L-DOPA treatment of Parkinson patients inhibits choroidal neovascularization in age related macular degeneration through dopamine D2 receptor activation

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Neovascular age-related macular degeneration (nAMD) remains a major cause of visual impairment, despite the continuous repeated intravitreal administration of anti-VEGF therapies that puts a considerable burden on patients, ophthalmologists and health care systems. Analyzing a retrospective cohort of more than one million nAMD patients receiving anti-VEGF treatment of the French nationwide insurance database, we here confirm that L-DOPA treated parkinsons disease (PD) patients have a significantly delayed age of onset for nAMD and reduced need for anti-VEGF therapies. Using MPTP-induced PD- and laser-induced nAMD- mouse models in combination with the standard PD treatment of L-DOPA / DOPA-decarboxylase inhibitor, we here demonstrate that an L-DOPA treatment-induced increase of dopamine receptor 2 (DR2) signaling, and not the PD itself, is likely responsible for the inhibition of choroidal neovascularization. While explaining an intriguing epidemiological observation, our findings show that systemic DR2 agonists might constitute a much sought after therapy to reduce the need for anti-VEGF therapy in nAMD patients.