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Epigenetic Regulation of PFC Maturation in Adolescents

Brain development is a complex process that, at the molecular level, involves an intricate network of genes and their proteins. In addition to being maturation-specific and time-dependent, certain genes are highly regulated by internal and external cues. Epigenetics is a phenomenon whereby environmental stimuli can influence the expression of genes and therefore plays a key role in developmental processes. By acting upon a complex regulatory network, the environment is able to modulate genetic function without altering the actual genome. There is currently little research examining the epigenetic regulation of brain development in postnatal periods such as adolescence. During this important time period, essential structural changes and subsequent functional modification occurs. It is therefor critical that we understand how epigenetic processes such a DNA methylation orchestrate and regulate postnatal processes and the impact these changes will have throughout the rest of the lifespan. Despite evidence demonstrating ongoing maturation of the prefrontal cortex (PFC) through adolescence, little is known about the changes in gene expression and epigenetic regulators that bring about this maturational transformation. ***The goal of this proposal is to determine the role of two epigenetic regulators, DNA methylation and telomere silencing, in adolescent brain maturation of the rat PFC, and then determine how experience and pharmacologics modify these processes.***

We expect to identify the specific functions that DNA methylation and telomere silencing play in adolescent maturation of the PFC. We will determine if these two epigenetic processes are involved in the differential rates of maturation that have been demonstrated in different regions of the PFC, and in males versus females. We also anticipate that environmental manipulations, both prior to and during adolescence, will delay maturation of the PFC and this developmental protraction will be the result of epigenetic modulation. These studies will advance the basic understanding of adolescent PFC development, by answering fundamental questions about two distinct regulators of the epigenome. This research will improve our basic understanding of gene by environment interactions in a complex system, impacting future epigenetic studies at both the cellular and organism level. In addition, this program of research will provide a strong and innovative teaching environment for the next wave of trainees.