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| Paper | Model | Exposure | Results |
| Placental Glucose Transporter Expression Is Regulated by Glucocorticoids <https://academic.oup.com/jcem/article/84/4/1445/2864464>  T.Hahn 1999 | Human placental extracts from term pregnancy treated with triamcinolone (TA)  E21 Rat placentas from rats injected with 0.38mg/kg TA once at E16  Mouse E17 placentas from GR transgenic mice using antisense RNA – this antisense is in the mother, but in placenta GR protein expression was reduced by 28% | TA in human cells and rats  GR KO model using antisense RNA in mice | Human TB cells had GLUT1 on MVM, GLUT3 on endothelial cells  GLUT1 mRNA and protein was reduced after TA  GLUT3 mRNA unaffected, but protein decreased  In rat and mouse, GLUT1 and GLUT3 localized in STB, CTB and endothelial cells(weakest in CTB)  In rats, fetal and placental wts were reduced by 73% and 53%, respectively at E21.  Implantation number unaffected  GLUT1 and GLUT3 mRNA and protein was reduced after TA  Placental wt of transgenic mice reduced by 28%, offspring of transgenic mice were 20% lighter  GLUT1 mRNA and protein was reduced  GLUT3 mRNA and protein increased  This suggests that GC may act via the GR to regulate GLUT expression in the placenta (since GC downregulates GR in placentas and other tissues) |
| Corticosterone alters materno-fetal glucose partitioning and insulin signaling in pregnant mice  Vaughan OR , 2015  <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4358686/> | 2 Mice cohorts given corticosterone in drinking water at two intervals:  1. E11-E16  2. E14-E19  The cort was designed to produce plasma cort levels that are high and similar to concentrations reported in heat/light stressed dams  Unidirectional materno-fetal clearance of non-metabolizable glucose was assessed | FIRST STUDY (ACCORDING TO THEM) TO DETERMINE *IN VIVO* GLUCOSE TRANSPORT IN CORT TREATED MICE IS REDUCED at E19  CORT in water given to mice | *Cool findings: Fetal glucose needs increase with pregnancy, maternal glucose passes to fetus through diffusion along concentration gradient*  *Transplacental glucose transport is not insulin-dependent since placental TBs do not express GLUT4 (Hay, 2006) Some have seen increased glucose placental transport in diabetic pregnant women so this is still not 100% confirmed. Localization of GLUT4 in human placentas remains unclear (from Hay 2006)*  Dams treated with cort where hyperinsulinemic but normoglycemic  On D19, transplacental 3Hmethyl-D-glucose clearance decreased by 33%, but this was normalized when mice were pair-fed (given food as much as controls eat to reduce increased food intake upon cort tx)  Cort reduced fetal weight by 8% and 19% at D16 and D19, respectively  Placental weight was reduced at both points  Number of viable pups was unaffected  At D19, materno-fetal clearance and fetal accumulation of glucose tracer was lower than controls at E19. No difference in clearance or accumulation at D16  Placental *Slc2a1&3* (GLUT 1 and 3) mRNA expression increased at E16, no change in expression on E19 🡪 THUS THE DECREASE IN TRASNPORT AT E19 WAS UNRELATED TO TRASNPORTER EXPRESSION CHANGE , SAME WITH E16 WHERE TRASNPORT WAS UNCHANGED BUT TRANSPORTER EXPRESSION DECREASED. HENCE OTHER TRASNPORTERS MAY BE INVOVLED  *Redd1* expression increased on D19 but not D16 with cort and was in sync with the reduced transplacental glucose transport at D19  No change in placental *Igf2* expression  On D16, pAkt was reduced 🡪 less active Akt |
| Maternal corticosterone regulates nutrient allocation to fetal growth in mice  Vaughan OR , 2012  <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3515836/> | 2 Mice cohorts given corticosterone in drinking water at two intervals:  1. E11-E16  2. E14-E19 | Corticosterone given in water | *Cool fndings: System A is for neutral amino acid transport which occurs via sodium-dependent active transport into the placenta then from the placenta they follow concentration gradient*  Fetal weight reduced in both  At D16, no effect on materno-fetal transfer of labeled amino acid  Fetal and placental weight reduced by 7% on D16  On D19, fetus weight decreased by 16% and placental weight was 11% smaller  Fetal weight negatively correlated with maternal corticosteroid levels at E19 but not E16  Number of viable pups per litter was unchanged with maternal cort tx  Fetal accumulation of MeAIB was not changed at E16, but placental accumulation was 35% more (expression of placental transporters was up as well, mentioned below)  At E19, placental and fetal MeAIB accumulation was reduced by 40-50%, after tx from E14-E19 (although placental transporter snat1 increased and others did not change)  Oppositely at E19, from dams treated E11-E16 (3 days post tx), fetal accumulation and clearance were 38% higher but placental accumulation was unchanged 🡪 longer term effects of GC tx after cessation of tx  At E16, *Slc38a1 and 2* expression in placenta was increased, *Slc38a4* was unchanged  At E19, *Slc38a1*expression increased, but no change in *Slc38a2 or 4*  Placentas weighed less at E16 but volume of zones did not differ. No difference in zone at E19  Reduced vascularity shown by less fetal capillaries in the labyrinthine zone by 55% at E16 |
| Dexamethasone stimulates placental system A transport and trophoblast differentiation in term villous explants. Placenta. 2010;31(2):97–105.  Audette MC, 2010  <https://www.ncbi.nlm.nih.gov/pubmed/20045184> | Human placental explants from term-pregnancies in healthy women | Term placentas collected from healthy women  Placental explants incubated with radiolabeled 14C-MeAIB for different periods  Dex added at 10^-6 M | *Cool findings: Sodium-dependent system A transporters located on both MVM and BM and transports small neutral amino acids and the non-metabolized synthetic analogue, N-methylated aminoisobutyric acid (MeAIB), which is used to assess System A activity.*  *System A contains SNAT1,2 and 4 only encoded by Slc38a1,2 and 4.*  Dex treatment increased placental uptake of MeAIB at 10-6M but not at 10-8M 🡪 stimulated system A activity at 10-6M with 30% increase of MeAIB uptake 🡪 they hypothesize that this increase in system A activity after 48h incubation may be due to acute upregulation/compensation which does not reflect permanent placental changes in transport rate  No change in mRNA expression of SNAT1,2 or 4 with Dex tx. increased hCG secretion suggesting increased regeneration of cells  No effect on placental apoptosis |
| Cortisol stimulates system A amino acid transport and SNAT2 expression in a human placental cell line (BeWo) American The Journal of Physiology. 2006;291(3):E596–E603.  Jones HN,2006  <https://www.ncbi.nlm.nih.gov/pubmed/16621896> | BeWo choriocarcinoma cell line used with 14CMeAIB infusion to assess transport of system A aa  Mannitol was included to assess passive component of MeAIB transepithelial transport (they then calculated ration of mannitol to MeAIB) | Cortisol was added to incubated cells at concentrations 5nM-2.5uM for up to 24 hours | *Cool findings: system A insufficiency is implicated in development of IUGR*  *System A transports small non-branched AA like alanine and glycine*  *SNAT4 is not expressed in BeWo cells!*  Cortisol did not affect passive transport of mannitol 🡪 passive permeability of membranes is unchanged  **Replacing sodium cations with Lithium cation inhibited 60% of the MeAIB transfer indicating that 60% of placental amino acid transfer is sodium-dependent thus 🡪 majority of placental transport depends on system A**  BeWo cells incubated with 1000nM cortisol had higher MeAIB transfer from apical to basolateral chambers over 20 minutes  SNAT1 mRNA was unchanged with cortisol tx at multiple concentrations  SNAT2 mRNA levels increased by 21% at 24h incubation of 1uM cortisol. Cort exposure of 2.5uM for 24 hours increase SNAT2 mRNA expression by 30%  Protein expression of SNAT1 was not assessed  Protein expression of SNAT2 by florescence staining showed increased expression with 1uM of cortisol for 24 hours |
| Antenatal dexamethasone treatment in midgestation reduces system A-mediated transport in the late-gestation murine placenta. Endocrinology. 2011;152(9):3561–3570  Audette MC , 2011  <https://www.ncbi.nlm.nih.gov/pubmed/21733830> | Pregnant mice treated with dex injected at E13.5 and E14.5 (midgestation exposure)  14C Mannitol was used as a negative control to ensure specificity of system  A transfer) | Dex 0.1mg/kg injection given to mice at E13.5 and E14.5  Transfer studies done at E12.5, E15.5 (24hr after tx) , E17.5 (72h after tx) and E18.5 (96h after tx)  Subset of dams were allowed to deliver their pups  First study to assess effects of antenatal GC on placental system A transport in vivo | In saline injected controls, placental and fetal weights increased from E12.5 to E15.5 to E18.5. Placental 14CMeAIB transfer also increased which was consistent with increases in system A gene expression of SNAT1, 2 and 4 as pregnancy progressed.  Mannitol transfer also increased from E15.5 to E18.5 in control and dex placentas as pregnancy progressed (makes sense)  Effects of Dex: Treatment from E13.5 and E14.5 did not alter 14CMeAIB transfer at E15.5 or E17.5, but **transfer was reduced at E18.5 in male and female placentas** (long-term after treatment cessation).  14C Mannitol transfer did not differ between control vs Dex male and female placentas on E15.5 and E18.5 🡪 passive diffusion was unaltered (they used mannitol to determine specificity of system A transport, negative control)  SNAT1,2 and 4 mRNA expression was unchanged with Dex tx in male and female placentas  Fetal weights at E15.5, E18.5 or at birth was unchanged.  No change on placental weight at E15.5, E17.5 and E18.5 in males. In females there was no change at E15.5 or E17.5, but placental weight was reduced at E18.5. 🡪 the reduced female placental weight at E18.5 increased the fetal:placental ratio at E18.5  No change in placental labyrinth or junctional zone proportions w.r.t. total placental area  No difference in maternal or ftal plasma corticosterone concentrations at E18.5 (mais c’est normal parce que it’s ages after the exposure, non? Oui oui) |
| Sex specific changes in placental growth and MAPK following short term maternal dexamethasone exposure in the mouse. Cuffe JS , 2011  <https://www.ncbi.nlm.nih.gov/pubmed/21974799> | Pregnant mice treated with Dex 1ug/kg/h for 60 hours (2.5 days) via a minipump at E12.5  Placentas collected at E14.5 (2 days- 48 hours) and at E17.5 (after 5 days of initial exposure, after 2.5 days from end of exposure) | Dex via minipump for 60 hours starting at E12.5 (so till E15) | Reduced fetal body weight at E14.5 in males and females, but not at E17.5.  Reduced female placental weight at E14.5 but not E17.5. Male placental weight was unchanged in both days.  HSD11B2 mRNA expression increased in females at E14.5, protein expression increased in females at E17.5. No change in mRNA or protein at other times and no change at all with male placentas. (not that I care about HSD11B2 since dex is not inactivated by it anyways)  *Igf2* expression not affected by Dex at either age.  MAPK  GLUT1, GLUT3, SNAT 1, SNAT2 and SNAT4 gene expression was unaltered after Dex at E14.5 and E17.5  No differences in placental areas or gross morphology  Female junctional zone cross sectional area was smaller at E14.5 (they used *in situ* hybridization to localize spongiotrophoblast marker, spongioTBs are expressed in junctional zone only) and whole placental cross sectional area was smaller |
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| Synthetic Glucocorticoid Reduces Human Placental System A Transport in Women Treated With Antenatal TherapyAudette MC <https://academic.oup.com/jcem/article/99/11/E2226/2836194> |  |  |  |
| <https://www.hindawi.com/journals/bmri/2018/5106174/>  Excess Hydrocortisone Hampers Placental Nutrient Uptake Disrupting Cellular Metabolism  Maria Mateos R 2018 |  |  |  |
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| Regulation of Nutrient Transport across the Placenta LAGER S AND POWELL TL 2012  <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3523549/>  REVIEW ON PLACENTAL TRASNPORT INFLUENCED BY MULTIPLE FACTORS/CONDITIONS |  |  |  |
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