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PPARγ activation ameliorates postoperative cognitive decline probably through suppressing hippocampal neuroinflammation in aged mice.

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Abstract

Neuroinflammation plays a key role in many neurodegenerative disorders, including postoperative cognitive decline (POCD). Growing evidence has demonstrated that activation of the peroxisome proliferator-activated receptor-γ (PPARγ) attenuates the inflammatory response and improves cognitive dysfunction associated with many neuropsychiatric disorders. We hypothesize that down-regulation of PPARγ is linked to neuroinflammation and the subsequent cognitive deficits observed in an animal model of POCD. In the present study, the POCD animal model was established by performing an exploratory laparotomy under isoflurane anesthesia in 20-month-old male C57BL/6 mice. Behavioral tests, inflammatory biomarkers, including tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), interleukin-1β, ionized calcium-binding adaptor molecule-1 (IBA1)-positive cells, as well as glial fibrillary acidic protein (GFAP)-positive cells and brain-derived neurotrophic factor (BDNF), were measured. Herein, we showed that surgery induced profound impairment in cognition that was associated with significant decreases in PPARγ and BDNF expression, and significant increases in IL-1β, IBA1-positive cells, and GFAP-positive cells in the hippocampus. As expected, the PPARγ agonist pioglitazone attenuated the surgery-induced inflammatory changes and rescued the associated cognitive impairment. However, these beneficial effects were abolished by the PPARγ specific antagonist GW9662, suggesting a pivotal role of the PPARγ pathway in the pathogenesis of POCD. Taken together, our results provide evidence that down-regulation of PPARγ may be involved in neuroinflammation and subsequent POCD, and suggest that activation of PPARγ by pioglitazone may represent a new way to prevent or treat POCD.

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