HISTONE DEACETYLASE (HDAC) INHIBITORS REDUCE THE *IN VITRO* AND *IN VIVO* NEUROINFLAMMATORY RESPONSE IN MICE

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Histone deacetylation plays a central role in the regulation of transcription of several genes. Inhibitors of histone deacetylases (HDAC) are currently evaluated in several clinical trials and emerge as neuroprotective agents. Indeed, histone acetylation balance is impaired during neurodegenerative conditions. Given that histone acetylation affects the extent of inflammatory response, in the present study, we investigated the effect of two potent HDAC inhibitors, namely SAHA and ITF2357, on histone acetylation and proinflammatory molecules expression in glial cells. Pharmacological inhibition of HDACs strongly reduced in a dose-dependent manner mRNA and protein levels of iNOS, COX-2, TNF-α and IL-β in LPS-challenged cultured mouse glial cells. However, the LPS-induced DNA binding activity of NF-κB, a transcription factor crucial for the expression of several cytokines, was not affected by both HDAC inhibitors. Also, the anti-inflammatory effects of HDAC inhibitors persisted even in the presence of cycloheximide suggesting that the mechanism of the anti-inflammatory properties of HDAC inhibitors do not involve the synthesis of newborn proteins. We next evaluated the effect of HDAC inhibition in a classical *in vivo* model of neuroinflammation such as microinjection of LPS in the mouse striatum. Importantly, intraperitoneal administration of ITF2357 (10mg/Kg) suppressed neuroinflammation in LPS challenged mice. Taken together, data demonstrate that pharmacological inhibition of HDACs may be of relevance to the treatment of neuroinflammatory disorders.