

Epigenetic Drugs for Major Depressive Disorder: A Critical Appraisal of Available Studies

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Abstract : Major depressive disorder (MDD) is a common and important psychiatric disorder. Several clinical features of MDD suggest an epigenetic basis for its pathogenesis. Since epigenetics (heritable changes in gene expression not involving changes in DNA sequence) may underlie the pathogenesis of MDD, epigenetic drugs such as DNA methyltransferase inhibitors (DNMTi) and histone deacetylase inhibitors (HDACi) may be useful for treating MDD. The available literature indexed in Pubmed on preclinical drug trials of epigenetic drugs for the treatment of MDD was investigated. The search terms we used were 'depression' or 'depressive' and 'HDACi' or 'DNMTi'. Among epigenetic drugs, it was found that there were 3 preclinical trials using HDACi and 3 using DNMTi for the treatment of MDD. All the trials were conducted on rodents (mice or rats). The animal models of depression that were used were: learned helplessness-induced animal model, forced swim test, open field test, and the tail suspension test. One study used a genetic rat model of depression (the Flinders Sensitive Line). The HDACi that were tested were: sodium butyrate, compound 60 (Cpd-60), and valproic acid. The DNMTi that were tested were: 5-azacytidine and decitabine. Among the three preclinical trials using HDACi, all showed an antidepressant effect in animal models of depression. Among the 3 preclinical trials using DNMTi also, all showed an antidepressant effect in animal models of depression. Thus, epigenetic drugs, namely, HDACi and DNMTi, may prove to be useful in the treatment of MDD and merit further investigation for the treatment of this disorder.

Keywords : DNA methylation, drug discovery, epigenetics, major depressive disorder

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