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Anti-apoptotic effect of memantine against staurosporine- and low-potassium-induced cell death in cerebellar granule cells: a development-dependent effect

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Abstract:
Memantine, a NMDA receptor antagonist used in several experimental models of neuronal cell injury, is a neuroprotective agent that can attenuate neuronal apoptosis connected with over-stimulation of NMDA receptors. In the present study, we evaluated the impact of memantine on apoptosis in primary cerebellar granule cell (CGC) cultures at 7 and 12 day *in vitro* (DIV). Cell death was induced by staurosporine (St, 0.5 μM) or by decreasing the level of potassium in the culture medium (LP, 5 mM KCl). Both treatments induced cell death in CGC with higher cell-damaging effects at 12 DIV and 7 DIV neurons for St and LP, respectively. Memantine (0.1–2 μM) partially attenuated St-induced apoptosis only in 7 DIV CGC as assessed by DNA fragmentation and LDH release, but not caspase-3 activity. During LP-induced apoptosis, memantine decreased LDH release and DNA fragmentation, but not affected caspase-3 activity in 7 and 12 DIV CGC. Interestingly, we found no beneficial effects of other NMDA antagonists, including a competitive antagonist such as AP-5 (100 μM) and an uncompetitive antagonist such as MK-801, (1 μM). In conclusion, our data suggest that the anti-apoptotic effects of memantine in CGC are developmentally regulated and its neuroprotective action occurs through an NMDAR-independent mechanism.

Key words:
apoptosis, NMDA receptor, cerebellar neurons, caspase-3, MK-801, AP-5