INNOVATE
EVIDENCE-BASED MENTAL HEALTH RESEARCH

Immune Activation and Schizophrenia

Getting sick or having a case of the flu is a common part of our day-to-day lives. However, women who get sick while pregnant may have another risk to consider. Recent research has shown that there is a link between a mother's immune response being triggered due to sickness and an increased risk of having a child who will develop schizophrenia and autism.[2] To be clear, the research is still being conducted and risk assessments are still unknown. Not every woman exposed to infection during pregnancy will give birth to offspring with abnormal brain development. But the question remains--what makes some women more susceptible?

To answer this question, Melissa Bauman, Ph.D., Associate Professor Department of Psychiatry and Behavioral Sciences, was awarded one of 23 Pilot Awards by the Behavioral Health Center of Excellence. Bauman's study is entitled "Evaluating Gene X Environment Risk Factors for Neuropsychiatric Disorders in a Rat Model of Prenatal Immune Challenge to Develop Disease Prevention Strategies."

Previous epidemiological studies have shown that children of mothers who get the flu during pregnancy have an increased risk for schizophrenia and autism.[1] However, Bauman and others have previously demonstrated that it is not the actual virus or infection itself that increases this risk, but the activation of the mother's immune response. When the immune response is activated the body releases cytokines, or small proteins, that regulate this response. An elevated concentration of cytokines during fetal development corresponds to a higher risk for abnormal brain development. Bauman's study looks at the underlying mechanism that affects the developing brain by taking into account other factors such as genetic susceptibility, sex of the fetus, intensity of the infection and the timing and degree of the immune response.

Animal Model Benefits

Bauman's research works in parallel with a rodent model and a non-human primate model that will rapidly inform preventive prenatal care in humans. Animal models are needed to understand how complex genetic and environmental risk factors produce neuropsychiatric disorders. The benefits of using well-designed preclinical animal

"Dr. Bauman's research is critical to understanding how maternal health contributes to brain development, and its implications for neurodevelopmental and psychiatric disorders. Her translational work will open doors to greater discoveries."

- Tara Niendam, Ph.D.,
Assistant Professor of Psychiatry, UC Davis, Director of Operations, UC Davis SacEDAPT Clinic

models are extensive. While the pace of research is generally slow and methodical, animal model researchers can have a larger sample size with faster turnaround. In addition, there are similarities in social, behavioral, and cognitive aspects in both rodent and nonhuman primate models that can be translated to the human model. Finally, by using genetically modified samples, one is able to get a better understanding of underlying mechanisms and isolate variables.

Bench-to-Bedside

Not all women who get sick during pregnancy have children with psychiatric disorders. Knowing this, Bauman and her team, including Katherine Ku, junior specialist, and Milo Careaga, postdoctoral fellow, look at genetic factors that work in tandem with the environmental inputs and ultimately lead to higher risk for developing schizophrenia.

There is a strong genetic component in addition to the environmental aspects that contribute to a mother's vulnerability. This genetic susceptibility will be studied in a rat model. Bauman's team will compare the behavior of offspring with and without a gene implicated in schizophrenia. This information will then be combined with behavioral responses to environmental risk factors and allow the lab to isolate factors that can be targeted thereapeutically. One such environmental factor is timing of the immune response. Bauman predicts that the timing of infection matters, and whether the immune response is activated early or late in the pregnancy will affect the offspring's risk. This may translate to interventions during a specific trimester for pregnant women during flu season.

Basic Science

By understanding the basic science of what actually occurs during fetal development and maternal immune response activation, Bauman can begin to design and test novel therapeutic approaches to mitigate the effects on brain development. "Research in prenatal risk factors has the potential to make progress fairly rapidly. I can foresee a time when we are able to able to identify women who are vulnerable, monitor their pregnancy and determine which interventions provide the most protection for the fetal brain as it develops," stated Bauman.

The bridge between basic science and public policy is clear for Bauman as a scientist and a mother. "Research can translate into information for human health and help inform women about how to manage infections and risk factors during pregnancy. This is a women's health issue."

What does this mean for pregnant women?

Not all women who are pregnant and get sick will have children with neurodevelopmental disorders. This research studies the genetic and environmental risk factors for development of neuropsychiatric disorders, specifically schizophrenia and autism. By understanding the combination of genetic and environmental risk factors and how they interact, novel preventive treatments for babies at risk can be developed.

1. Smith SE, Li J, Garbett K, Mirnics K, Patterson PH. Maternal immune activation alters fetal brain development through interleukin-6. J Neurosci. 2007 Oct 3;27(40):10695-702. PubMed PMID: 17913903; PubMed Central PMCID: PMC2387067.

2. Canetta SE, Brown AS. Prenatal Infection, Maternal Immune Activation, and Risk for Schizophrenia. Transl Neurosci. 2012 Dec 1;3(4):320-327. PubMed PMID: 23956839; PubMed Central PMCID: PMC3744366.

Behavioral Health Center of Excellence at UC Davis

UC Davis launched the Behavioral Health Center of Excellence in October 2014 to advance mental health research and policy with initial funding from the Mental Health Services Act. The Innovate series highlights the Center's $4.3 million Research Pilot Award program.

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