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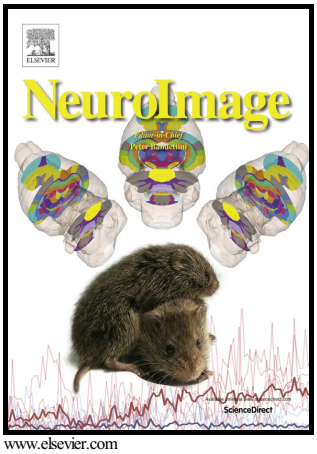

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Altered adenosine 2A and dopamine D2 receptor availability in the 6-hydroxydopamine-treated rats with and without levodopa-induced dyskinesia

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ABSTRACT

Several lines of evidence imply alterations in adenosine signaling in Parkinson's disease (PD). Here, we investigated cerebral changes in adenosine 2A receptor ($A_{2A}R$) availability in 6-hydroxydopamine (6-OHDA)-lesioned rats with and without levodopa-induced dyskinesia (LID) using positron-emission tomography (PET) with [^{11}C]preladenant. In parallel dopamine type 2 receptor (D_2R) imaging with [^{11}C]raclopride PET and behavioral tests for motor and cognitive function were performed. **Methods:** Parametric $A_{2A}R$ and D_2R binding potential (BP_{ND}) images were reconstructed using reference tissue models with midbrain and cerebellum as reference tissue, respectively. All images were anatomically standardized to Paxinos space and analyzed using volume-of-interest (VOI) and voxel-based approaches. The behavioral alternations were assessed with the open field test, Y-maze, novel object recognition test, cylinder test, and abnormal involuntary movement (AIM) score. In total, 28 female Wistar rats were included. **Results:** On the behavioral level, 6-OHDA-lesioned rats showed asymmetry in forepaw use and deficits in spatial memory and explorative behavior as compared to the sham-operated animals. 15-Days of levodopa (L-DOPA) treatment induced dyskinesia but did not alleviate motor deficits in PD rats. Intranigral 6-OHDA injection significantly increased D_2R binding in the lesioned striatum (BP_{ND}: 2.69±0.40 6-OHDA vs. 2.31±0.18 sham, +16.6%; p=0.03), whereas L-