Input from the medial septum regulates adult hippocampal neurogenesis

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Neural progenitors in the subgranular zone (SGZ) of the dentate gyrus (DG) of the hippocampal formation are continuously proliferating and new granule neurons are generated throughout adult life. The factors that control this process are largely unknown. In the present study, it was investigated whether a partial lesion of one of the main nuclei projecting to the hippocampus, the medial septum (MS), affects adult neurogenesis. Rats were injected with the thymidine analogue 5-bromo-2'-deoxyuridine (BrdU) and five days later excitotoxic lesion of the MS was applied by infusion of either 30 nmol or 60 nmol of N-methyl-D-aspartate (NMDA). NMDA infusion resulted in a significant reduction of the number of GABAergic cells one week after the lesion, whereas the cholinergic cells remained relatively unaffected. Only the highest concentration of NMDA significantly decreased the number of cholinergic cells. Hippocampal neurogenesis was significantly affected by MS lesion. The septohippocampal denervation reduced survival of newly generated cells with approximately 40%. Both concentrations of NMDA had opposite effects on the number of proliferating progenitors in the SGZ. Animals lesioned with 30 nmol of NMDA had more mitotic cells than the ones lesioned with 60 nmol. The present study reveals a function for the MS in the regulation of adult neurogenesis. The observation that excitotoxic lesion of the MS had a detrimental effect on both viability of GABAergic septal neurons and on survival of newly formed dentate granule neurons, suggests that GABA is a major factor in the survival of newly formed neurons.

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