

Inter-correlation between Placental Genes Regulating Fetal Glucocorticoid Exposure and IGF2 in Maternal Severe Obesity: A Mechanism for Higher Birth Weight?

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INTRODUCTION



- 1) Exposure to prenatal maternal obesity is associated with high birth weight.
- 2) One potential biological mechanism is altered placental regulation of fetal growth.
- 3) Excess fetal glucocorticoid exposure associates with lower birth weight and placental Insulin-like Growth Factor (IGF2) may be modulated by glucocorticoids.

Hypothesis: The expression profiles of placental genes leading to reduced glucocorticoid exposure and increased IGF2 mRNA level correlate with higher birth weight in severely obese pregnancy.

MATERIALS & CLINICAL PROTOCOL

LEAN control
BMI ≤ 25 Kg/ m²
N (placenta) = 42

VERY SEVERELY OBESE (SO)
BMI ≥ 40 Kg/ m²
N (placenta) = 49

No antenatal STEROIDS
No GESTATIONAL DIABETES
No PRETERM BIRTH

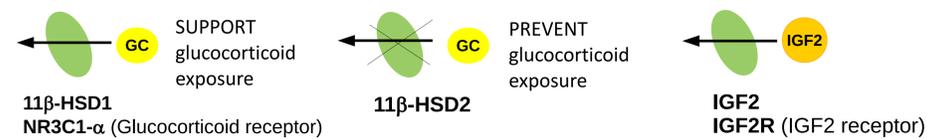
PLACENTA

INFANT ANTHROPOMETRY

Birth weight, birth length, BMI and their British Standard deviation-scores (SDS) (Pan & Cole 2012). This allowed the adjustment of gestational age & gender.

PLACENTAL GENE EXPRESSION ANALYSIS

RT-QPCR was performed in triplicates with RocheLightcycler™. YWHAZ and TBP were used as composite housekeeping genes. RNA integrity was verified with Agilent Bioanalyser (Mina et al., 2015).

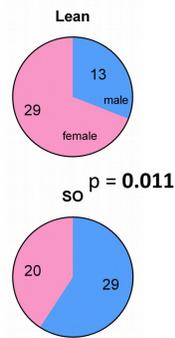


RESULT 1: MEASUREMENTS AT BIRTH

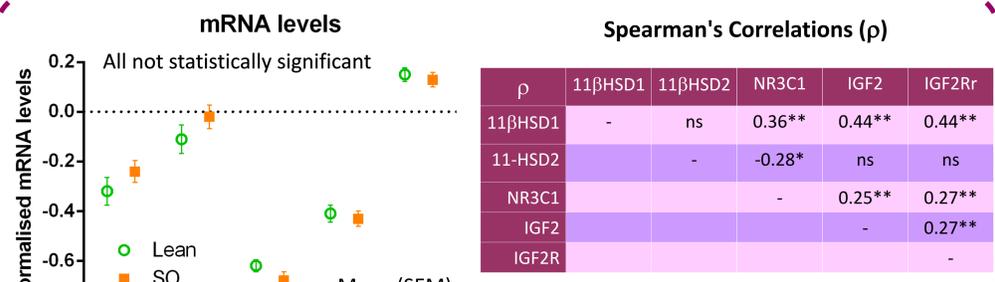
Anthropometry Output	LEAN	SO	p
Birth weight (grams)	3457.79 (433.54)	3578.16 (643.39)	0.307
Birth length (cm)	52.91 (2.59)	54.13 (3.48)	0.11
Birth BMI (Kg/ m ²)	12.28 (1.17)	12.00 (1.92)	0.477
SDS birth weight	0.06 (0.92)	0.44 (1.18)	<u>0.096</u>
SDS birth length	1.23 (1.17)	1.72 (1.60)	0.151
SDS BMI	-0.91 (1.10)	-0.95 (1.40)	0.903

Data displayed = mean (SD). P values were obtained from student's T-test. Length of gestational age was not significantly different by maternal obesity status.

- Infants of SO pregnancy in this subgroup were not heavier, longer and/or had higher higher BMI.
- Due to the significant difference in fetal sex composition it is important to adjust for sex in the downstream analysis.



RESULT 2: OVERALL GENE EXPRESSION

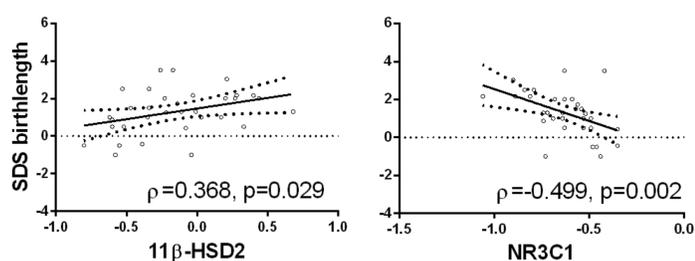


- The placental gene expressions did not differ according to maternal obesity status.
- The strong inter-correlation data were consistent with the data from our previous work (Mina et al., 2015).

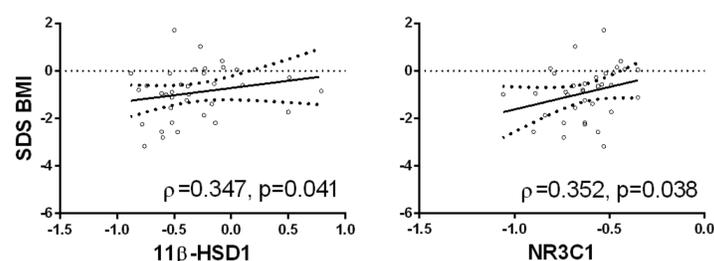
RESULT 3: CORRELATION BETWEEN ANTHROPOMETRIC OUTPUT & GENE EXPRESSION

INVOLVING GLUCOCORTICOID- LINKED PLACENTAL GENE EXPRESSIONS

SDS BIRTH LENGTH

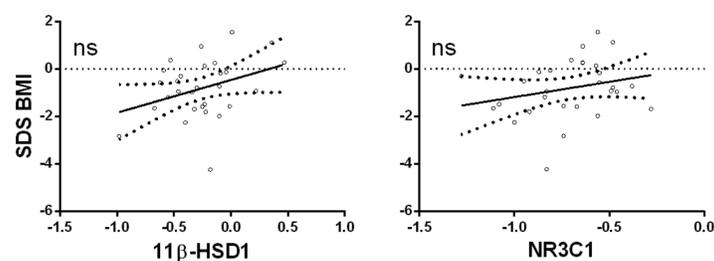
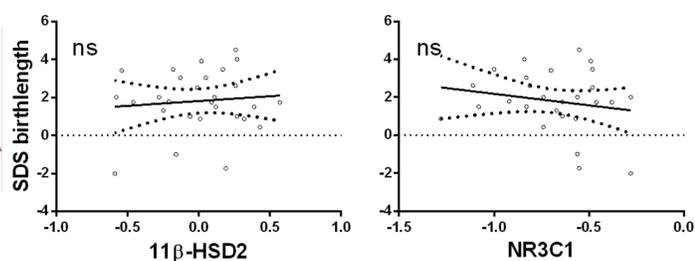
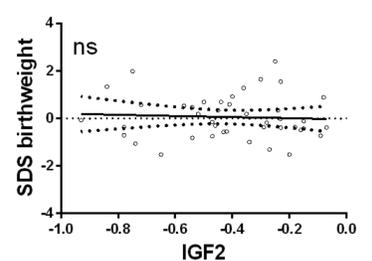


SDS BMI



INVOLVING PLACENTAL IGF2

SDS BIRTH WEIGHT



The correlation data between placental genes supporting MORE in utero GLUCOCORTICOID exposure and SHORTER birth length were absent in SO group.

The correlation data between placental genes supporting MORE in utero GLUCOCORTICOID exposure and HIGHER birth BMI were absent in SO group.

The correlation data between HIGHER placental IGF2 exposure and HIGHER birth weight were observed in SO group only.

DISCUSSION, CONCLUSION, FURTHER STUDIES

- Our inter-correlation findings in the placental mRNA profiles support the biological findings elsewhere that IGF2 family could be downstream targets of glucocorticoid signalling (Vaughan et al., 2012)
- The correlation data between placental genes and body compositions at birth are in line with our hypothesis.
- Works to expand the placental pool to enable association analysis are currently undertaken.

ACKNOWLEDGEMENT

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REFERENCE

- Mina T, Raikkonen K, Riley S, Norman J, Reynolds R., 2015. Psychoneuroendocrinology 59: 112-122.
- Vaughan O, Sferuzzi-ferri A, Fowden A., 2012. J Physiol 590(21):5529- 5540.