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BDNF inhibition of LPS-induced microglial activation in Parkinson's disease

Ting-Ting Yang[1], Yu-Min Kuo[2], Wei-Hung Kuo, Shu-Chi Wang[1], Ming-Jia Jou[1] and Chao-Tien Hsu[3]

[1]I-Shou University, Taiwan

[2]National Cheng Kung University, Taiwan

[3]Kaohsiung Medical University, Taiwan

Microglial Activation (MA) and Dopaminergic (DA) neuron loss are features of aging brain in Parkinson's disease (PD). Although the etiology of PD remains unclear, age and inflammation are known PD risk factors. Because Reduced Brain-Derived Neurotrophic Factor (BDNF) are associated with DA neuron loss in the Substantia Nigra (SN), age and LPS-related BDNF/ TrkB signaling pathway for MA and DA neuron loss in PD have been characterized. Infusing recombinant BDNF into the SN of mice at 6-month-old by osmotic mini-pump for 3 months, we found BDNF inhibited LPS-evoked area of MA in SN, striatum, hippocampus. Exposure to LPS induced phosphorylation of p38, JNK and GSK3, which then increased phosphorylation of NF-κB. Phosphorylated NF-κB translocated into nucleus and bound to CBP and other co-activators. The NF-κB-CBP complex then induced transcription of inflammatory-related genes. Exogenous supplement with BDNF or endogenous up-regulating the expression of BDNF by exercise inhibited MA. Potential suppressive mechanisms of BDNF on MA might depend on three pathways: (1) BDNF induced Erk activation, which then phosphorylates CREB. Activated CREB inhibited NF-κB activity through competition for limited amounts of CBP. Activated CREB was also known to induce transcription of anti-inflammatory genes. Furthermore, activated CREB might also induce a positive feed forward production of BDNF, (2) BDNF actives Akt, which inhibited the activation of GSK3, resulting in a decrease of NF-κB activation and an increase of CREB activation and (3) BDNF up-regulated MKP-1, which then reduced the LPS-induced phosphorylation of p38 and JNK.

Biography

Ting-Ting Yang is the Professor of Neuroscience at School of Medicine and a Senior Fellow of School of Chinese Medicine for Post-Baccalaureate at I-Shou University. She has completed her Master's level training and Doctoral training in Cellular and Molecular Biology at Nagasaki University. The major focus of her ongoing research is the investigation of disease and treatment-induced changes in gene and protein expression profiles that regulate neuro-energetics and neuroplasticity signaling pathways in neurodegeneration disease including Alzheimer's disease and Parkinson's disease.

tingting.taiwan@gmail.com

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