Cerebral Ischemia and the Developing Brain

Introduction

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The Princeton Conference has focused almost exclusively on cerebrovascular disease in the mature, or adult, brain. This session at the 25th Princeton Conference was quite unique in that the focus was on cerebral ischemia in the developing brain, ie, in both preterm and term infant. Hypoxic-ischemic injury to the developing brain is a major cause of acute mortality and chronic neurological morbidity in infants and children. Statistics suggest an incidence of systemic asphyxia in 2 to 4/1000 full-term births and an incidence approaching 60% in low birth weight, premature newborns.\textsuperscript{1,2} Between 20% to 50% of asphyxiated newborns with hypoxic-ischemic encephalopathy die within the newborn period, and up to 25% of the survivors go on to exhibit permanent neuropsychological handicaps, including mental retardation, cerebral palsy, epilepsy or learning disability. Care of the fetus and newborn human infant at risk for developing cerebral hypoxia-ischemia is clearly a high priority in current health care, and an understanding of the pathophysiology of perinatal hypoxic-ischemic brain damage is essential to the design of effective therapeutic interventions.

Much of our current understanding of the pathophysiology of hypoxic-ischemic brain damage derives from the vast body of experimental literature on stroke in the adult brain. From these studies, it is now well established that a cerebral hypoxic-ischemic event severe enough to cause cellular energy depletion initiates a cascade of events including early events of acidosis, glutamate excitotoxicity, and generation of reactive oxygen species, followed by prolonged periods of delayed cell death and inflammation.\textsuperscript{3} To a certain extent this cascade is also characteristic of hypoxic-ischemic damage in the immature brain but with some very notable, and important, differences. Whereas the immature brain has long been considered to be “resistant” to the damaging effects of hypoxia-ischemia, we now appreciate that this is not the case but that hypoxic-ischemic injury in the immature brain is different from that in the adult and actually exhibits periods of heightened sensitivity to injury depending on the developmental stage of the brain at the time of injury. Thus, it must be appreciated that the effects of the cascade of events initiated by hypoxia-ischemia will be determined by what normal developmental processes are occurring in the brain at the time of injury, and what developmental processes occur subsequent to the injury.

In this regard, hypoxic-ischemic injury to the preterm brain differs substantially to that in the term brain. Aspects and outcomes of injury along the developmental timeline are presented in this symposium.

References

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