Maternal choline intake alters the epigenetic state of fetal cortisol-regulating genes in humans.

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BACKGROUND: The in utero availability of methyl donors, such as choline, may modify fetal epigenetic marks and lead to sustainable functional alterations throughout the life course. The hypothalamic-pituitary-adrenal (HPA) axis regulates cortisol production and is sensitive to perinatal epigenetic programming.

OBJECTIVE: As an extension of a 12-wk dose-response choline feeding study conducted in third-trimester pregnant women, we investigated the effect of maternal choline intake (930 vs. 480 mg/d) on the epigenetic state of cortisol-regulating genes, and their expression, in placenta and cord venous blood.

RESULTS: The higher maternal choline intake yielded higher placental promoter methylation of the cortisol-regulating genes, corticotropin releasing hormone (CRH; P=0.05) and glucocorticoid receptor (NR3C1; P=0.002); lower placental CRH transcript abundance (P=0.04); lower cord blood leukocyte promoter methylation of CRH (P=0.05) and NR3C1 (P=0.04); and 33% lower (P=0.07) cord plasma cortisol. In addition, placental global DNA methylation and dimethylated histone H3 at lysine 9 (H3K9me2) were higher (P=0.02) in the 930 mg choline/d group, as was the expression of select placental methyltransferases.

CONCLUSIONS: These data collectively suggest that maternal choline intake in humans modulates the epigenetic state of genes that regulate fetal HPA axis reactivity as well as the epigenomic status of fetal derived tissues.

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