Differential regulation of dopamine release by *N*-methyl-D-aspartate receptors in rat striatum after partial and extreme lesions of the nigro-striatal pathway

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Abstract

The participation of *N*-methyl-D-aspartate (NMDA) receptors on dopamine(DA) efflux in the striatum of anaesthetized rats, which had their DAnigrostriatal pathway previously lesioned with different doses of 6-hydroxydopamine (6-OH-DA), was assessed by in vivo microdialysismethodology. In addition, the in vivo basal DA and dihydroxy-phenyl-acetic acid (DOPAC) effluxes and the effect of local K^+-depolarization on DA release were also evaluated in the striatum of these 6-OH-DA treated rats. Lesioned rats were divided in three groups corresponding to animals with 25–75%, 75–95% and >95% of striatum tissue DA depletion, respectively. Striatal DA tissue depletion between 25–75% occurred in parallel with a 30% reduction in DA extracellular levels, with a moderate 10% increase in basal fractional DA efflux, and with no statistical changes in the fractional DA efflux induced by NMDA (500 μM) receptor stimulation by reverse dialysis. Rats with higher DA tissue depletion (between 75–95%) exhibited a 60% reduction in DA extracellular levels in the striatum and this reduction occurred in parallel with a modest rise in basal fractional DA efflux, but with a striking decrease in the NMDA-induced fractional DA efflux. In rats with extreme or >95% of striatal DA tissue depletion, basal fractional DA efflux in the striatum increased quite substantially along with a recovery in the ability of NMDA receptor stimulation to induce fractional DA release. The >95% striatal DA-depleted rats also exhibited a significant decrease in tissue and extracellular DOPAC/DA ratio when compared to sham and partially DA-depleted rats. In contrast to the previous results, fractional DA efflux induced by reverse dialysis with K^+ (40 mM) remained the same in the striatum of sham and all groups of DA-tissue depleted rats. The present findings suggest the existence of at least three features associated to the regulation of basal and NMDA-induced extracellular levels of DA in the striatum of rats as a function of striatal tissue DA depletion produced by 6-OH-DA. They also support the view that a differential regulation of basal and NMDA-induced DA extracellular levels occur in partial and extreme DA-depleted striatum after 6-OH-DA treatment. Such findings may have implications as regard to the participation of the NMDA receptor in the compensatory mechanisms associated to the progress of Parkinson's disease, as well as in the therapeutic treatment of this neurological disorder.