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Modulation of Post-Traumatic Neurogenesis and Recovery by Ketamine

Abstract

Traumatic brain injury (TBI) is a devastating condition associated with long-term morbidity, including depression and memory deficits. Although most of the brain has limited regenerative ability after birth, neurogenesis continues in the adult hippocampus and is greatly increased after TBI, possibly contributing to functional recovery. Constitutive adult neurogenesis is modulated by a host of factors, including activation of neurotransmitter receptors and feedback from neighboring astrocytes, both of which influence neuronal stem cells and developing neurons. The N-Methyl-D-Aspartate-type glutamate receptor plays an essential role in the proliferation and survival of adult-born neurons, and is inhibited by several anesthetic drugs, including ketamine. Ketamine is increasingly being utilized in the management of TBI patients, and thus might potentially impact the neurogenic response and patient recovery after TBI. We hypothesize that ketamine exposure after TBI attenuates neurogenesis. To test this hypothesis, we are utilizing a mouse model of TBI in conjunction with post-injury ketamine infusion. Our preliminary data suggest that neurogenesis after TBI is indeed impaired by ketamine, which also appears to also induce a disproportionate reduction in astrocyte formation after injury. We will conduct behavioral analyses on mice after TBI to determine whether ketamine exposure hampers hippocampal-dependent learning and mood-related behaviors during recovery. The findings of this study will bolster our knowledge of constitutive and post-injury neurogenesis and their clinical implications, and eventually guide TBI treatment choices to improve patient outcomes.