ABUSE AND NEGLECT IN CHILDHOOD: THE IMPACT ON BEHAVIOR DEVELOPMENT AND NEUROENDOCRINOLOGY

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Abstract: Neglect and abuse, particularly during infancy and the early stages of life, can lead to epigenetic regulation of genes involved in stress-response, behavioral disinhibition, and cognitive-emotional systems. This stress induces long-lasting effects on the HPA axis. Objective: Demonstrate that abuse and neglect produce neurobiological abnormalities in affected individuals. Introduction: Programming of the HPA axis, one of the key mechanisms that contribute to altered metabolism and the response to stress, often involves epigenetic modification of the glucocorticoid receptor (GR) gene promoter, which influences tissue-specific GR expression patterns and response to stressful stimuli. Stress-mediated epigenetic modifications may be more pronounced during the stress-vulnerable, early-life period where brain regions implicated in emotionality and stress reactivity, such as the hippocampus, amygdala, and the prefrontal cortex, are undergoing rapid changes in dendritic density, myelination, and synaptic plasticity. Epigenetics is the study of mitotically and/or meiotically heritable changes in gene function that are not explained by changes in DNA sequence. Preclinical, epidemiological, and clinical studies suggest a strong link between exposure to stress, dysregulation of the HPA-axis, and susceptibility to neuropsychiatric illnesses. Methods: Research articles in Pubmed acquis. Results: Abuse and neglect in childhood cause neuroendocrine disorders that cause behavioral changes in later life. Discussion: In response to stress, the hypothalamic paraventricular nucleus (PVN) releases corticotropin-releasing hormone (CRH) and arginine vasopressin (AVP), which enter the hypophysial portal circulation and stimulate the synthesis and secretion of adrenocorticotropin (ACTH) into the peripheral circulation. ACTH initiates the production and secretion of glucocorticoid from the adrenal cortex. In cases of exposure to trauma or chronic stress, negative-feedback regulation of the HPA-axis becomes disrupted, leading to aberrant glucocorticoid levels that can persist even in the absence of additional stressors. In the rat, glucocorticoid overexposure decreases the expression of GR and reduction of GR levels by only 30–50% results in significant neuroendocrine, metabolic and immunological disorders. An epidemiological study that examined hundreds of thousands of patients who were prescribed glucocorticoids (i.e., iatrogenic Cushing’s syndrome) for non-psychiatric disorders found a significant increase in cases of depression, suicide, mania, and anxiety associated with glucocorticoid therapy. Glucocorticoid administration to adolescent animals is capable of inducing loss of DNA methylation and an increase in expression of FKBP5, a chaperone protein and primary regulator of intracellular GR-signaling, which has been implicated in numerous association studies of depression, bipolar disorder, and PTSD. Methylation alterations observed in the glucocorticoid response element (GRE) persisted into adulthood and were associated with anxiety-like behavior. Conclusion: Altered glucocorticoids levels cause deregulation of the HPA-axis negative feedback and disturbances in glucocorticoid signaling, which can have a negative impact on behavior by epigenetic control of genes that regulate mood and neurotransmission. Thereby, early-life adversity increases risk of psychiatric disorders, such as major depressive disorder (MDD) and posttraumatic stress disorder.
(PTSD),\textsuperscript{18,19} besides suicide in susceptible individuals by disrupting the development of stable emotional, behavioral and cognitive phenotypes.\textsuperscript{20}

Acknowledgements: Professor Edward Ziff and professor Elizabeth Castelon Konkiewitz

References


