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NR2B antagonist ifenprodil improves abnormal forelimb movement induced by D1R agonist SKF38393 in hemiperkinsonian rats

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Objectives: The antiparkinsonian effect of N-methyl-D-aspartate receptor subtype 2B (NR2B) antagonists remain controversial. To determine the effects of NR2B antagonist on Parkinson's disease (PD), the effect of a single administration of D1R agonist SKF38393 (SKF) and NR2B antagonist ifenprodil or co-administration of ifenprodil and SKF were investigated using the cylinder test.

Methods: We performed the cylinder test to estimate the number of forelimb use per 15 min as a measure of motor activity 30 min after administration of SKF(1.0, 2.0, 3.0 mg/kg), 0.1 mg/kg ifenprodil or co-administration of SKF and ifenprodil. Next, to identify the brain areas influenced by SKF and ifenprodil, neurons with SKF-induced c-Fos expression were analysed in various brain regions in hemi-PD following the administration of SKF, with and without ifenprodil.

Results: The administration of SKF increased a frequency of forelimb-use in dose-dependent manner, mostly via the facilitation of the frequent use of parkinsonian paw. The combined administration of SKF and ifenprodil completely reversed the SKF-induced abnormality in bilaterally coordinated movement of the forelimb in hemi-PD without affecting the facilitatory effect of SKF on motor activity. The co-administered ifenprodil also modulated the SKF-induced c-Fos expression in the striatum and the subthalamic nucleus (STN).

Conclusion: We conclude that the ameliorative effect of ifenprodil on the motor deficits in hemi-PD is resulted from the improvement of the SKF-induced excessive use of parkinsonian paw, and that the STN and/or the striatum in the lesioned hemisphere are possible targets for the antiparkinsonian effect of the NR2B antagonist.

Biography

Habata has study his PhD in Kitasato University School of Medicine. He is a Kitasato University Lecturer, Master of Engineering and an Occupational Therapist of Japan for 30 years.

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