

## **The Role of Histone-Deacetylase-Inhibitors in Neuroprotection**

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Epigenetic is a term used to describe states of gene expression that are not due to changes in DNA sequence. One of the most studied epigenetic phenomenon is histone tail modification via methylation and acetylation.

The acetylation or deacetylation of histone N-terminal tails alter the interaction between histones and DNA in chromatin, and this chromatin remodeling has been identified as a key step in gene expression regulation. In general, hyperacetylation is associated with transcriptional activation, whereas hypoacetylation is associated with repression. The quantity and activity of histone acetyltransferases (HAT) and histone deacetylases (HDAC) are finely balanced in neurons under normal conditions. This acetylation homeostasis is greatly impaired, shifting towards deacetylation in neurodegenerative diseases.

Drugs that prevent a resulting histone deacetylation in a disease can help restore transcription. These compounds, known as HDAC inhibitors (HDACi), affect histones as well as transcription factors that are regulated by acetylation. HDACi are divided into four groups: 1. short-chain fatty acids (e.g. Sodium butyrate (NaB), Valproic acid (VPA), 2. hydroxamic acids (e.g. trichostatin A (TSA), suberoylanilide hydroxamic acid (SAHA), 3. cyclic tetrapeptides and 4. benzamides.

NaB and VPA were the first known HDACi and together with TSA recently attracted attention as neuroprotective drugs. It has been suggested that their action is linked to a large extent to direct inhibition of HDAC, causing histone hyperacetylation. Among others, the extracellular signal-regulated kinase pathway and the inhibition of proapoptotic molecules are further involved in HDACi-mediated protection.

Our data revealed that VPA significantly delayed cell death in rat retinal ganglion cells (RGC) after optic nerve crush.