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Altered placental neurotrophins and adverse neurodevelopment in female offspring of women with polycystic ovary syndrome

Wang F, Wu Y, Zhu Y, Qu F
Women's hospital, Medical School, Zhejiang university, China, China

Objective

Polycystic ovary syndrome (PCOS) is one of the most common female endocrine disorders. It is characterized by excess androgens and abnormal follicle development. Pregnancy exacerbates hyperandrogenemia in women with PCOS. However, offspring health risk of PCOS is poorly studied. The altered placental expression of neurotrophins may lead to abnormal fetal growth and brain development. Epigenetic mechanisms are widely involved in offspring development. The current study is aimed to investigate the neurodevelopment of female offspring of women with PCOS and to explore the underlying mechanism in placenta. ".

Methods

Twelve PCOS patients, 25 controls undergoing selective cesarean section and their female offspring were recruited in obstetric unit. The maternal blood, placenta and umbilical cord blood were collected. Dubowitz neurologic examination of the newborn was used to assess the newborns. We performed quantitative realtime-PCR (qRT-PCR), enzyme-linked immunosorbent assay (ELISA), immunofluorescence (IF) and bisulfite genomic sequencing PCR (BSP).

Results

In PCOS group, whereas no significant difference in birthweight and APGAR score, there was a slight reduction in placental weight. The total score and the behavior subscale of the Dubowitz scoring system were lower among infants from women with PCOS compared with controls. The digital ratio which could be influenced by prenatal androgens was comparable between PCOS and control group. Using ELISA and qRT-PCR, altered levels of neurotrophins, including nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF), were found in umbilical cord and placentae of PCOS group compared with controls. IF further confirmed the change of neurotrophin protein expression in trophoblast. We analyzed the cytosine phosphate guanine (CpG) islands of BDNF and NGF gene in placentae with BSP, unfortunately we did not observe any considerable difference between PCOS individuals and controls.

Conclusion

The female offspring of women with PCOS appear adverse neurodevelopment, which may partially due to differential placental production of neurotrophins including NGF and BDNF, although their DNA methylation change in placenta is probably not the cause.