Differential regulation of glutamate, aspartate and *γ*-amino-butyrate release by *N*-methyl-D-aspartate receptors in rat striatum after partial and extensive lesions to the nigro-striatal dopamine pathway

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Abstract

The in vivo microdialysis methodology was used to assess the effect of *N*-methyl-D-aspartate (NMDA) receptor ligands on glutamate (GLU), aspartate (ASP) and *γ*-aminobutyrate (GABA) extracellular levels in the striatum of anaesthetized rats, after damage to the dopamine (DA) nigrostriatal pathway by injections of different doses of 6-hydroxydopamine (6-OH-DA) seven days earlier. The 6-OH-DA treated rats were divided into two groups, corresponding to animals with 20–80% (partial) and 85–99% (extensive) striatal DA tissue depletion, respectively. In rats with partial DA depletion, the striatal extracellular ASP levels significantly increased after intrastriatal dialysis perfusion with MK-801 (100 μM), an antagonist of NMDA receptors. In addition, a change in the pattern of local NMDA (500 μM)- induced efflux of ASP was observed in the striatum of these rats. However, in these partially DA-depleted striata no changes were found in basal extracellular levels of GLU, ASP and GABA or in NMDA- and MK-801-mediated effluxes of GLU and GABA relative to striata from sham rats. In contrast, rats with extensive striatal DA depletion exhibited a significant increase in ASP and GABA extracellular striatal levels, after intrastriatal dialysis perfusion with NMDA. In addition, the MK-801-mediated stimulation of extracellular ASP levels was accentuated along with the appearance of a MK-801 mediated increase in extracellular striatal GLU. Finally, basal extracellular levels of ASP, but not of GLU and GABA, were found to increase in extensive DA-depleted striata when compared to sham and partially DA-depleted striata. Thus, a differential regulation of basal and NMDA receptor-mediated release of transmitter amino acids occur seven days after partial and extensive DA-depleted striatum by 6-OH-DA-induced lesions of the nigrostriatal DA pathway.

These findings may have implications as regards the participation of NMDA receptors in the compensatory mechanisms associated with the progress of Parkinson’s disease, as well as in the treatment of this neurological disorder.