

The impact of parental and developmental stress on DNA methylation in the avian hypothalamic-pituitary-adrenal axis

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Abstract

The hypothalamic-pituitary-adrenal (HPA) axis coordinates an organism's response to environmental stress. The responsiveness and sensitivity of an offspring's stress response may be shaped not only by stressors encountered in an organism's early post-natal environment, but also by stressors in their parent's environment. Yet, few studies have considered how stressors encountered in both of these early life environments may function together to impact the developing HPA axis. Here, we manipulated stressors in the parental and post-natal environments in a population of house sparrows (*Passer domesticus*) to assess the impact of these stressors on changes in DNA methylation in a suite of genes within the HPA axis. We found that nestlings that experienced early life stress across both life-history periods had higher DNA methylation in a critical HPA axis gene, the glucocorticoid receptor (NR3C1). In addition, we found that the life-history stage when stress was encountered impacted some genes (HSD11B1, NR3C1, and NR3C2) differently. We also found evidence for the mitigation of parental stress by post-natal stress (in HSD11B1 and NR3C2). Finally, by assessing DNA methylation in both the brain and the blood, we were able to evaluate cross-tissue patterns; while some differentially methylated regions were tissue-specific, we found cross-tissue changes in NR3C2 and NR3C1, suggesting that blood may be a potential biomarker for DNA methylation of specific genes. Our results provide a crucial first step in understanding the mechanisms by which early life stress in different life history periods contributes to changes in the epigenome of the HPA axis.

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