セサミンは脳出血時の p44/42 MAPK および ミクログリアの活性化を抑制し、神経保護効果を発揮する

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Sesamin suppresses activations of microglia and p44/42 MAPK pathway, which confers neuroprotection in rat intracerebral hemorrhage

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ABSTRACT: Thrombin plays important roles in the pathology of intracerebral hemorrhage (ICH). The recruitment of activated microlgia, accompanied by thrombin-induced phosphorylation of the mitogen-activated protein kinase (MAPK) family, contributes to ICH-associated neuron loss. Here we investigated the possibility that sesamin, a lignan of sesame seed oil, is a natural candidate as an inhibitor of microglial activation and MAPK pathways under ICH insults. Sesamin (30-100 μM) suppressed thrombin-induced nitric oxide (NO) production by primary-cultured rat microglia via inhibition of inducible NO synthase (iNOS) protein expression, independently of the antioxidative effect. Sesamin selectively inhibited p44/42 MAPK phosphorylation in the MAPK family (p38 and p44/42) involved in iNOS protein expression in primary-cultured rat micrgolia. An in vivo rat ICH model was prepared by intrastriatal injection of 0.20 U collagenase type IV unilaterally. ICH evoked the phosphorylation of p44/42 MAPK, microglial proliferation with morphological change into the activated ameboid form, and neuron loss. The phosphorylation of p44/42 MAPK was inhibited by intracerebroventricular administration of 30 nmol sesamin. Sesamin prevented ICH-induced increase of microglial cells in the preihematomal area. Notably, ramified microglia, the resting morphology, were observed in brain sections of the animals administrated sesamin. Sesamin furthermore achieved neuroprotection in the perihematomal area but not in the hematomal center. These results suggest that sesamin is a promising natural product as a novel therapeutic strategy based on the regulation of microglial activities accompanied by the activated p44/42 MAPK pathway in ICH.

抄録　脳出血発作時には、MAPKs のリン酸化を伴うミクログリアの活性化が炎症性拡散因子の遊離促進につながり、その病態形成の一翼を担うことをこれまで明らかにしてきた。本研究は、ゴマの種子に含有されるリグナンの一種であるセサミンが、トロンビンによる上記各因子の活性化を抑制し、神経細胞をレスキューすることを示した

ものである。

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