中文題目：周邊發炎反應對腦部CB1受體表現的影響

英文題目：Brain CB1 receptor expression following lipopolysaccharide-induced inflammation

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Background and Aim: Cannabinoid 1 receptors (CB1) are highly expressed on presynaptic terminals in the brain where they are importantly involved in the control of neurotransmitter release. Alteration of CB1 expression is associated with a variety of neurological and psychiatric disorders. There is now compelling evidence that peripheral inflammatory disorders are associated with depression and cognitive impairments. These can be modeled in rodents with peripheral administration of lipopolysaccharide (LPS), but central effects of this treatment remain to be fully elucidated. As a reduction in endocannabinoid tone is thought to contribute to depression, we asked whether the expression of CB1 in the central nervous system (CNS) is altered following LPS treatment.

Methods: Male CD1 mice were divided into 6 groups: i) LPS 100 μg/kg 6 h; ii) LPS 1 mg/kg 6 h; iii) saline 6 h; iv) LPS 100 μg/kg 24 h; v) LPS 1 mg/kg 24 h; vi) saline 24 hours. LPS and an equal amount of saline were injected intraperitoneally, and brain tissue was collected according to the specific time point. Immunohistochemistry study was performed using 3 different primary antibodies respectively: Iba-1, rabbit anti-CB1 C-terminal antibody and rabbit anti-CB1 N-terminal antibody. Quantification and colocalization of immunoreactivity were analyzed by Olympus FluoView 1000 confocal microscope using the 60X objective. Immunoreactivity of each antibody was analyzed by FV10-ASW2.1 software. The change of CB1 and TNF-α mRNA level was evaluated by quantitative polymerase chain reaction (PCR).

Results: CD1 mice received LPS (0.1-1 mg/kg, ip) and 6 hours later activated microglial cells were observed only in circumventricular organs and only at the higher dose. At 24 hours, activated microglial cells were identified in other brain regions, including the hippocampus, a structure implicated in some mood disorders. Immunohistochemistry and real-time PCR were utilized to evaluate the change of CB1 expression 24 hours after inflammation. LPS induced an increase of CB1 mRNA in hippocampus and brainstem. Subsequent immunohistochemical analysis revealed reduced CB1 in hippocampus, especially in CA3 pyramidal layer. Analysis of co-localization with markers of excitatory and inhibitory terminals indicated that the decrease in CB1 expression was restricted to glutamatergic terminals.

Conclusions: Despite widespread microglial activation, these results suggest that peripheral LPS treatment leads to limited changes in CB1 expression in the brain.