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| Paper | Methods/Exposure | Results |
| (Hahn *et al.*, 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% | Human TB cells had GLUT1 on MVM, GLUT3 on endothelial cells  GLUT1 mRNA and protein 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 weights reduced by 73% and 53%, respectively at E21.  Implantation number unaffected  GLUT1 and GLUT3 mRNA and protein 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 |
| (Vaughan *et al.*, 2015) | 2 Mice cohorts given corticosterone in drinking water at two intervals:  1. E11-E16  2. E14-E19  The dose 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 | On D19, transplacental 3Hmethyl-D-glucose clearance decreased by 33%  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  *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 |
| (Vaughan *et al.*, 2012) | 2 Mice cohorts given corticosterone in drinking water at two intervals:  1. E11-E16  2. E14-E19 | 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  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 |
| (Audette *et al.*, 2010) | Human placental explants from term-pregnancies in healthy women  Placental explants incubated with radiolabeled 14C-MeAIB for different periods  Dex added at 10-6 M | 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  No change in mRNA expression of SNAT1,2 or 4 with Dex.  No effect on placental apoptosis |
| (Jones *et al.*, 2006) | BeWo choriocarcinoma cell line used with 14CMeAIB infusion to assess transport of system A aa  Cortisol was added to incubated cells at concentrations 5nM-2.5uM for up to 24 hours | BeWo cells incubated with 1000nM cortisol had higher MeAIB transfer from apical to basolateral chambers over 20 minutes  SNAT1 mRNA was unchanged with cortisol 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 showed increased expression with 1uM of cortisol for 24 hours by 11% |
| (Audette *et al.*, 2011) | Pregnant mice treated with 0.1mg/kg dex injected at E13.5 and E14.5 (midgestation exposure)  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 | 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.  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).  SNAT1,2 and 4 mRNA expression was unchanged with Dex in male and female placentas at E15.5, 17.5 and 18.5 (despite reduced transfer at E18.5)  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 fetal plasma corticosterone concentrations at E18.5 |
| (Cuffe *et al.*, 2011) | Pregnant mice treated with Dex 1ug/kg/h minipump for 60 hours (2.5 days) via a minipump starting 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) | 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.  *Igf2* expression not affected by Dex at either age.  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.  Whole placental cross sectional area was smaller. |
| (Audette *et al.*, 2014) | Used placental extracts from pregnancies treated with GC who delivered at various times during gestation.  Women recruited if they received 2 doses of celestone (betamethasone 12 mg intramuscular ~12 hours apart) at 23.6 and 33.9 weeks of gestation  Groups:  1. mom who delivered preterm 24h-14 days after tx  2. who delivered 14d-after treatment but still delivered before term  3.who received GC but delivered at term | Fetuses born 24hours-14 days after the GC treatment (preterm delivery) had reduced birth weight compared to fetuses born 14days post treatment until term (term pregnancies).  No difference between birth weight of GC treated fetuses at term and term controls (not treated with GC)  Placentas of fetuses delivered between 24h-14d after the tx had significantly lower weights compared to placentas from 14d-term deliveries with GC.  Uptake of 14CMeAIB by placental explants from GC treated moms who delivered 14d-term or at term after the treatment had reduced system A activity compared to placentas from preterm delivery.  Placentas from preterm delivery (24h-14d post GC) had no change in MeAIB uptake compared to control term placentas  Placentas of GC treated moms who delivered at term had significantly reduced system A transport compared to control term placentas.  Expression of placental AA transporters:  No effect of SNAT 1 or SNAT2  SNAT4 gene expression was reduced in placentas of GC treated moms at term compared to GC treated placentas of fetuses born 14d-term after GC treatment |
| (Mateos *et al.*, 2018) | Placentas obtained from healthy women who delivered at term. Placental explants cultured with or without GC hydrocortisone 1mg/ml (2.75 mM) | Placentas incubated with 1mg/ml hydrocortisone had unchanged 3H-2DOG uptake, but higher concentrations of 2mg/ml and 20mg/ml showed reduced DOG uptake by 30-40%  Expression of GLUT1 was not changed with all concentrations  GLUT3 mRNA expression was increased with 2mg/ml incubation only  GLUT1 protein expression was increased at 1mg/ml, 2mg/ml and 20mg/ml of hydrocortisone  Fatty acid oxidation was reduced by 25%, 50% and 75% in explants treated with 1, 2 and 20 mg/ml, respectively  Fatty acid esterification (to make TG or to undergo oxidation) was also reduced at all concentrations, consistent with the fact that there was less oxidation.  Lipoprotein lipase activity was reduced significantly by 40% and 80% at 2 and 20 mg/ml doses, respectively (LPL is needed to allow uptake of fatty acids that will then become esterified and undergo oxidation or become TG)  Mitochondrial activity in placental explants was significantly reduced at 20mg/ml only, but TUNEL analysis showed no differences in apoptosis  Hence, glucose and lipid uptake were reduced in placentas despite available nutrients |
| (Baisden *et al.*, 2007) | Pregnant mice injected with 0.5mg/kg intraperitoneal dexamethasone on E15, E16 and E17 to mimic multiple course of antenatal GC treatment | At E20, dex placentas were pale and weighed less.  Dex treatment was not associated with fetal death.  Trophoblasts in labyrinth and junctional zones were swollen with loss of TB in junctional zone (marked by empty space in H&E stain)  Downregulation of 1212 genes and up-regulation of 1382 genes 🡪 decreased expression of genes involved in cell division with mixed responses on genes regulating glucose, cholesterol and steroid metabolism  No difference in gene expression of *Igf1 or 2* |
| (Braun *et al.*, 2013) | Mothers who received a single course of betamethasone treatment during pregnancy  Single course is 2 x 12 mg betamethasone in 2 consecutive days given intramuscularly  Collected maternal plasma at 4 timepoints:  1.prior to first GC administration  2. 24 hours after first GC administration and right before the second dose of 12mg betamethasone  3. 48 hours after the first GC tx (24h after second dose)  4. Finally, one sample collected during delivery at 4-5cm cervical dilation | Single Betamethasone treatment was associated with reduced fetal growth and reduced head circumference.  Birth weight was reduced by 18.2% after betamethasone.  Placental width was reduced by 5.5% with insignificant but reduced surface area by 14.7%  Birth weight was positively associated with placental surface area.  Betamethasone increased STB cell circumference and cell surface. |
| (Langdown & Sugden, 2001) | Pregnant rats given dexamethasone by subcutaneous infusion at E15 via a pump at a dose of 100 or 200 ug/kg body wt/day  Sac at E21 | Reduced fetal and placental weights that was dose-dependent, the 200 dex dose had a larger impact on weight reduction  No effect of dex on gestation length or offspring number or viability  Maternal blood showed higher but insignificant blood glucose when dex treated at 200 dose.  Fetal hypoglycemia was evident and showed 36% and 49% reduction in fetal plasma glucose at 100 and 200 ug dex, respectively.  Increase in placental GLUT1 protein expression by 1.6 and 1.9 fold at 100 and 200 ug/kg/day dex doses, respectively.  Increased GLUT3 protein expression by 2.3 fold only with the 200 ug dex dose. |
| (Dupouy *et al.*, 1987) | Dex treated rats at E15 till E21 with dexamethasone acetate in drinking water at 10ug/ml dose | 21 day old rats offspring from stressed dams showed reduced headless body weight (- 66%)  Lower offspring hypothalamic Corticotropin releasing factor content and concentration from 21-day old rats of stressed dams (-57 and -67%, respectively )  Lower pituitary ACTH content (-93 %) and lower plasma ACTH levels.  Lower adrenal corticosterone concentrations (-74%) and lower plasma corticosterone levels.  Severe atrophy of adrenals with reduced absolute adrenal weight (- 83%) and reduced relative adrenal to body weight |
| (Ain *et al.*, 2005) | Rats injected subcutaneously with 100ug dexamethasone acetate in 0.1% ethanol at E13.  Pump was then implanted to release 200ug dex acetate/kg body wt/day  Sac on E20 | Dex did not affect litter size or fetal viability.  Significant reduction of fetal and placental weights.  Decrease of junctional zone. *Igf2* mRNA expression but no effect on it in labyrinth zone 🡪 can be a contributor to placental growth restriction  Decrease protein expression of phosphorylated/active Akt, but no effect on total Akt 🡪 attenuated Akt signaling |
| (Ali Khan *et al.*, 2011) | Review: Compiled studies from humans that used betamethasone during pregnancy. | 10 out of 17 studies reported significant reduction in birthweight of infants exposed to antenatal GC, while other 7 studies reported no relation 🡪 studies methods varied largely!  All studies used betamethasone.  5 out of 9 studies reported reduced head circumference  Birth length and ponderal index: 2 out of 5 studies reported reductions in these  Overall 🡪 synthetic GCs contribute to reduced birth size but there is a lot unknown and studies conflict in their used methods, results and measured variables. |
| (Lesage *et al.*, 2004) | Rats exposed to stress by being in a plastic cylinder in a lighted environment 3x/day for 45 minutes each during last week of gestation.  Sac at E20 | Fetuses of stressed dams had reduced body weights in males and females 🡪 IUGR  Fetal plasma glucose and corticosterone levels were reduced but leptin was unchanged.  Effect of antenatal stress on offspring:  24-month old male rats had unchanged weights after antenatal exposure of stress  Basal plasma corticosterone levels were higher but not significant  Plasma leptin was reduced  OGTT showed higher plasma glucose levels in antenatally stressed rats at all timepoints (0, 60 and 120 minutes tested), but insulin secretion was similar. |