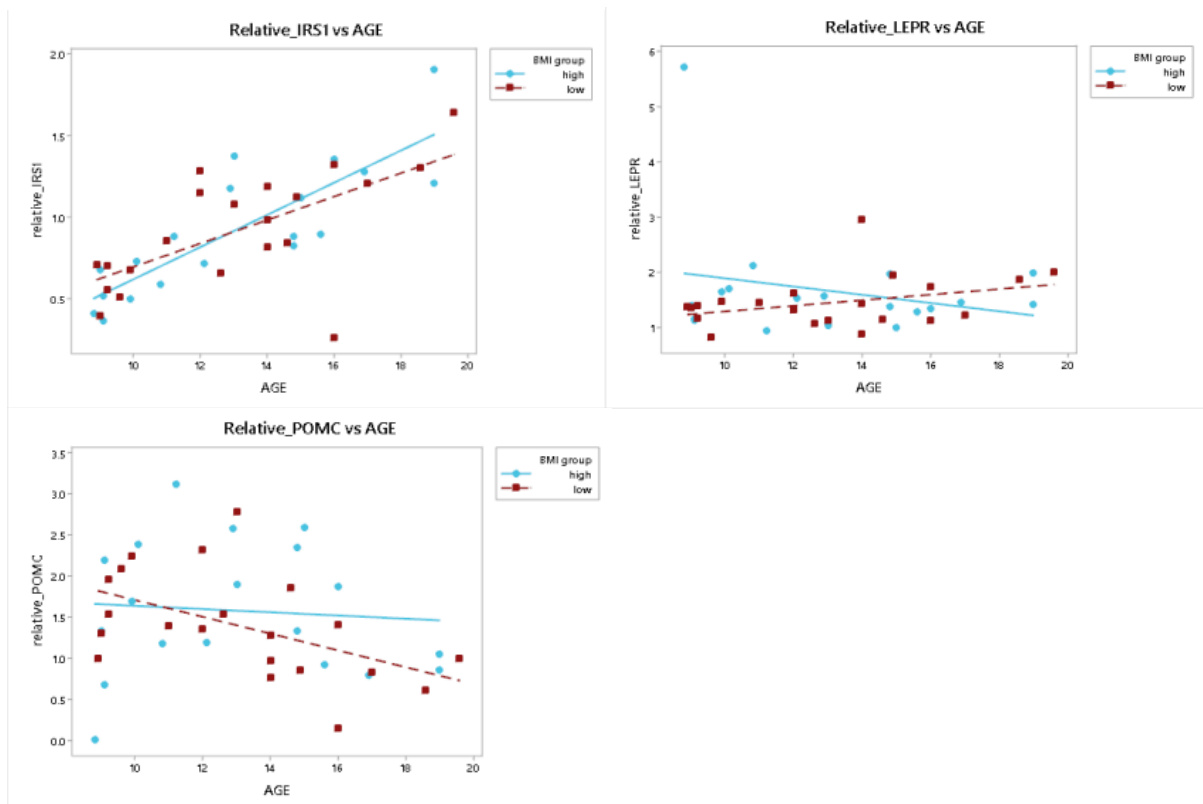
Using standard counts 9 significantly enriched KEGG pathways (180 genes) were affected in a two-way analysis (BMI * fetal age), including focal adhesion, and signalling pathways Rap1 and PI3K-Akt.

Learning:

Over the course of the scholarship, I was taught a number of techniques. These included: the designing of primers and the creation of cDNA for RT-qPCR, the running and analysis of the qPCR using LightCycler480 software, H+E staining, gel electrophoresis, mounting paraffin slices of adrenal samples, and Ki67 immunohistochemistry (IHC).

Overall, our findings suggest that maternal obesity has subtle effects on the fetal adrenal gland via the leptin pathway.

The findings of this vacation scholarship will be presented at Fertility2022, ePoster #Maternal overweight may interfere with first and second trimester human fetal adrenal development



Figures show the relative expression of IRS1, LEPR, and POMC against fetal age compared to a reference gene.