Medical Xpress

New research shows critical role of placenta in brain development

April 21 2011

Research at the Keck School of Medicine of the University of Southern California's (USC) Zilkha Neurogenetic Institute shows for the first time that the human placenta plays an active role in synthesizing serotonin, paving the way to new treatment strategies that could mitigate health impacts such as cardiovascular disease and mental illness.

The groundbreaking findings, conducted with researchers from Vanderbilt University as part of a Silvio Conte Center of Excellence grant from the National Institute of Mental Health, offer conclusive evidence that the placenta provides serotonin to the fetal forebrain, not through the mother's blood supply, as theorized for the past 60 years. The research, "A transient placental source of serotonin for the fetal forebrain," will be published in the journal *Nature* on April 21, 2011.

"Our research indicates that the placenta actually synthesizes serotonin, and the serotonin is released from the placenta into the fetal bloodstream where it can reach the fetal brain," said lead author Alexandre Bonnin, Ph.D. "The placenta was seen as a passive organ, but we now know that it has significant synthetic capabilities and has a much more critical role in developmental programming of the fetus than previously thought."

Bonnin's work with Pat Levitt, Ph.D., director of the Zilkha Neurogenetic Institute and corresponding author on the paper, included the invention of a unique technology known as a "placentometer" that monitors substances that pass through the mouse placenta from mother to fetus. This technology can incorporate genetic models of human

disease, and could lead to targeted therapies that treat the mother without affecting the fetus, or vice versa.

"The findings by Dr. Bonnin and his collaborators open the door for future studies examining the potential role for targeted interventions in high-risk pregnancies where a perturbed intrauterine environment might negatively impact fetal brain development," said Istvan Seri, professor of pediatrics, Keck School, and director, Center for Fetal and Neonatal Medicine at Children's Hospital Los Angeles. "However, it will take many more basic, translational and clinical trials and many years until we can provide evidence that approaches like this one work."

Serotonin, a neurotransmitter known to affect wellbeing in humans, also has been implicated in brain, cardiac and pancreas development.

In the early stages of development, neurons that synthesize serotonin develop in the fetal hindbrain, where heart, respiration and other critical functions reside, eventually building their way up to the forebrain, the home of higher cognition and emotional regulation. The study shows that during this gap between hindbrain and forebrain serotonin development, the placenta is an important source of serotonin to the forebrain – a process that could be affected by the mother's nutrition, since her diet is the only source for the essential amino acid tryptophan.

"An altered capacity of the placenta to make and release serotonin could affect the levels of serotonin in the human forebrain as it does in the mouse," said Levitt. "Developmental programming of the fetal brain can set the stage for adult-onset health impacts including heart disease, diabetes and mental illness."

The research relates to a growing body of evidence that subtle, deleterious effects on the fetus as it develops could lead to a lifetime of chronic mental health problems, including anxiety disorders, learning

and emotional disabilities and depression.

"Bonnin's research may be of particular importance for early onset brain disorders, such as autism, Asperger's syndrome and pediatric obsessive-compulsive disorder, where investigators are considering a role for serotonin based on human genetic studies," said Randy Blakely, Ph.D., director of the Vanderbilt Conte Center and a collaborator on the paper.

More information: Alexandre Bonnin, Nick Goeden, Kevin Chen, Melissa L. Wilson, Jennifer King, Jean C. Shih, Randy D. Blakely, Evan S. Deneris, Pat Levitt. "A transient placental source of serotonin for the fetal forebrain." *Nature*, April 2011.

Provided by University of Southern California