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## Imparment of synaptic activity through reduced CaMKII activity in Parkinson's disease model mice

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Parkinson's disease (PD) patients frequently reveal deficit in cognitive functions during the early stage in PD. The dopaminergic neurotoxin, MPTP-induced neurodegeneration causes an injury of the basal ganglia and is associated with PD-like behaviors. In this study, we demonstrated that deficits in cognitive functions in MPTP-treated mice were associated with reduced calcium/calmodulin-dependent protein kinase II (CaMKII) autophosphorylation and impaired long-term potentiation (LTP) induction in the hippocampal CA1 region. Mice were injected once a day for 5 days with MPTP (25mg/kg i.p.). The impaired motor coordination was observed one or two week after MPTP treatment as assessed by rota-rod and beam-walking tasks. In immunoblotting analyses, the levels of tyrosine hydroxylase protein and CaMKII autophosphorylation in the striatum were significantly decreased 1week after MPTP treatment. By contrast, deficits of cognitive functions were observed three-four weeks after MPTP treatment as assessed by novel object recognition and passive avoidance tasks but not Y-maze task. Impaired LTP in the hippocampal CA1 region was also observed in MPTP-treated mice. Concomitant with impaired LTP induction, CaMKII autophosphorylation was significantly decreased three weeks after MPTP treatment in the hippocampal CA1 region. Finally, the reduced CaMKII autophosphorylation was closely associated with reduced AMPA-type glutamate receptor subunit 1 (GluR1; Ser-831) phosphorylation in the hippocampal CA1 region of MPTP-treated mice. Taken together, decreased CaMKII activity with concomitant impaired LTP induction in the hippocampus likely account for the learning disability observed in MPTP-treated mice.

### Biography

Kohji Fukunaga first discovered calcium/calmodulin-dependent protein kinase II (CaMKII) from brain. He received his PhD degrees from Kumamoto University School of Medicine in 1985. During 1988 to 1990, he worked as research fellow in Vanderbilt University (HHMI) under Professor TR Soderling. In 2002, he was appointed a Professor and Chairman in the faculty of graduate school of pharmaceutical sciences. He was Editor-in-Chief of Journal of Pharmacological Sciences (Elsevier) since 2012. He is interested in disease-modifying drug development for neurodegenerative disorders and psychiatry diseases such as autism and mental retardation.

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