Targeting the cannabinoid receptor CB2 in a mouse model of l-dopa induced dyskinesia

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L-dopa induced dyskinesia (LID) is a debilitating side-effect of the primary treatment used in Parkinson's disease (PD), l-dopa. Here we investigate the effect of HU-308, a cannabinoid CB2 receptor agonist, on LIDs. Utilizing a mouse model of PD and LIDs, induced by 6-OHDA and subsequent l-dopa treatment, we show that HU-308 reduced LIDs as effectively as amantadine, the current frontline treatment. Furthermore, treatment with HU-308 plus amantadine resulted in a greater anti-dyskinetic effect than maximally achieved with HU-308 alone, potentially suggesting a synergistic effect of these two treatments. Lastly, we demonstrated that treatment with HU-308 and amantadine either alone, or in combination, decreased striatal neuroinflammation, a mechanism which has been suggested to contribute to LIDs. Taken together, our results suggest pharmacological treatments with CB2 agonists merit further investigation as therapies for LIDs in PD patients. Furthermore, since CB2 receptors are thought to be primarily expressed on, and signal through, glia, our data provide weight to suggestion that neuroinflammation, or more specifically, altered glial function, plays a role in development of LIDs.