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ROLE OF NEUROGENESIS IN DISTINGUISHING RELEVANT FROM IRRELEVANT MEMORIES

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Background: In this study we examine potential mechanisms by which the stimulation of hippocampal neurogenesis may generate an antidepressant effect.

Methods: Study-1: Adult male rats (N=24) were trained to segregate relevant from irrelevant spatial cues (spatial segregation); tested on this task four and 8-weeks later; then exposed (on week 8) to a modified version of the task that conflicted with the memory of the initially learned experience (mnemonic segregation); and then euthanized to detect hippocampal neurogenesis. Study-2: Adult rats (N=24) were trained in the spatial segregation task; three-days later, half were re-tested on the same task and half the tested on the modified task (mnemonic segregation); and euthanized immediately to detect neurons that were synaptically active during task performance.

Results: Study-1: Good performers on the modified task (mnemonic segregation) had significantly greater rates of hippocampal neurogenesis, but the increase was only in immature neurons and not in new neurons that had completed maturation. Performance on spatial segregation task was unrelated to proficiency in mnemonic segregation or rates of neurogenesis. Study-2: Performance on the mnemonic segregation unrelated to neurogenesis rates, but inversely correlated to synaptic activation of mature hippocampal neurons, which in turn inversely correlated with immature neuron rates.

Conclusion: Taken together, the data suggests that neurogenesis facilitates detection of subtle changes to experiences established over several weeks (not days); this occurs prior to forming synapses; and maybe associated with suppression of mature hippocampal neurons that presumably mediate older, interfering, experiences.