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THE NEUROEPIGENETIC ROLE OF HISTONE ACETYLATION IN THE CAUSE AND TREATMENT OF MAJOR DEPRESSIVE DISORDER

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Major depressive disorder (MDD) is a chronic, multifactorial depressive syndrome of intricate etiology that ranks high in the Global Burden of Diseases (GBD) and is one of the subjects undergoing intense study in contemporary research. Various studies over the past decade reveal a significant influence of epigenetics in the pathophysiology of MDD including DNA methylation, histone modifications (methylation, acetylation, phosphorylation, crotonylation, and β-hydroxybutyrylation), mechanisms of non-coding RNAs, and microRNA biogenesis. The latest studies have revealed that epigenomic interaction between specific risk genes and environmental factors, such as severe exposure to stressful events are intensely related to MDD pathogenesis thus causing transcriptional changes and generation of stable changes in gene expression leading to maladaptive neuronal plasticity.

This study evaluates the latest information about the present understanding of the role of epigenomics contributing to MDD – especially the role of histone acetylation and the value of histone deacetylase inhibitors (HDACi) for MDD treatment, which will provide further insight into the disease and will assist in identifying biomarkers that would improve the progress of preclinical and clinical studies for diagnosis, and treatment.

PubMed and Google Scholar databases were used as the main search tools – in search of studies compatible with different combinations of keywords including ‘major depressive disorder’, ‘early life stress’, ‘epigenetics’, ‘histone modification’, ‘histone acetylation’ that were released in the time-frame between January 2007 and December 2022. The found sources were carefully read, selected, and summarized.

An epigenomic impact due to histone acetylation is present in MDD via adverse environmental factors. Metabolic pathways of histone acetylation were found to be interrelated to the epigenetic regulation transcribing genes for neuroplasticity dynamics and the formation of memory. HDACi were validated to hold antidepressant effects to treat MDD.

Epigenomics due to histone acetylation provides clarification in comprehending the relationship between adverse environmental factors and the cause of chronic and severe effects of MDD. Focusing on histone acetylation may offer a more elaborative interpretation of the mechanism of MDD and might open a new direction for MDD treatment. Although clinical trials assessing the antidepressant effects of HDACi in humans haven’t been done yet, as an emerging field, epigenomic studies may reach extraordinary conclusive insights using complete analysis of the epigenome as far as to predict the onset of the disorder and provide advanced modes of epigenetic therapy.