Learning more about the link between polycystic ovary syndrome and mental health

November 2 2015

Dr. Elisabet Stener-Victorin is a senior lecturer and research group leader at Karolinska Institutet's Department of Physiology and Pharmacology. Credit: Mats Rundgren

Women with polycystic ovary syndrome (PCOS) have high levels of

androgens in their blood, which has been assumed able to affect fetal development during pregnancy. An international team of researchers led from Karolinska Institutet in Sweden has now identified a hormonal mechanism that might explain why women with PCOS run a higher risk of developing symptoms of mental ill-health, such as anxiety and depression, in adulthood. The results, which are based on animal studies, are presented in the journal *PNAS*.

PCOS affects more than one in ten women of fertile age, and is characterised by small follicles inn one or both ovaries, high levels of testosterone in the blood and irregular periods. Women with PCOS also have problems with obesity and insulin resistance, which puts them at greater risk of developing type 2 Diabetes. They are also more likely to have mental health issues.

"Over 60 per cent of these women are diagnosed with at least one psychiatric symptom, such as anxiety, depression or an eating disorder, and suicide is much more common amongst women with PCOS than amongst healthy controls," says principal investigator Elisabet Stener-Victorin, researcher at the Department of Physiology and Pharmacology at Karolinska Institutet.

It is also known that daughters of women with PCOS are more likely to develop the condition, while the sons tend to have problems with obesity and insulin resistance. One of the causes has been assumed to be due to the greater in-utero exposure to male hormones (androgens) via the mother's blood, but the biological mechanism is unclear.

In the present '*PNAS*' study, the researchers have examined what happens when pregnant rats and their fetuses are exposed to excessive doses of testosterone to mimic the conditions of pregnant women with PCOS. They studied the impact on the placenta and on fetal growth and monitored the offspring - of both sexes - to adulthood, when their

behaviour was then tested.

Their results show that both male and female offspring exposed to testosterone in a late fetal stage display a higher degree of anxiety-like behaviour as adults than individuals born under normal circumstances. Further experiments allowed the researchers to establish that the testosterone exerts the greatest effect on the amygdala, a region of the brain that plays a part in emotional regulation and behaviour linked to both positive and negative emotions.

The group found evidence of disturbances in the activity of the gene regulating the androgen receptor in the amygdale of offspring, and noted changes in the receptors for a type of oestrogen and in the genes that regulate serotonin and GABA, signal substances in the brain known for their involvement in the regulation of anxious behaviour.

"But when the androgenic and oestrogenic receptors were blocked by two different drugs, the animals were protected against the development of the anxiety-like behaviour in adulthood," says Dr Stener-Victorin. "Our results indicate a hitherto unknown biological mechanism that can help us understand why the daughters and sons of women with PCOS develop anxiety as adults."

More information: Maternal testosterone exposure increases anxiety-like behavior and impacts the limbic system in the offspring, *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1507514112

Provided by Karolinska Institutet

polycystic-ovary-syndrome-mental.html