β_3-adrenoceptor agonist protects dopaminergic neurons in the 6-hydroxydopamine model of Parkinson's disease.

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Oxidative stress has been implicated in the progression of neurodegenerative disorders, including Parkinson's disease. We have previously demonstrated that noradrenaline increases the level of intracellular glutathione (GSH) in astrocytes via β_3-adrenoceptor stimulation and protects co-cultured neurons from oxidative stress-induced death by increasing the supply of GSH from astrocytes. In addition, we have reported that the intraperitoneal administration of SR58611A, a β_3-adrenoceptor agonist, increases the level of GSH in ventral midbrain. In the present study, we investigated the effects of SR58611A on the degeneration of dopaminergic neurons induced by 6-hydroxydopamine (6-OHDA) in C57BL/6 mice. Mice were injected with 6-OHDA into the right striatum, and the degeneration of dopaminergic neurons was evaluated by tyrosine hydroxylase (TH) immunohistochemistry. At 14 days after the intrastriatal injection of 6-OHDA, the number of TH-positive cells was decreased in substantia nigra, and this decrease was attenuated by treatment with SR58611A (once a day 5 mg/kg, i.p. for 3 days). These results suggest that SR58611A attenuates 6-OHDA-induced degeneration of dopaminergic neurons by increasing brain GSH levels and that β_3-adrenoceptor agonists may be useful as novel therapeutic agents for the treatment of Parkinson's disease.