Suberoylanilide hydroxamic acid, a histone deacetylase inhibitor, protects dopaminergic neurons from neurotoxin-induced damage

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Several evidence suggest that the pathogenesis of neurodegenerative diseases such as Alzheimer’s disease, Parkinson’s disease, Huntington’s disease and amyotrophic lateral sclerosis may include epigenetic dysregulation in the brain. Suberoylanilide hydroxamic acid (SAHA) was found to inhibit histone deacetylase (HDAC) and has a broad spectrum of epigenetic activities. SAHA has also been tested for the treatment of neurodegenerative diseases such as Huntington’s disease and spinal and bulbar muscular atrophy (SMA) models. However, the majority of these studies focused on the effect of SAHA on neurons while neglecting the possible role of glial cells in the pathogenesis of neurodegeneration. The main purpose of their study was to investigate the neuroprotective effect and the underlying mechanism of SAHA by using a series of midbrain primary cultures which contain dopaminergic neurons. They found that (1) SAHA protected dopaminergic neurons from spontaneous or neurotoxin-induced cell death in the cultures; (2) neurotrophic factors such as GDNF and BDNF released from astroglia played a critical role in SAHA-induced neuroprotection; and (3) SAHA induced the expression of neurotrophic factors from astroglia through induction of histone acetylation. They suggest that SAHA can be a potential drug for treatment of neurodegenerative diseases such as Parkinson’s disease. The novel neurotrophic and neuroprotective effects of SAHA demonstrated in this study suggest that further study of this HDAC inhibitor could provide a new therapeutic approach to the treatment of neurodegenerative diseases.