Neuroprotective effects of vinpocetine and its major metabolite cis-apovincaminic acid on NMDA-induced neurotoxicity in a rat entorhinal cortex lesion model

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Vinpocetine (ethyl-apovincaminate, Cavinton), a synthetic derivative of the Vinca minor alkaloid vincamine, has been used now for decades for prevention and treatment of cerebrovascular diseases predisposing to development of dementia. Both vinpocetine and its main metabolite cis-apovincaminic acid (cAVA) exert a neuroprotective type of action. Bilateral N-methyl-D-aspartate (NMDA)-induced neurodegeneration in the entorhinal cortex of rat was used as a dementia model to confirm the neuroprotective action of these compounds in vivo. NMDA-lesioned rats were treated 60 min before lesion and throughout 3 postoperative days with a 10mg/kg intraperitoneal dose of vinpocetine or cAVA. Behavioral tests started after termination of drug treatment and consisted of novel object recognition, social discrimination, spontaneous alternation in Y-maze, and spatial learning in Morris water maze. After behavioral testing brains were perfused with fixative and the size of the excitotoxic neuronal lesion and that of microglial activation around the lesion assayed quantitatively on brain sections immunostained for neuron-specific nuclear protein (NeuN) and integrin CD11b, respectively. Entorhinal NMDA lesions impaired recognition of novel objects and the new social partner, and suppressed spontaneous alternation and spatial learning performance in the Morris maze. Both vinpocetine and cAVA effectively attenuated the behavioral deficits, and significantly decreased lesion size and the region of microglia activation. Both lesion-induced attention deficit and learning disabilities were markedly alleviated by vinpocetine and cAVA. The morphological findings corroborated the behavioral observations and indicated reduced lesion size and microglia activation especially after vinpocetine treatment which supports an in vivo neuroprotective mode of action of vinpocetine and a less potent action of cAVA.