SYNAPTIC PHYSIOLOGY

Environmental influences

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Ongoing neurogenesis in specific regions of the adult brain can be modulated by physiological stimuli, such as exercise, and can also be upregulated by traumatic brain injury, but does the development of neurons in different contexts result in differences in their functional properties? New findings published by Lindvall and colleagues show that development in a pathological environment has a profound effect on the electrophysiological properties of adult-born hippocampal neurons.

Despite the promise of strategies to harness endogenous neurogenesis to repair the damaged brain, it is not yet clear whether the presence of these new-born neurons is beneficial or detrimental after injury. In particular, it is not clear whether neurons developing within the environment of the injured brain mature with the same properties as the neurons that they replace. To tackle this problem, the authors assessed the functional properties of neurons born in the subgranular zone (SGZ) of the dentate gyrus of rats following status epilepticus, a type of experimental damage known to upregulate hippocampal neurogenesis.

New-born neurons were labelled by injecting a retrovirus engineered to carry the gene for green fluorescent protein (GFP) into the hippocampus. Several weeks later, following migration and integration of the cells into the granule cell layer (GCL), GFP-labelled cells were examined using whole-cell patch clamp recordings. For comparison, in a second group of animals neurogenesis was stimulated non-pathologically using voluntary wheel running. Although the intrinsic membrane properties of the neurons were similar, there were significant differences in the synaptic properties of the newly integrated neurons in the two groups, highlighting the importance of the environment in which the neurons develop.

GCL neurons born after status epilepticus were shown to have a lower frequency of spontaneous excitatory postsynaptic currents, suggesting that overall excitatory synaptic input to these cells was reduced. Short-term plasticity, assessed by measuring paired-pulse facilitation of the postsynaptic response after repeated stimulation of an incoming excitatory pathway, was also modified at synapses on neurons born after injury. In agreement with these findings, the authors demonstrated that the probability of glutamate release was reduced at these synapses. By contrast, the new-born cells had increased inhibitory input and paired-pulse depression was reduced at inhibitory synapses. The authors showed that this was at least in part due to a decrease in $GABA_B$ (γ-aminobutyric acid type B) receptor expression or sensitivity.

This study provides an indication of the importance of the environment in which adult-born neurons differentiate for their functional properties. Further experiments will be required to determine the factors that are crucial for causing the effects of the epileptic brain on synaptic function and whether these new-born neurons benefit or harm the injured brain. However it is intriguing to note that the changes observed might be expected to reduce excitability in the epileptic brain, providing new hope for therapeutic strategies that are based on this approach.

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