Placental expression of neurokinin B and its receptor NK3R is increased in women with polycystic ovary syndrome: results of a preliminary study.

Georgios Markantes, Fotios Markatos, Neoklis Georgopoulos

e-ECE 2021, Sunday 23 May 2021

Funding

This research is co-financed by Greece and the European Union (European Social Fund - ESF) through the Operational Programme “Human Resources Development, Education and Lifelong Learning 2014-2020” in the context of the project “Exploring the developmental theory for polycystic ovary syndrome: the role of alterations in placental gene expression and in fetal DNA methylation (MIS: 5047128).”

Polycystic Ovary Syndrome (PCOS)

- Commonest endocrinopathy in young women
- Manifestations of hyperandrogenism
- Menstrual disturbances – infertility
- High risk of adverse pregnancy outcomes

PCOS & Placenta

- Altered placental structure

- Altered steroidogenic function

- Potential implications

  (1) obstetric complications of PCOS pregnancies

  (2) PCOS heritability – developmental origin

[intrauterine hyperandrogenemia → placental dysfunction → adverse hormonal/nutritional environment → metabolic/reproductive disturbances]

Neurokinin B (NKB)

- Decapeptide of the tachykinin family (neuropeptides)
- Encoded by the TAC3 gene
- Acts via interaction with G-protein coupled receptors (neurokinin 1, 2, 3 receptors – NK1R, NK2R, NK3R)
- Neurotransmitter – expression & action in hypothalamus (KNDy neurons – regulation of GnRH secretion)

Neurokinin B & Placenta

- Significant increase of NKB during pregnancy – placental origin
- Physiological role (regulation of uterine blood supply)?

- Increased NKB production in IUGR, preterm labor
- Possible role in the pathogenesis of pre-eclampsia

- PCOS?

Our study

- **Objective**: compare the placental mRNA expression of NKB, NK1R, NK2R and NK3R in women with PCOS vs controls
- **Setting**: single-center, prospective, case-control study
- **Participants**: 20 women (10 PCOS and 10 controls) with spontaneous conception and singleton, uncomplicated, term pregnancies

Our study

- **Placental sampling**: tissue collected within 15min of placental delivery – full-depth samples 1x1cm from 3 areas – removal of maternal decidua and chorionic plate tissues – division of each sample in 0.5-1cm^3 pieces – immediate submersion in RNAlater solution and storage at -20^o C

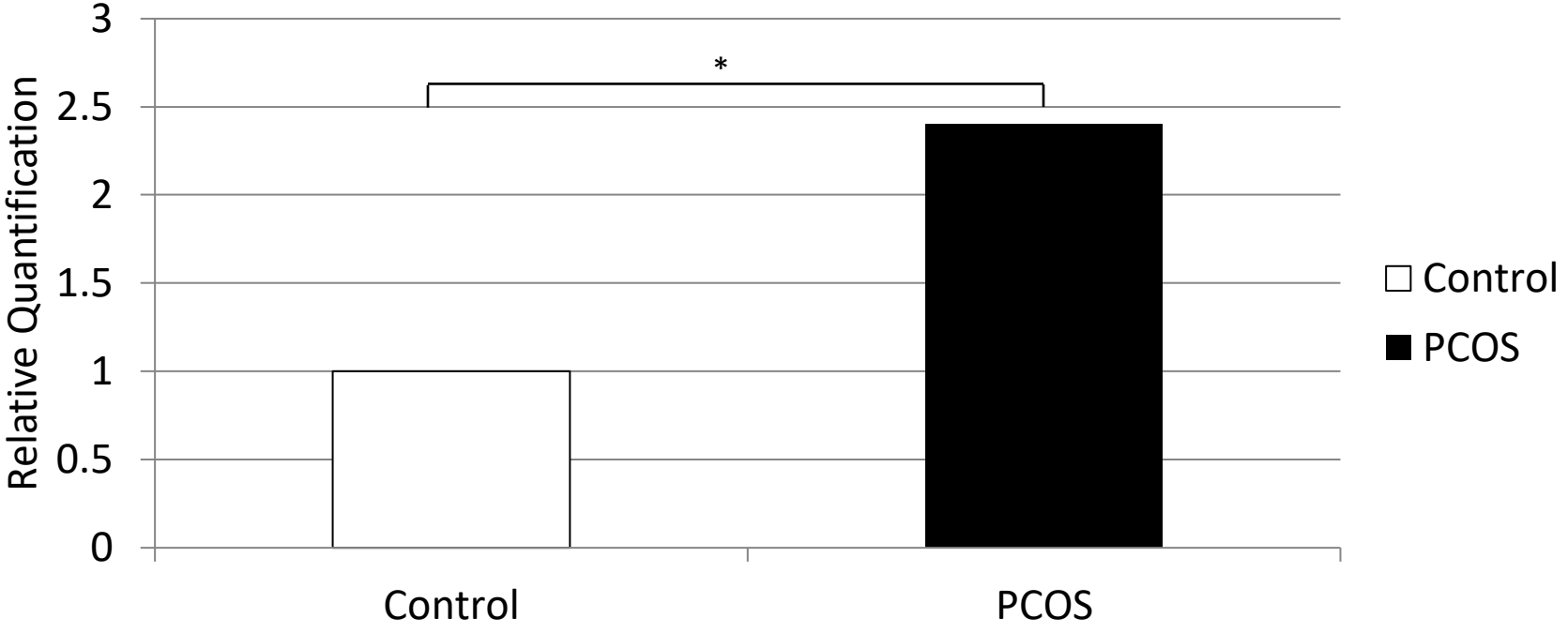
- **Gene expression**: isolation of total RNA – cDNA synthesis – RT-PCR with specific primers and SYBR Green (determination of the Ct value for each sample, reactions run in triplicates) – relative mRNA expression estimated by the ΔΔCT method, using β-actin as reference (housekeeping gene)

Results

	Controls	PCOS	p
Age (years)	31.9±6.4	33.6±3.5	ns
BMI (kg/m^2)	29.8±5.9	31.3±3.6	ns
Gestational Age (weeks)	38.7±1.4	39.4±0.8	ns
Mode of delivery (VD/CS)	6/4	3/7	ns
Offspring sex (M/F)	6/4	7/3	ns
Offspring birth weight (g)	3348±374	3459±447	ns

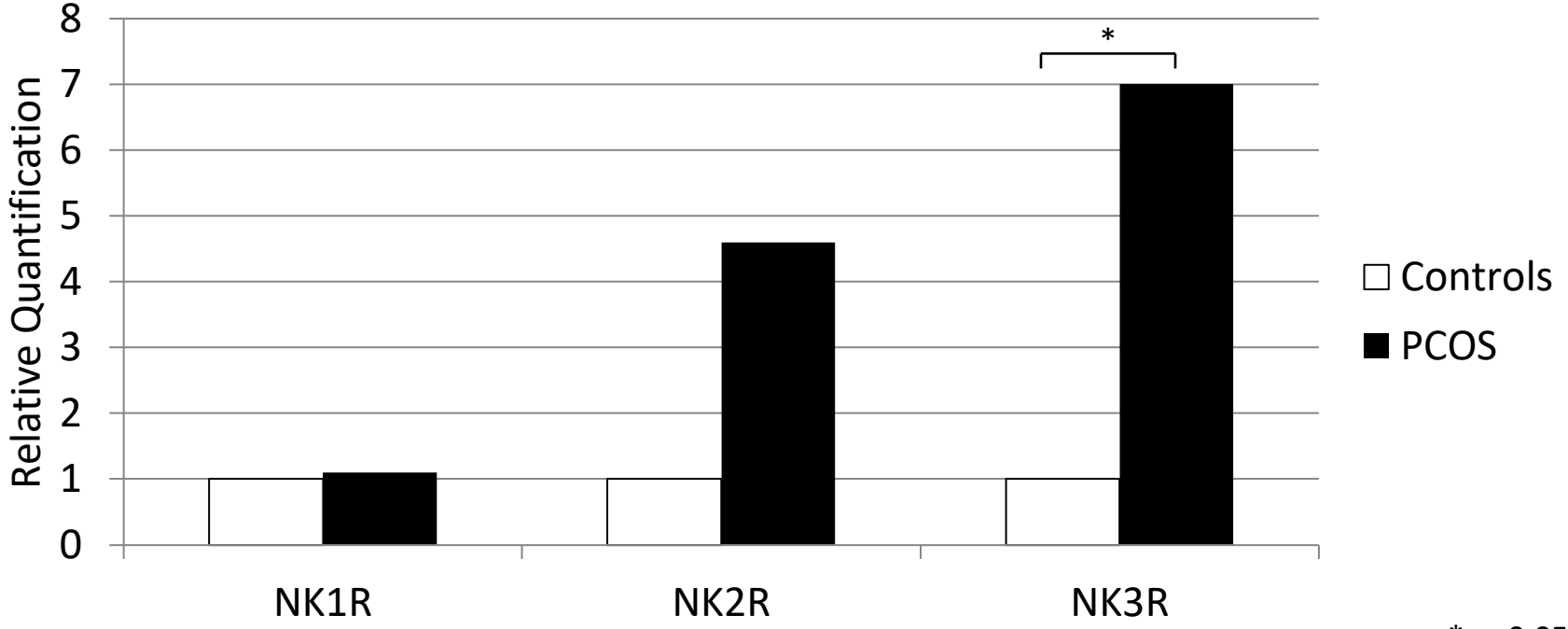
VD: vaginal delivery, CS: cesarean section, M: male, F: female

NKB mRNA expression



* $p<0.05$

NK1R, NK2R, NK3R mRNA expression



* $p<0.05$

Conclusions – Further implications

- Increased NKB and NK3R mRNA expression in PCOS placenta
- Preliminary findings – small sample
- NKB as mediator in placental alterations of PCOS?
- Dependence of NKB and its receptors expression on PCOS phenotype, sex steroid levels, glucose, insulin?
- Role of NKB in PCOS heritability?

Thank You
For Your Attention