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Exposure to early life stress and glucocorticoids: Mechanisms of system-wide epigenetic effects

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Exposure to early life stress (ELS) is a well-known major risk factor for developing psychiatric and behavioral disorders later in life. Both prenatal and postnatal stressors have long-lasting impact on adult pathological states. Epigenetic mechanisms have been shown to be involved in the embedding of these long-term changes. In a model of early life adversity in rhesus macaques, we have shown that differential rearing leads to long-lasting epigenetic alterations in two different tissues, the prefrontal cortex (PFC) and T cells. One of the mechanisms that might lead to these epigenetic alterations in multiple tissues is a long-lasting disruption of the stress hormone system by excessive glucocorticoids (GCs) release after ELS exposure. Using human hippocampal progenitor cells (HPCs), we have recently identified long-lasting DNA methylation alterations induced by GCs exposure, where a significant portion of these marks were initiated early during cellular proliferation and differentiation stages and persisted in mature neurons. Moreover, a significant overlap was observed between our GR-induced epigenetic changes in HPCs and sites previously associated with child abuse in postmortem human hippocampus and blood cells, suggesting similar long-lasting GR-induced epigenetic alterations in the brain and in peripheral tissues reflecting GC actions during ELS. A mechanistic understanding of the long-term epigenetic consequences of stress using a translational approach may allow novel, targeted intervention and prevention strategies for behavioral, psychiatric and other stress-associated disorders.

Biography

Nadine Provencal has completed her PhD in Epigenetics at McGill University in collaboration with the Research Group on Psychosocial Maladjustment in Children (GRIP) in 2013. Thereafter, she continued her training through Post-doctoral research at the University of Montreal and Max-Planck Institute of Psychiatry. She has published more than 15 papers in high impact international journals and received a prestigious Postdoctoral Fellowship from the Canadian Institute of Health Research (CIHR) and has been awarded the 2014 Richard Todd Award from the International Society of Psychiatric Genetics for her outstanding contribution to the genetics of child psychiatry.

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