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Sanguinarine alleviates post-stroke cognitive impairment in rats by modulating the p38 MAPK signaling pathway

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Post-stroke cognitive impairment (PSCI) is common, but the understanding of its cognitive impairment mechanisms and available treatment options are limited. Sanguinarine (SG) has shown promising neuroprotective potential, but its effects and mechanism in PSCI remain unexplored. This study established a rat stroke model via middle cerebral artery occlusion (MCAO) surgery. SG was administered intraperitoneally at doses of 1.0, 2.5, or 6.25 mg/kg. Cognitive function and neuronal injury were assessed using a novel object recognition test, the Y-maze, Nissl staining, and TUNEL staining. Neuroinflammation and the activation levels of p38 mitogen-activated protein kinase (MAPK) were evaluated by ELISA, western blot, and immunofluorescence. The results showed that MCAO rats demonstrated cognitive impairments, increased neuronal apoptosis, and heightened neuroinflammation. Treatment with 6.25 mg/kg SG significantly improved cognitive function in stroke rats, as evidenced by an increased recognition index and more time spent in the novel arm of the Y-maze. SG alleviated neuronal injury and reduced neuronal apoptosis in MACO rats. Furthermore, SG treatment downregulated the pro-inflammatory cytokines tumor necrosis factor-α and interleukin (IL)-1β and upregulated the anti-inflammatory cytokine IL-10 in a dose-dependent manner, while also inhibiting the activation of p38 MAPK in MCAO rats. Notably, the co-administration of SG with anisomycin (a p38 MAPK activator) reversed these effects. Molecular docking experiments also demonstrated a strong binding affinity between SG and p38 MAPK. In conclusion, SG alleviates neuroinflammation and neuronal apoptosis by inhibiting p38 MAPK activation in PSCI, highlighting its potential as a multi-target therapeutic agent.

Keywords: Middle cerebral artery occlusion (MACO), Neuroinflammation, Apoptosis, Anisomycin