American College of Neuropsychopharmacology

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Sex Differences in Fetal Brain Development May Explain Risk of Co-Occurring Depression and Cardiovascular Disease

WAIKOLOA, HI (December 4, 2011) –A new study suggests that the development of the stress response circuitry, areas of the brain that are important in how we respond to every day stress, our mood and cardiac function, may be important for understanding male-female differences in the risk for developing co-occurring depression and cardiovascular disease during adulthood. Co-occurring depression and cardiovascular disease is significantly more common in women than in men[1] and will be the number one cause of disability worldwide by 2020[2]. The study was presented today at the American College of Neuropsychopharmacology (ACNP) annual meeting.

Led by Jill Goldstein, PhD, Professor of Psychiatry and Medicine at Harvard Medical School and Director of Research at the Connors Center for Women's Health and Gender Biology at Brigham and Women's Hospital, the research team found that adult women who were exposed to preeclampsia, a pregnancy condition marked by a mother's high blood pressure, or to conditions that restricted fetal growth during their prenatal development, were at significantly higher risk for the co-occurrence of depression and cardiovascular disease during adulthood, particularly in women[3]. Specifically, the researchers found that immune activation abnormalities in mothers during their pregnancy had lasting sex-specific effects on their offspring's response to stress, depression and cardiac regulation.

"Understanding the early signs and pathways to this common co-occurrence will help us think about how we can intervene earlier, before adult onset of these disorders occurs," said Goldstein.

This research expands on a National Institutes of Health (NIH) cohort study that systematically followed mothers through pregnancy and their children through the first seven years of life. During pregnancy, mothers' blood was taken and stored at NIH for 40 years. Over the last 20 years, Goldstein and her colleagues have followed many of the adult offspring from this cohort into their late 40s.

In this study, Goldstein and her colleagues analyzed the mothers' prenatal blood and identified indicators of immune activation (associated with preeclampsia and fetal growth restriction) to which the developing fetus was exposed. They looked at the impact of these immunological indicators on the development of the stress response circuitry in the male and female offspring's brain. Stress response circuitry includes brain regions that show some of the largest

sex differences in the brain. These regions develop differently in males and females during fetal development and function differently in men and women in adulthood.

Given that these brain regions also regulate mood and cardiac function, Goldstein hypothesized that disruptions in the development of this brain circuitry during fetal development would result in the sex-specific vulnerability to depression and cardiac disease in adulthood.

Goldstein and her colleagues re-recruited adults who were exposed to prenatal immune activation, as well as unexposed adult siblings, to look at how these potential vulnerabilities developed over 40-50 years. Psychiatric interviews, cognitive testing, electrocardiocardiogram data, and blood were collected. Participants also underwent functional brain imaging using a stress challenge task, during which hormones and heart rate measures were collected.

Results showed significant associations between mothers immunologic responses during fetal development and sex-specific deficits in exposed adults' stress response brain activity, hormones and cardiac dysregulation 40 years later.

The studies were funded by the National Institute of Mental Health and NIH Office of Research on Women's Health.

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ACNP, founded in 1961, is a professional organization of more than 900 leading scientists, including four Nobel Laureates. The mission of ACNP is to further research and education in neuropsychopharmacology and related fields in the following ways: promoting the interaction of a broad range of scientific disciplines of brain and behavior in order to advance the understanding of causes, prevention and treatment of diseases of the nervous system including psychiatric, neurological, behavioral and addictive disorders; encouraging scientists to enter research careers in fields related to these disorders and their treatment; and ensuring the dissemination of relevant scientific advances in these disorders.

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