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PEA prevented early BBB disruption after cerebral ischaemic/reperfusion (I/R) injury through regulation of ROCK/MLC signaling

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Abstract

Palmitoylethanolamide (PEA) offers a strong protection against BBB disruption and neurological deficits after cerebral ischaemic/reperfusion (I/R) injury. To date, these BBB protective effects of PEA are mainly attributed to PPARα-mediated actions. However, whether PEA protects against BBB disruption through direct regulation of cytoskeletal microfilaments remains unknown. Here, we identified PEA as a Rho-associated protein kinase (ROCK2) inhibitor (IC_{50} = 38.4 ± 4.8 μM). In vitro data suggested that PEA reduced the activation of ROCK/MLC signaling and stress fiber formation within microvascular endothelial cells (ECs) after oxygen-glucose deprivation (OGD), and consequently attenuated early (0-4 h) EC barrier disruption. These actions of PEA could not be blocked by the PPARα antagonist GW6471. In summary, the present study described a previously unexplored role of PEA as a ROCK2 inhibitor, and propose a PPARα-independent mechanism for pharmacological effects of PEA.

Keywords: Blood–brain barrier (BBB); Cerebral ischaemic; Myosin light chain (MLC); Palmitoylethanolamide (PEA); Reperfusion (I/R) injury; Rho-associated protein kinase (ROCK).

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