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Early-life undernutrition induces sex-specific effects on the sympatho-adrenal response to stress in sheep

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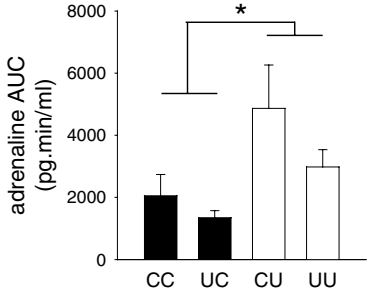
Altered adrenocortical and sympatho-adrenal activity may mediate the link between the early-life environment and cardiovascular and metabolic abnormalities in later life(1). Nutrition in early postnatal life has previously been demonstrated to have long-term effects on adult pituitary and adrenocortical responsiveness to stress(2). The aim of the present study was to determine the long-term effects of nutrient restriction in early pre- and postnatal life on adult sympatho-adrenal function in sheep.

Ewes received either 100% (C; *n* 39) or 50% nutritional requirements (U; *n* 41) from 1 d of gestation to 31 d of gestation and 100% thereafter. Male and female offspring were then fed either *ad libitum* (CC, *n* 22; UC, *n* 19) or to reduce body weight to 85% of target from 12 weeks to 25 weeks postnatal age (CU, *n* 17; UU, *n* 22) and *ad libitum* thereafter. At age 2.5 years catheters were inserted into the carotid artery and jugular vein under general anaesthesia. Basal arterial blood pressure was derived from the mean of recordings taken on three separate days under control conditions. Sympatho-adrenal responses to a stress test were assessed by transporting the sheep in their carts from their normal holding room to a different empty room followed by 30 min isolation (transport and isolation (TI) test). Plasma adrenaline and noradrenaline concentrations were measured before (-15 and -1 min) and during (10, 20 and 30 min) the test by radioimmunoassay (2 CAT RIA; Labor Diagnostika Nord, Nordhorn, Germany). Heart-rate responses to the TI test were measured by an implanted loop recorder (Reveal®; Medtronic Inc, Minneapolis, MN, USA). Data were analysed by ANOVA.

There were no significant differences between sex or group in basal heart rate or blood pressure. The adrenaline output (as given by area under curve (AUC)) during the TI test was significantly ($P<0.05$) enhanced in female sheep (Figure), but not male sheep that were exposed to postnatal undernutrition, regardless of the prenatal nutrient environment. There was no difference between sex or group in heart-rate response during the TI test.



The sex-specific effects of the postnatal nutrient environment on adrenomedullary output in response to stress follow a similar pattern to previous observations on pituitary–adrenocortical responsiveness in these animals(2). This finding suggests a generalised effect of postnatal undernutrition at the level of the adrenal. The absence of an accompanying increase in heart rate could reflect a down-regulation in cardiac β-adrenergic pathways or altered parasympathetic tone.

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1. Phillips DI, Jones A & Goulden PA (2006) *Ann N Y Acad Sci* **1083**, 28–36.
2. Poore KR, Cleal JK, Newman JP, Boullin J, Noakes D, Hanson MA & Green LR (2006) *Early Hum Dev* **82**, 537(F-15).