Neuroprotection

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Brain injury evolves over time, often taking days or even weeks to fully develop. It is a dynamic process that involves immediate oxidative stress and excitotoxicity followed by inflammation and preprogrammed cell death. This talk will present a brief overview of mechanisms of neuroprotection in the developing brain. Although the focus is on ischemic injury, the conclusions drawn apply to any type of brain insult—epileptic seizures, trauma, or ischemia.

Strategies of neuroprotection include salvaging neurons through the use of targeted pharmacotherapies, protecting neurons through preconditioning, and repairing neurons by enhancing neurogenesis. Drug therapies and interventions like hypothermia that dampen the impact of immediate and downstream postinjury events are only modestly effective in protecting the brain from ischemic injury. In experimental models, complete or true protection can be achieved only through preconditioning, a process during which an animal develops tolerance to an otherwise lethal stressor. Although of no clinical use, preconditioning models have provided valuable insight into how repair systems work in the brain. Cumulative evidence indicates that the same genes that are upregulated during preconditioning, those mediating true protection, are also upregulated during injury and repair. Specifically, hypoxic preconditioning and hypoxic-ischemic insult have been shown to induce hypoxia inducible factor-1 (HIF-1) and its target survival genes, vascular endothelial growth factor (VEGF), and erythropoietin (Epo) in rodents. Of particular interest is the upregulation of Epo, a growth factor that may have therapeutic potential in the treatment of ischemic stroke. At this time, however, the postinjury enhancement of neurogenesis and angiogenesis appears to offer the best hope for long-lasting functional recovery following brain injury.

Bibliography

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