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Neurology Congress 2018: Modulation of cell viability by L-DOPA via the ERK and JNK-c-Jun systems in dopaminergic neuronal cells - Myung Koo Lee - Chungbuk National University

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Parkinson's disease (PD) is caused by the degeneration of dopaminergic neurons in the substantia nigra-striatal locale. L-3,4-dihydroxyphenylalanine (L-DOPA) is the most much of the time recommended sedate for controlling the side effects of PD. Be that as it may, the significant levels of L-DOPA lead to cell demise by producing receptive oxygen species in dopaminergic neuronal and PC12 cells. As of late, it has been accounted for that the intracellular cyclic AMP levels expanded because of cytotoxic degrees of L-DOPA and different medicines with non-poisonous L-DOPA (MT-LD) diminished dopamine biosynthesis in PC12 cells. In this examination, the impacts of L-DOPA on dopaminergic neuronal cell demise through the ERK1/2 and JNK1/2-c-Jun frameworks were researched. In PC12 cells, MT-LD actuated cell endurance by means of PKA-transient ERK1/2 enactment, and afterward it prompted separation through the Epac-supported ERK1/2 framework. MT-LD at first upgraded c-Jun phosphorylation (Ser73), yet later instigated c-Jun phosphorylation (Ser63) and c-Jun articulation, which consequently prompted the cell demise process. In the 6-hydroxydopaminelesioned rodent model of PD (6-OHDA injury), L-DOPA organization (10 mg/kg) secured against neurotoxicity through c-Jun phosphorylation (Ser73) for quite a long time. Be that as it may, L-DOPA organization (10 or 30 mg/kg) indicated neurotoxicity through c-Jun phosphorylation (Ser63) and c-Jun articulation by means of ERK1/2 phosphorylation for 34 weeks. Also, gynosaponin TN-2 from ethanol concentrate of G. pentaphyllum (GP-EX) ensured against L-DOPA-prompted neurotoxicity in PC12 cells. Gypenosides and GP-EX additionally indicated the defensive impacts on long haul L-DOPA organization in 6-OHDA sore. Our information demonstrate that ceaseless treatment of L-DOPA causes neurotoxicity by means of the cyclic AMP-ERK1/2-c-Jun framework in dopaminergic neuronal cells and GP-EX may fill in as an adjuvant specialist for PD. Late Publications 1. Shin K S, Park H J, Park K H, Lee K S, Jeong S W, Hwang B Y, Lee C K and Lee M K (2018) Effects of gynosaponin TN-2 on L-DOPA-instigated cytotoxicity in PC12 cells. Neuro Report 29(1):1-5. 2. Zhao T, kim K S, Shin K S, Park H J, Kim H J, Lee K E and Lee MK (2017) Gypenosides improve memory shortages in MPTP-lesioned mouse model of Parkinson's disease rewarded with L-DOPA. BMC Complementary and Alternative Medicine 17(1):449. 3. Park K H, Shin K S, Zhao T, Park H J, Lee K E and Lee M K (2016) L-DOPA regulates cell practicality through the ERKc-Jun framework in PC12 and dopaminergic neuronal cells. Neuropharmacology 101:87-97. 4. Shin K S, Zhao T, Park K H, Park H J, Hwang B Y, Lee C K and Lee M K (2015) Gypenosides constrict the improvement of L-DOPA-incited dyskinesia in 6-hydroxydopamine-lesioned rodent model of Parkinson's disease. BMC Neuroscience 16:23. 5. Shin K S, Zhao T, Choi H S, Hwang B Y, Lee C K and Lee M K (2014) Effects of gypenosides on tension issue in MPTP-lesioned mouse model of Parkinson's disease. Mind Res 1567:57-65.

L-DOPA causes neurotoxicity by balancing the Epac-ERK framework in PC12 cells. This examination researched the impacts of a solitary treatment with L-DOPA and various medicines with L-DOPA (MT-LD) on ERK1/2 and JNK1/2-c-Jun frameworks. In PC12 cells, a harmful L-DOPA fixation (200 μM) incited supported ERK1/2 and JNK1/2 phosphorylation that was restrained by the Epac inhibitor brefeldin A, however not by the PKA inhibitor H89. This ERK1/2 and JNK1/2 phosphorylation was additionally hindered by ERK1/2 (U0126) and JNK1/2 (SP600125) inhibitors, separately, however supported ERK1/2 phosphorylation was not influenced by JNK1/2 phosphorylation. A non-poisonous L-DOPA fixation (20 μM) incited c-Jun phosphorylation (Ser73) by means of transient ERK1/2 phosphorylation, while the harmful L-DOPA focus actuated c-Jun phosphorylation (Ser63) and c-Jun articulation by means of Epac-supported ERK1/2-JNK1/2 phosphorylation, which at that point improved separated caspase-3 articulation. MT-LD (20 μM) at first upgraded c-Jun phosphorylation (Ser73) (for 1–4 days), yet later (5–6 days) initiated c-Jun phosphorylation (Ser63) and c-Jun articulation. In the 6-hydroxydopamine-lesioned rodent model of Parkinson's disease, L-DOPA organization (10 mg/kg) ensured against neurotoxicity through c-Jun phosphorylation (Ser73) for 1 fourteen days. Be that as it may, L-DOPA organization (10 or 30 mg/kg)

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demonstrated neurotoxicity through c-Jun phosphorylation (Ser63) and c-Jun articulation by means of ERK1/2 phosphorylation for 3 a month. In this manner, in PC12 cells, non-poisonous L-DOPA treatment kept up cell endurance through c-Jun phosphorylation (Ser73). On the other hand, harmful L-DOPA treatment or the MT-LD (20 μM) initiated c-Jun phosphorylation c-Jun articulation by means of Epac-subordinate continued ERK1/2 and JNK1/2 phosphorylation, which in this manner prompted cell passing. These outcomes were approved by those acquired after long haul L-DOPA organization in a rodent model of Parkinson's disease. Our information show that L-DOPA causes neurotoxicity through the ERK1/2-c-Jun framework in dopaminergic neuronal cells.

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