Title: EARLY CARDIOVASCULAR AUTONOMIC DYSFUNCTION IS ASSOCIATED WITH PROGRAMMED HYPERTENSION FOLLOWING GESTATIONAL GLUCOCORTICOID ADMINISTRATION

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ABSTRACT BODY:
High gestational levels of glucocorticoid (GC) are associated with a number of pathologies, including increased incidence of hypertension in later life, referred to as programmed hypertension (PH, 1,2). The cause of PH is not fully understood, but may involve changes in renal and vascular function. However, high gestational GC also causes long-term changes in gene expression in various brain regions associated with altered hypothalamic pituitary axis (1), suggestive thatother central nervous system changes may also occur. We hypothesize that high gestation CG causes altered autonomic cardiovascular function, which may play a causative role in hypertension (2). In this study, we exposed pregnant rats to high steroid and examined the offspring for changes in spontaneous baroreflex gain (sBRG), pulse interval variability (PIV) and systolic blood pressure variability using radiotelemetry. Values expressed are mean ± SE.

At E15-E16, pregnant Sprague Dawley dams were administered with the synthetic GC dexamethasone (DEX; 200 $\mu g.kg^{-1}$ s.c.). The offspring (3-5 weeks) were anesthetised with ketamine (60 $mg.kg^{-1}$) and medetomidine (250 $\mu g.kg^{-1}$) and implanted with a blood pressure (BP) radiotelemetry transmitter. After 1 week recovery, 24 hr pulsatile BP was recorded in the unanaesthetized, freely moving rat, and sBRG, PIV and BPV were calculated. At week 11 (after the onset of hypertension) baroreflex function curves were constructed using sodium nitroprusside and phenylephrine

At week 5 postnatal, BP was not different in the offspring of DEX treated-dams than saline controls (DEX, 120.0±1.9 v control, 120.7±1.5 mmHg, P=0.8), however sBRG (DEX, 0.36±0.02 v control, 0.59±0.07 $ms.mmHg^{-1}$, P<0.01), very low frequency (3.24±0.28 v 4.76±0.57 $ms^{2,}$ P<0.05) and low:high frequency (0.17±0.01 v 0.26±0.02, P<0.05) components of PIV were reduced. At week 11, BP was higher in DEX-treated offspring than controls (145.7±4.3 v 120.3±2.4 mmHg, P<0.01) and sBRG remained reduced (0.31±0.04 v 0.50±0.06, P<0.05), while very low frequency and low:high frequency PIV were not different.. In addition, the baroreflex function curve was shifted to a higher BP and the slope of the curve was reduced in the DEX-treated offspring.

Our results show that following prenatal administration of DEX in the rat, cardiovascular autonomic function is already disturbed at week 5 postnatal, before the onset of hypertension,. Alterations in cardiovascular autonomic function may contribute to PH in this model.

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2. Moritz KM (2005). *Cell Tissue Res* **322**: 81–88.

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