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Ketamine and Parkinson´s disease

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Ketamine is an anesthetic that has been widely used in children and adults for decades. New applications of its known pharmacodynamics support its utility as multifaceted and life-saving drug. There is a range of new studies for the prophylactic or therapeutic role of ketamine in the drug-induced hyperalgesia, refractory pain, lung injury induced by mechanical ventilation and other inflammatory events, psychiatric disorders, antitumor, motor symptoms and neurodegeneration and others. Clinical and basic research have demonstrated that ketamine's action involves inhibition of NMDA and HCN1, upregulation of the AMPA receptors, decreases in the serotonin transporter activity, reduction in the production of Tumor necrosis factor α (TNF-α) and interleukin (IL)-6, inhibits transcription factor activator protein-1 and nuclear factor-κB (NF-κB) which regulates the production of proinflammatory mediators as COX-2 (Cyclooxygenase 2) and iNOS protein, inhibits TNF-α gene expression also by NF-κB suppression and acts on many other receptors and inflammatory cascades. The large variety of the ketamine effects relies on many factors. There are many plasma drug concentration-time curve for different administration routes and clinical conditions. Many specific effects accounts for chirality and its distinct isomers. Ketamine is a racemic mixture of R-ketamine and S-ketamine. S-ketamine has greater analgesic and anesthetic action than R-ketamine. Additionally, its metabolism generates hydroxynorketamine and activation of downstream synaptogenic signaling pathways. The ketamine effects on the nervous system include depressive disorder therapy and neuroprotective activity in stroke, neurotrauma, subarachnoid hemorrhage and status epilepticus. Studies have focus on its applications for excitotoxicity, neuroinflammation, and neuronal hyperexcitability. Sherman and Cols, 2016, reported on subanesthetic intravenous ketamine infusion treatment in Parkinson's Disease patients by 5 case studies. They demonstrated the long-lasting therapeutic benefit to reduce L-DOPA-induced dyskinesia, improve on time, and reduced depression. We aimed to review the possible association between neurodegenerative, neuroinflammatory and immunological mechanisms of Parkinson´s Disease and the underlying benefits of ketamine.

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