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Rosmarinic acid reverses the deleterious effects of repetitive stress and tat protein Khayelihle B Makhathini^{1*}, Musa V Mabandla¹ and William MU Daniels²

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Highlights

- (1) The rosmarinic acid attenuated anxiety-like behaviour induced by tat and stress
- (2) The rosmarinic acid has anxiolytic potential that produce the ability to neutralise stressinduced alterations to the HPA axis and BDNF
- (3) The rosmarininc acid is neuroprotective with respect to tat-mediated toxicity

Abstract

Human immunodeficiency virus type 1 (HIV) has infected more than 40 million people worldwide and is associated with central nervous system (CNS) disruption in at least 30% of these persons. The use of highly active antiretroviral therapy (HAART) has significantly reduced the systemic immunopathology associated with HIV, but the occurrence of neurological disorders continues to be reported in notable numbers. The present study evaluated the potential of rosmarinic acid to reverse the detrimental effects of an intracerebral injection of the viral protein tat. Control and tat-injected rats were also subjected to repetitive restrain stress (RRS) for 28 days, 6 hours per day, to investigate whether subsequent stress exposure would worsen the effects of tat. 14 days after the initiation of RRS, animals were treated with rosmarinic acid (10 mg/kg given intraperitoneally) daily until the end of the stress exposure period. We assessed locomotor activity and anxiety-like behavioral changes. We also measured plasma corticosterone levels and quantified the expression of mineralocorticoid receptors (MR), glucocorticoid receptors (GR) and brain-derived neurotrophic factor (BDNF) in the hippocampus. Rosmarinic acid attenuated anxiety-like behavior induced by tat and stress, reduced plasma corticosterone levels and increased the expression of hippocampal GR, MR and BDNF when compared to controls. These results suggest that rosmarinic acid may reverse

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