Impact of Gestational Inhalation of Nanoparticles on Glucose Transporters in Rat Placenta

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Particulate matter exposure can induce adverse health effects during pregnancy including fetal growth restriction. Glucose, a primary nutrient required for fetal growth, is transferred from maternal blood to the fetus via the placenta. Placental glucose transport relies on three glucose transporters (GLUT): GLUT1, GLUT3, and GLUT4. GLUT1 is the primary glucose transporter. We hypothesize that glucose transport in the placenta will be compromised following maternal inhalation of titanium dioxide nanoparticles (nano-TiO2) during pregnancy, impacting fetal glucose access and growth. Dams were exposed to nano-TiO2 as a surrogate for particulate matter in a whole-body inhalation chamber from gestational day (GD) 4 to GD19 and compared to naïve controls. Dams were fasted 16 hours before sacrifice on GD20. Placental tissue was isolated and sex of the corresponding fetus was determined. GLUT expression and localization were evaluated using qRT-PCR, immunohistochemistry (IHC), and immunofluorescence confocal microscopy. There was a significant decrease in GLUT3 mRNA expression of exposed placentas compared to control. IHC identified a significant decrease in GLUT1 protein (p=0.035) and significant increase in GLUT4 protein (p=0.001) of exposed placentas, with females driving this observation. Conversely, membrane localization of GLUT1 increased (p=0.056) while there was no difference for GLUT3 and GLUT4. Gestational nanoparticle inhalation decreases GLUT1 protein expression, but increases membrane localization. Interestingly, there is an upregulation of GLUT4, which may act as a compensatory mechanism to maintain fetal glucose. Overall, these studies demonstrate perturbations to placental glucose transport after maternal nano-TiO2 inhalation. Supported by NIH R25ES020721 and the American Society for Pharmacology and Experimental Therapeutics.