Programming Influences of Placental CRH on Fetal, Infant, and Child Development
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Background
A growing body of research suggests that the prenatal period represents a particularly sensitive developmental window during which intrauterine exposures play a key role in shaping or “programming” later offspring physiological and psychological functioning. The HPA and placental axis represents one of the major pathways by which gestational experiences may exert persisting influences.

We have proposed that prenatal exposure to placental CRH (pCRH) should be examined as a primary candidate for fetal programming. pCRH is of feto-placental origin and represents an indicator of fetal exposure and response to a variety of major stress signals, including increased maternal cortisol, increased norepinephrine and epinephrine, reduced uterine blood flow, nutritional deprivation, maternal cardiovascular disorders, and infection.

Presented here are data spanning the prenatal period through childhood which evaluate the influence of prenatal pCRH exposures on fetal, infant, and child development.

Method
- Prospective evaluations of natural variations in prenatal placental CRH at five gestational intervals (approximately 15, 19, 25, 31, and 36 weeks’ gestation) and assessment of offspring developmental from before birth to 9 years of age.
- Findings reported here are based on low risk, normative samples of healthy women and children and consider relevant pre- and postnatal influences, including maternal psychosocial state, obstetric risk, and sociodemographic factors.

Infant
- Fig. 5. Compared to children who exhibited typical growth profiles, children who exhibited catch-up growth within the first two years of life were exposed to higher levels of pCRH at 30 weeks’ gestation. Catch-up growth, a rapid and dramatic increase in body size, is a risk factor for developing metabolic disorder and obesity. N = 246
  Stout et al., 2015

Fetal
- Fig. 2. Fetuses exposed to higher concentrations of pCRH at 15 weeks’ gestation did not respond to a startling stimulus at 25 weeks’ gestation. High levels of pCRH early in pregnancy may be associated with delayed fetal maturation. N = 138
  Classi et al., 2008, Dev Neurosci

Neonatal
- Fig. 3. Compared with women who delivered at term, women who delivered preterm exhibited accelerated pCRH trajectories between 26 to 31 weeks’ gestation and elevated levels of pCRH at 31 weeks’ gestation. N = 203
  Sandman et al., 2006, Peptides

Brain Development
- Fig. 8-10. Prenatal exposure to increased pCRH levels at 31 weeks’ gestation was associated with cortical thinning, particularly in temporal areas, in 6-9 year-old children (e.g., left superior temporal, right temporal pole). Blue overlays indicate areas where the cortex is significantly thinner among these children. N = 79
  Ellman et al., 2008, Dev Psychobiol

Discussion
Our findings document links between elevated pCRH exposures and offspring developmental outcomes that begin prenatally and persist through 9 years of age. The prenatal period is a time of extremely rapid central nervous system development, during which the fetus is susceptible to intrauterine influences that confer risk or benefit. Because pCRH is of feto-placental origin, it may represent a salient indicator of fetal exposure or response to stress signals and subsequent alteration of developmental pathways related to fetal development, preterm birth, learning, memory, and emotion.

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