



Lídia Cantacorps Centellas

DIfE Potsdam

My name is Lídia Cantacorps Centellas and I am a postdoctoral researcher at the Neurocircuit Development and Function research group led by Dr. Rachel Lippert at the German Institute of Human Nutrition Potsdam-Rehbrücke (Germany). My current project is focused on studying the impact of lactational metformin exposure on offspring's growth and hypothalamic neuronal development in mice. Metformin is one of the glucose-lowering pharmacological agents approved for gestational diabetes, along with insulin. Even though it's known that metformin is capable to cross the placenta and, consequently, reach the foetus, its potential effects on baby's brain development are still unknown. Clinical studies have shown a trend to increased obesity-related parameters in 9-year-old children born to metformin-treated mothers during pregnancy; however, animal studies focusing on its effects on the brain development are still lacking. The correct foetal brain development is critical to keep a healthy body state. Alterations in the hypothalamic connectivity have been related to an increased likelihood to develop metabolic disorders later in life. Metformin promotes AMPK signalling, and overactivation of AMPK during development may have an impact on axonal growth, affecting the neuronal projection formation in the hypothalamus, which occurs during the perinatal period. Thus, our aim is to study the effects of metformin treatment during the lactation on intra-hypothalamic neuronal connectivity formation in mice. To do so, we established a mouse model of excessive gestational weight gain by exposing the lactating female mice to a high-fat diet (HFD) and a model of maternal obesity, by exposing the female mice to HFD before pregnancy and during both pregnancy and lactation periods in order to induce an insulin-resistant phenotype. The control group of mothers had access to an experimental control diet throughout the procedure. Metformin treatment was given during the lactation phase, as would be seen in the human scenario. Then, offspring mice were transcardially perfused at postnatal day 16 and brains were collected. Agouti-related peptide (AgRP) and proopiomelanocortin (POMC) neuronal projections at the paraventricular nucleus of the hypothalamus (PVH) were assessed by immunofluorescence staining and analysed by confocal microscopy. Our results show a differential response to antidiabetic treatment on offspring's development

WINNER PORTRAIT

dependent on the maternal metabolic status, as shown by distinct effects on offspring's metabolism and hypothalamic neuronal development. Furthermore, metformin treatment does not seem to be able to rescue the innervation impairments in the PVH induced by lactational HFD intake in male offspring, showing a potential sexual dimorphic effect.