

MRI	N	Unadjusted		Adjusted	
		b*	p	b*	p
MRI Lactate	175	0.001	0.94	0.006	0.52
MRI Lactate >0	52	0.010	0.11	0.021	0.02
MRI Lactate: NAA ratio	52	0.005	0.11	0.008	0.05

*b represents the change in MRI lactate level per unit change in arterial blood gas lactate.

50 Vitamin C supplementation mitigates the deleterious effects of chronic nicotine exposure on placental histology in a nonhuman primate model

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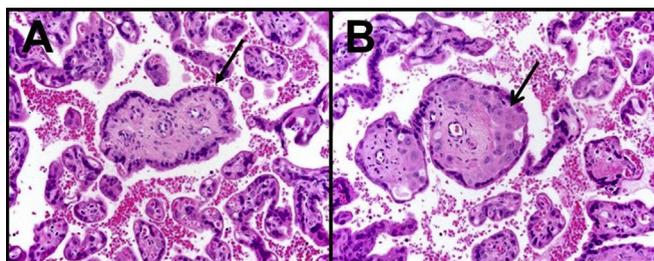
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OBJECTIVE: We previously demonstrated that prenatal nicotine (NIC) exposure decreases pulmonary function in macaques and maternal vitamin C (VC) supplementation attenuates these detrimental effects. Smoking during pregnancy is associated with placental histopathological features of hypoxia. We hypothesized that VC supplementation would ameliorate the placental morphologic features associated with smoking.

STUDY DESIGN: Histopathologic analysis of 24 placental samples from timed-pregnant rhesus macaques in 4 treatment groups consisting of: control (n=5), VC only (n=7) NIC only (n=4), and NIC/VC (n=8). NIC animals received 2mg/kg/day of nicotine bitartrate (equivalent to 0.7mg/kg/day free NIC levels in pregnant human smokers) by SQ mini pumps from days 26 to 160 (term, 165 days). VC groups received ascorbic acid at 50, 100 or 250mg/kg/day +/- NIC. Cesarean section was performed at 160 days and placental tissue processed for histology. A single blinded placental pathologist scored the placentas for villous cytotrophoblast (CTB) proliferation and syncytiotrophoblast (STB) maturation with increased sprouting. Chi-square was used for statistical analysis.

RESULTS: Villous CTB proliferation (Fig 1) was observed in 2/5 (40%) control cases and significantly more in NIC only animals 4/4 (100%) compared with the NIC/VC group 1/7 (14%), (p<0.05). STB sprouting was observed in all NIC only animals (4/4) but absent in control (0/5) and NIC/VC (0/8) animals, (p<0.001). There was no significant difference between VC dosing groups.

CONCLUSION: Prenatal NIC exposure in macaques results in CTB proliferation and STB sprouting, histologic markers of hypoxia seen in placentas of human smokers. These placental changes were ameliorated by VC. Significantly, VC at 50mg/kg/day demonstrated beneficial effects suggesting that effective intervention can be achieved with low dose supplementation to limit the deleterious effects of maternal smoking during pregnancy on placental hypoxic changes.



1A. Normal villous with normal stroma and small cytotrophoblasts rimming the villi (closed arrow) 1B. Abnormal villous with cytotrophoblasts proliferating into villous stroma (open arrow).

51 Programmed adipogenesis and obesity in offspring of obese dams

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OBJECTIVE: Maternal obesity during pregnancy is associated with offspring obesity. Monounsaturated C16 and C18 fatty acids are preferred substrates for triglyceride synthesis and fat deposition. Accordingly, an increased monounsaturated/saturated fatty acid ratio (Desaturation Index; DI) is associated with adipogenesis and obesity. We hypothesized that a maternal high fat diet programs fetal fatty acid metabolism so as to promote offspring obesity. To assess the role of maternal dietary fatty acids in programmed adiposity, we analyzed plasma and liver DI in pregnant rats and their offspring.

STUDY DESIGN: Female rats were fed a high fat diet (60% kcal) to create obesity (OB), and Control (Con) dams fed a normal diet (10% kcal) prior to mating. All pups were nursed by their respective dams and weaned to a normal diet. Blood and liver samples were collected from dams at term, and male offspring at age 1 day and 6 months. Plasma and liver fatty acids were analyzed by GC-MS and the DI determined. Values are means ±SE.

RESULTS: OB dams were significantly heavier (430±17 vs 330±5g), though OB newborns had similar birth weight as Controls. Both OB dams and their newborns had decreased plasma C16 DI (Dam, 0.03±0.004 vs 0.06±0.003; Newborn, 0.03±0.01 vs 0.06±0.01) and liver C16 DI (Dam, 0.01±0.001 vs 0.17±0.02; Newborn, 0.01±0.002 vs 0.03±0.003) as compared to Controls. At age 6 months, OB adult males were significantly heavier (800±27 vs 659±18g) with greater adiposity (26±3 vs 20±2%), triglyceride levels (126±15 vs 85±8mg/dl), and increased plasma (0.1±0.01 vs 0.06±0.01) and liver (0.09±0.01 vs 0.06±0.01) C16 DI, as compared to Control males.

CONCLUSION: A maternal high fat diet suppresses both maternal and newborn DI, indicating reduced endogenous lipogenesis. Maternal OB offspring exhibit increased DI despite a normal diet, indicating a programmed upregulated lipogenesis. Together, these findings suggest that maternal high fat diet-induced fetal programming alters hepatic fatty acid metabolism, contributing to adipogenesis and offspring obesity.