ABSTRACT
Excessive production of cytokines by microglia may cause cognitive dysfunction and long-lasting behavioral changes. Activating the peripheral innate immune system stimulates cytokine secretion in the central nervous system, which modulates cognitive function. Histone deacetylases (HDACs) modulate cytokine synthesis and release. Trichostatin A (TSA), an HDAC inhibitor, is documented to be anti-inflammatory and neuroprotective. We investigated whether TSA reduces lipopolysaccharide- (LPS-) induced neuroinflammation and cognitive dysfunction. ICR mice were first intraperitoneally (i.p.) injected with vehicle or TSA (0.3mg/kg). One hour later, they were injected (i.p.) with saline or Escherichia coli LPS (1mg/kg). We analyzed the food and water intake, body weight loss, and sucrose preference of the injected mice and then determined the microglia activation and inflammatory cytokine expression in the brains of LPS-treated mice and LPS-treated BV-2 microglial cells. In the TSA-pretreated mice, microglial activation was lower, anhedonia did not occur, and LPS-induced cognitive dysfunction (anorexia, weight loss, and social withdrawal) was attenuated. Moreover, mRNA expression of HDAC2, HDAC5, indoleamine 2,3-dioxygenase (IDO), TNF-?, MCP-1, and IL-1? in the brain of LPS-challenged mice and in the LPS-treated BV-2 microglial cells was lower. TSA diminished LPS-induced inflammatory responses in the mouse brain and modulated the cytokine-associated changes in cognitive function, which might be specifically related to reducing HDAC2 and HDAC5 expression.

Keywords: Trichostatin A, Histone deacetylases, Neuroinflammation

REFERENCES