

The amazing role of the placenta on fetal brain development Alexander Kofinas, M.D.

The placenta has been the most neglected human reproduction organ for ages. There exists a strange relationship between obstetricians and the placenta. Obstetricians have always been blaming the placenta for most of the pregnancy related complications. They are right, unfortunately. The problem is, however, that they have never made a serious effort to study the placenta and find ways to help its proper development; such treatment of the placenta could prevent most if not all of the complications for which the placenta is considered responsible. Thankfully, there are a lot of scientists from other disciplines that have produced a large volume of laboratory data regarding placental physiology, albeit not enough to resolve the important issues that cause placental failure and fetal adverse outcomes.

It was with great pleasure that I read the article published recently by Dr. Alexandre Bonnin in the basic sciences journal Nature. Dr. Bonnin works at the department of Cell and Neurobiology, Keck School of Medicine of USC, Los Angeles. Dr. Bonnin presented important evidence in experimental mice regarding the production of Serotonin by the fetal placenta. Serotonin is a neurotransmitter; it stimulates the brain neurons that create euphoria. Reduced serotonin levels in the brain are associated with depression and other psychiatric mood disorders. Until recently, we thought that in the early stages of pregnancy and before the fetal brain starts its own production, fetal serotonin is transported across the placenta from the mother. Dr. Bonnin with a well-designed study has proven otherwise. It is the placenta that produces the serotonin that the fetal brain needs in order to develop normally in the early formative months of pregnancy.

In the developed adult brain, serotonin is secreted by various neurons into the synapse (the space that connects one neuron to the next); as serotonin travels across the synaptic space, it transmits the electrical signal from the previous neuron to the next. Reduced amounts of serotonin lead to mood disorders and depression. In persons who use various stimulants, such as cocaine, the neurons are stimulated to produce more serotonin, which is responsible for the euphoria (high) drug addicts feel. In fetal life, and before the anatomical and functional formation of the brain neurons, serotonin has a much more important role to play. According to Dr. Bonnin's study, serotonin produced by the placenta is responsible for the development of the neurons in the brain. Bonnin and colleagues particularly focused their investigation on the developmental stage of the brain between gestational age 13.5 and 15.5 days. In mice, the gestation lasts 21-23 days under normal conditions. This gestational age in humans corresponds to approximately 25-27 weeks gestation; the later part of the second trimester. Although they did not directly study the effect of serotonin on brain development, there is evidence from other studies that serotonin influences the number of cerebral-cortical neurons, their location and how they connect to other parts of the brain. What it all means, is that the placenta provides signals to the brain; these signals regulate early development of the fetal brain cortex. And it does that by local production of serotonin by the superficial trophoblastic cellular layer that covers the chorionic villi. This is known as syncytiotrophoblast.

The elucidation of this placental miracle was a detective's work. Dr. Bonnin and colleagues removed placentas from the uterus and kept them in a special culture chamber by supplying

them with oxygen and nutrients. They connected the fetal umbilical vessels as well as the maternal uterine artery with tiny catheters. They infused tryptophan – the amino acid that is the basis for serotonin production - in the uterine placental artery and measured the presence of serotonin in the fetal circulation exiting the placenta. They found that within 15 minutes after tryptophan infusion, serotonin levels in the umbilical vein increased significantly. This is clear and indisputable evidence that the placenta produces serotonin.

At Kofinas Perinatal, we have always believed that a healthy placenta is the most important contribution for the creation of a healthy pregnancy and a normal neonate. ***We have always struggled to make sure that we preserve placental function to its maximum possible.*** This is the only way we can be certain that the baby will be protected and receive all the necessary nutrients to grow according to its genetic potential. With Dr. Bonnin's discovery however, we now know that the placenta is not only a passive supplier of nutrients for the fetal brain but a brain architect too; by the regulation of fetal serotonin levels at specific gestational ages, the placenta designs the structural development and functional inter-neuronal connections that possibly determine the personality and emotional state of the unborn and future adult. Such knowledge gives tremendous gratification for our relentless efforts over the years to educate obstetricians and patients alike about the importance of a healthy placenta and the pursuit of innovative ways to treat placentas and prevent the dreadful consequences of placental insufficiency.