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Stress hormone during pregnancy linked to IQ in children

Higher levels of the stress hormone cortisol during the third trimester of pregnancy may impede intelligence quotient (IQ) scores in boys aged 7 years old, according to research presented at the 26th European Congress of Endocrinology in Stockholm. Surprisingly, cortisol levels in the blood are not associated with IQ scores in girls, but higher urine cortisone levels improved their scores. The findings highlight the important role cortisol plays in fetal development in boys and girls independently.

Prenatal exposure to cortisol — a steroid hormone that helps the body respond to stress — is needed for fetal development and is thought to affect cognitive function in children later in life. During pregnancy, the levels of cortisol increase and pregnant women carrying girls generally secrete more cortisol than those with boys. However, in the placenta, the enzyme 11 β -hydroxysteroid-dehydrogenase type 2 (11 β -HSD2) regulates the amount of cortisol that reaches the fetus by converting cortisol to its inactive form known as cortisone.

Researchers from the Odense University Hospital in Denmark have previously shown that children between the ages of one and three have more advanced speech and language skills when their mothers have high levels of cortisol during their third trimester. Now, in this study, the researchers analyzed data on the cortisol and cortisone levels of 943 pregnant women during the third trimester and on the IQ tests of their 943 children aged 7 years old, from the Odense Child Cohort. They found that pregnant women carrying a boy had lower cortisol levels circulating in their blood than those women carrying a girl. In addition, boys exposed to higher cortisol levels in the womb scored lower on IQ tests at age 7. Girls the same age scored better on IQ tests when their mothers had higher levels of urine cortisone.

"To our knowledge, this is the first study investigating the association between urine cortisone levels during pregnancy and IQ scores in children," said lead author, Dr Anja Fenger Dreyer. "While other studies have only looked at cortisol circulating in the blood during pregnancy and child IQ, we are the first to look at urine samples as well as blood samples and to investigate boys and girls separately."

Dr Fenger Dreyer added: "Our results show that girls may be more protected by the activity of placental 11β -HSD2, whereas boys may be more vulnerable to prenatal exposure of maternal physiological cortisol."

"Although our previous study showed prenatal cortisol exposure was positively associated with language development, in this study prenatal cortisol exposure — 'directly' by serum cortisol and 'indirectly' by urine cortisone — is negatively associated with IQ scores," continued Dr Fenger Dreyer.

"This may mean that the high levels of prenatal cortisol exposure might have a temporary effect on a child's cognitive development. It should also be noted that the vocabulary in toddlers was reported by parents in our previous study, while child IQ in this study was assessed by trained psychologists."

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<u>Abstract</u> P312

Maternal Cortisol Levels in Pregnancy and Intelligence Quotient in Children at 7 Years of Age. Odense Child Cohort.

Background: Maternal cortisol levels increase during pregnancy and prenatal cortisol exposure have been linked to cognitive function in childhood. Higher activity of the enzyme 11 β -hydroxysteroid-dehydrogenase type 2 (11 β -HSD2) downregulates the amount of maternal cortisol crossing the placenta by inactivation of cortisol to cortisone. In childhood, boys perform significantly poorer in tests of intelligence than girls.

Aim: To investigate associations between maternal 3rd trimester cortisol or cortisone and child IQ at 7-years-of-age, and to consider the impact of child sex.

Method: Odense Child Cohort is a prospective observational cohort study. In this current study, 943 mother-child dyads were included. Exposure was maternal 24 hour urine (u-) cortisol and cortisone, and fasting morning serum (s-) cortisol, obtained in 3rd trimester of pregnancy and measured by liquid chromatography–tandem mass spectrometry. Outcome was child intelligence at age 7 years assessed by trained psychologists using the Wechsler Intelligence Scale for Children version V. Estimations of full scale intelligence quotient (FSIQ) and verbal comprehension index (VCI) were calculated.

Results: Women carrying a boy had significantly lower s-cortisol levels than women carrying a girl (825 vs. 865 nmol/L, p = 0.005). Girls had a significant higher score in FSIQ (101.2 vs. 98.2, p < 0.001) and VCI (101.1 vs. 98.9, p = 0.004) compared to boys. In girls, levels of maternal u-cortisone were positively associated with VCI (B (95%-CI) = 6.2 (1.2; 11.2). In boys, maternal s-cortisol was negatively associated with FSIQ (B (95%-CI) = -3.9 (-6.5; -1.3)) and VCI (B (95%-CI) = -4.4 (-7.0; -1.9)). Child sex had a significant interaction with u-cortisone and s-cortisol in the associations.

Conclusion: Lower prenatal cortisol exposure of the fetus seems beneficial for cognitive development at 7-years-of-age. Girls were protected against high cortisol exposure via the inactivation of cortisol to cortisone by 11β -HSD2, while boys were more susceptible to high maternal cortisol levels. Child sex differences in prenatal cortisol exposure and cognitive development should be considered in future studies.

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Notes for Editors

1. For further information about the study, and to arrange an interview with the authors, please contact the ECE 2024 press office:

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- The study "Maternal Cortisol Levels in Pregnancy and Intelligence Quotient in Children at 7 Years of Age. Odense Child Cohort." is a poster presentation that will take place on Saturday 11 May 2024 at the European Congress of Endocrinology at the Stockholm International Fairs (Stockholmsmässan) in Stockholm, Sweden.
- 3. The 26th European Congress of Endocrinology (ECE) is held at the Stockholm International Fairs (Stockholmsmässan) in Stockholm, Sweden, on 11-14 May 2024. See the full scientific programme here: <u>https://ese-hormonesapps.m-anage.com/ece2024/en-GB/pag</u>
- 4. The <u>European Society of Endocrinology</u> (ESE) is at the centre of Europe's endocrine community. Its vision is to shape the future of endocrinology to improve science, knowledge and health. Through its events, publications, grants and advocacy work, ESE shares the best knowledge in endocrine science and medicine across Europe and beyond. ESE and its partner societies jointly represent a community of over 20,000 endocrinologists. ESE informs policymakers on health decisions at the highest level through advocacy efforts across Europe.