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MMP-2 and MMP-9 in Drug-Provoked Developmental Neuroapoptosis

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Matrix metalloproteinases (MMPs) are zinc-dependent endoproteases with multiple roles in morphogenesis, cell death, and tissue regeneration. The aim of the present study was to investigate potential role of MMP-2/-9 in the pathogenesis of neuroapoptosis provoked by MK-801 or phenobarbital in the developing rodent brain. Seven-day-old rats or mice were drug-injected and pups were sacrificed at different survival times. Tissues from various brain regions were studied for expression of MMP-2/-9 by standard RT-PCR, western blotting, gelatin zymography and TUNEL immunohistochemistry. We found an increased number of TUNEL-positive cells 24 h after administration of MK-801 or phenobarbital. There was no significant increase in MMP-2/-9 mRNA expression, protein level or gelatinolytic activity observed in conjunction with drug-induced neuroapoptosis. The extent of neurodegeneration was not altered in MMP-9 TG rats and was increased in MMP-9 KO mice. Treatment with the broad metalloproteinase inhibitor GM6001 did not protect against drug-induced apoptosis. Our results suggest that activation of MMP-2/-9 does not contribute to pathogenesis of neuroapoptosis caused by NMDA antagonists or $GABA_A$ agonists in the developing rodent brain.

Key words: Matrix metalloproteinases, neuroapoptosis, MK-801, phenobarbital, GM6001.