Effects of unpredictable variable prenatal stress (UVPS) on *bdnf* DNA methylation and telomere length in the adult rat brain.

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In utero exposure to stress can shape neurobiological and behavioral outcomes in offspring, producing vulnerability to psychopathology later in life. Animal models of prenatal stress likewise have demonstrated long-term alterations in brain function and behavioral deficits in offspring. For example, using a rodent model of unpredictable variable prenatal stress (UVPS), in which dams are exposed to unpredictable, variable stress across pregnancy, we have found increased body weight and anxiety-like behavior in adult male, but not female, offspring. DNA methylation (addition of methyl groups to cytosines which normally represses gene transcription) and changes in telomere length (TTAGGG repeats on the ends of chromosomes) are two molecular modifications that result from stress and could be responsible for the long-term effects of UVPS. Here, we measured methylation of *brain-derived neurotrophic factor (bdnf)*, a gene important in development and plasticity, and telomere length in the brains of adult offspring from the UVPS model. Results indicate that prenatally stressed adult males have greater methylation in the medial prefrontal cortex (mPFC) compared to non-stressed controls, while females have greater methylation in the ventral hippocampus compared to controls. Further, prenatally stressed males had shorter telomeres than controls in the mPFC. These findings demonstrate the ability of UVPS to produce epigenetic alterations and changes in telomere length across behaviorally-relevant brain regions, which may have linkages to the phenotypic outcomes.

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