

## **F2 fetal nephron number and weight benefits of endurance exercise training for females born small on high fat diet**

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Uteroplacental insufficiency is the major cause of intrauterine growth restriction in Western society and is associated with cardiorenal disease, which is exacerbated by “second hits” such as pregnancy and overweight/obesity. We reported that F2 fetuses have nephron deficits, which contribute to the development of F2 high blood pressure in males during adulthood (Gallo *et al.*, 2013). The aim of this study was to determine if F2 male nephron deficits of mothers born small are exacerbated by a high fat maternal diet and whether endurance exercise training can prevent these deficits.

This study was approved by the University of Melbourne Animal Ethics Committee. Uteroplacental insufficiency was induced by bilateral uterine artery ligation (Restricted) or sham (Control) surgery on E18 in F0 female Wistar-Kyoto rats with anesthesia induced by 4% Isoflurane and 650ml/min oxygen flow. F1 female offspring were fed a chow or high fat (43% kcals from fat) diet from 5 weeks to mating (20 weeks) and throughout pregnancy. Female rats were exercised on a treadmill 4 weeks before mating and throughout pregnancy. Post mortems were conducted at E20 and maternal dorsal fat, fetal kidneys and tails were collected (n = 9/10). Each post mortem was conducted in accordance with previous literature (Gallo *et al.*, 2013). The sex of each fetus was determined at E20 and was confirmed using qPCR analysis on fetal tails. Male fetal nephron number was quantified using unbiased stereology and maternal and fetal body weights were measured at E20, in addition to fetal kidney and placental weights. Data were initially analysed by a 3-way ANOVA and presented as mean ± SEM.

Restricted and Control female rats that were exposed to a high fat diet were significantly heavier with more dorsal fat than females on a chow diet. Exercise prevented dorsal fat gain in Restricted high fat diet compared to sedentary. F2 male nephron deficit was present in mothers born small regardless of diet (-18-42%). High fat diet reduced F2 male nephron number in Control mothers (-29%). Exercise prevented the high fat fed induced nephron deficits in F2 males of both Control and Restricted mothers (+22-50%). There was no treatment, diet or exercise effect in F2 male fetal body weight, placental weight and kidney weight.

In summary, we have demonstrated that females born small are at a greater risk of increased adiposity. F2 male fetal nephron deficits in mothers exposed to a high fat diet were prevented by the life style intervention of endurance exercise. These data suggest that exercise during pregnancy, in obese mothers born small, may prevent the development of F2 male high blood pressure.

Gallo LA, Tran M, Cullen-McEwen LA, Denton KM, Jefferies AJ, Moritz KM & Wlodek ME. (2013). Transgenerational programming of fetal nephron deficits and sex-specific adult hypertension in rats. *Reprod Fertil Dev* **26**, 1032-1043.