Effects of 2G on gene expression of stress-related hormones in rat placenta

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Understanding the effects of spaceflight on mammalian reproductive and developmental physiology is important to future human space exploration and permanent settlement beyond Earth orbit. Fetal developmental programming, including modulation of the HPA axis, is thought to originate at the placental-uterine interface, where both transfer of maternal hormones to the fetus and synthesis of endogenous hormones occurs. In healthy rats, fetal corticosterone levels are kept significantly lower by 11βHSD-2, which inactivates corticosterone by conversion into cortisone. Placental tissues express endogenous HPA axis-associated hormones including corticotropin-releasing hormone (CRH), pre-opiomelanocortin (POMC), and vasopressin, which may contribute to fetal programming alongside maternal hormones. DNA methylase 3A, 11βHSD-2, and 11βHSD-1, which are involved in the regulation of maternal cortisol transfer and modulation of the HPA axis, are also expressed in placental tissues along with glucocorticoid receptor and may be affected by differential gravity exposure during pregnancy. Fetuses may respond differently to maternal glucocorticoid exposure during gestation through sexually dimorphic expression of corticosterone-modulating hormones. To elucidate effects of altered gravity on placental gene expression, here we present a ground-based analogue study involving continuous centrifugation to produce 2g hypergravity. We hypothesized that exposure to 2g would induce a decrease in 11βHSD-2 expression through the downregulation of DNA methylase 3a and GC receptor, along with concurrent upregulation in endogenous CRH, POMC, and vasopressin expression. Timed pregnant female rats were exposed to 2G from Gestational day 6 to Gestational day 20, and comparisons made with Stationary Control (SC) and Vivarium Control (VC) dams at 1G. Dams were euthanized and placentas harvested on G20. We homogenized placental tissues, extracted and purified RNA, synthesized cDNA, and quantified the expression levels of the genes of interest relative to the GAPDH housekeeping gene, using RT-qPCR and gene-specific cDNA probes. Elucidation of glucocorticoid transfer and synthesis in the placenta can provide new insights into the unique dynamics of mammalian development in microgravity and guide future multi-generational studies in space.