大学院特別講義

新潟脳神経研究会特別例会の御案内

日　　時：令和５年 11 月 17 日(金) 16:00～17:00

場　　所：脳研究所 Ａ棟１階　検討会室

Differential Roles of Dopamine D2R Isoforms in Neuronal Excitability, Spine Formation and Dyskinesia-Like Behavior

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The basal ganglia circuitry including the striatum is involved in the pathophysiology of Parkinson's disease and drug-induced dyskinesia. Modulating the activity of striatal neurons by the dopamine D2 receptor (D2R) can greatly impact motor control and movement disorders. D2R exists in two isoforms: D2L (long form) and D2S (short form). Here we assessed whether changes in the D2L and D2S expression levels would alter striatal neuronal and synaptic activity, spine formation, and L-dopa-induced dyskinesia-like behavior. We showed that D2L deficiency or increased ratio of D2S to D2L altered the effect of the D2R agonist quinpirole on neuronal excitability depending on the types of striatal neurons. In addition, we found the frequency of inhibitory postsynaptic currents was reduced in cholinergic interneurons (ChIs) in D2L KO mice compared to WT mice. Furthermore, D2L deficiency resulted in reduced dendritic spine density in ChIs in D2L KO mice. We also demonstrated that D2L KO mice displayed markedly enhanced dyskinesia-like behavior in response to chronic treatment of L-dopa or quinpirole compared to WT mice, suggesting that D2S plays a greater role than D2L to dopamine agonist-induced dyskinesia-like behavior. Our findings reveal new molecular and cellular mechanisms for causing ChIs abnormality seen in Parkinson's disease and suggest new factors contributing to the pathophysiology of L-dopa-induced dyskinesia-like behavior.

どうぞ奮ってご参加ください。　　（担当：脳研究所 動物資源開発研究分野）

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