ジベンゾイルメタン誘導体は、マウスミクログリア細胞株 BV-2 のリポ多糖誘発 NO 産生を阻害する

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A dibenzoylmethane derivative inhibits lipopolysaccharide-induced NO production in mouse microglial cell line BV-2

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ABSTRACT Microglial activation has been suggested to play important roles in various neurodegenerative diseases by phagocytosis and producing various factors such as nitric oxide (NO), proinflammatory cytokines. Excessive production of NO, as a consequence of increased inducible nitric oxide synthase (iNOS) in microglia, contributes to the neurodegeneration. During a search for compounds that regulate endoplasmic reticulum (ER) stress, a dibenzoylmethane derivative, 2,2'-dimethoxydibenzoylmethane (DBM 14-26) was identified as a novel neuroprotective agent. We previously reported in cultured astrocytes that DBM 14-26 protected hydrogen peroxide-induced cell death and inhibited lipopolysaccharide (LPS)-induced NO production. In the present study, we assessed the effects of DBM 14-26 on microglia using the mouse cell line BV-2 and found that DBM 14-26 inhibited LPS-induced iNOS expression and NO production also in microglia. DBM 14-26 also suppressed LPS-induced IL-1b expression. Conditioned medium of BV-2 cells stimulated by LPS significantly decreased cell viability of neuron (human neuroblastoma SH-SY5Y cells) compared with the absence of LPS. Conditioned medium of BV-2 cells stimulated by LPS in the presence of DBM 14-26 did not significantly decreased cell viability of neuron. These results indicate that microglial activation by LPS causes neuronal cell death and DBM 14-26 protect neuron through the inhibition of microglial activation. Functional regulation of microglia by DBM 14-26 could be a therapeutic candidate for the treatment of neurodegenerative diseases.

抄録 ミクログリアの活性化は、食作用および一酸化窒素（NO）、炎症性サイトカインなどのさまざまな産生因子により、さまざまな神経変性疾患で重要な役割を果たすことが示唆されている。本研究では、マウス細胞株 BV-2 を使用しジベンゾイルメタン誘導体 (DBM) 14-26 がミクログリアに及ぼす影響を評価し、DBM 14-26 がミクログリアで LPS 誘導 iNOS 発現と NO 産生を阻害することを発見し、そして DBM 14-26 がミクログリアの活性化の阻害を通じてニューロンを保護することを明らかにした。DBM 14-26 によるミクログリアの機能的調節は、神経変性疾患の治療の候補となる可能性がることを示した内容である。

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