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Evidence for a reduction in renal oxidative stress following juvenile obesity in offspring born to sheep nutrient restricted during early kidney development

Hernan Fainberg[1], Amanj Saeed[1], Asrar Rashid[1], David Gardner[2], Helen Budge[1] and Michael Symonds[1]

[1]*Centre for Reproduction and Early Life, University of Nottingham, Nottingham, UK and* [2]*School of Veterinary Medicine and Science, University of Nottingham, Nottingham, UK*

Obesity is associated with an increase in reactive oxygen species (ROS) and the development of renal damage. It has previously been demonstrated that exposure to a period of maternal nutrient restriction (NR), between early gestation and -mid-gestation, prevents the occurrence of glomerulosclerosis that follows juvenile obesity(1). The aim of the present study was to elucidate whether this adaptation is accompanied by a reduction in renal ROS production.

Pregnant sheep (*n* 26) were randomly assigned to a normal (7 MJ/d) or nutrient-restricted diet (3.5 MJ/d; NR) from day 30 to day 80 of gestation (term 147 d) and fed to requirements at all other times. Nutrient-restricted (NR-O; *n* 11) and obese (O; *n* 7) offspring groups were reared in an environment of restricted activity and increased energy-dense food to promote fat deposition and, thus, obesity following weaning at 10 weeks postnatal age. The lean group (L; *n* 8) remained out to pasture. All sheep were humanely killed at 1 year of age and kidneys sampled for NO determination (Nitric Oxide Synthase Assay Kit, Colorimetric, Calbiochem, Nottingham, UK) superoxide dismutase (SOD) activity measurement (Superoxide Dismutase Assay Kit II, Calbiochem, Nottingham, UK) and immunoblotting for SOD1 and SOD2. All animal procedures had local Animal Ethics Committee approval and were performed in accordance with UK legislation.

SOD2 abundance showed an increase in O offspring compared with L animals (arbitrary units; O, 128 (SE 6.5); L, 105 (SE 6.5); $P<0.01$)), whereas the SOD1 abundance was similar. However, the SOD activity was higher in NR-O animals compared with O animals (U/ml; O, 0.03 (SE 0.004); NR-O, 0.06 (SE 0.009); $P<0.05$). In addition, NO oxidation was lower in the NR-O offspring compared with O offspring (NO_x (μM)/(protein μg/μl); O, 1.56 (SE 0.3); NR-O, 0.87 (SE 0.1); $P<0.05$).

Exposure to nutrient restriction over the period of early kidney development when followed by juvenile obesity is associated with an increase in renal SOD activity and reduction in NO concentrations. These adaptations may reduce the production of ROS and contribute to avoidance of the early renal damage induced by obesity. The factors that may protect offspring born to nutrient-restricted mothers from early onset of glomerulorsclerosis induced by obesity are currently being investigated.

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1. Williams PJ, Kurlak LO, Perkins AC, Budge H, Stephenson T & Keisler D (2007) Hypertension and impaired renal function accompany juvenile obesity: the effect of prenatal diet. *Kidney Int* **72**, 279–289.