OXIDATIVE AND ISCHEMIC DAMAGE IN THE HYPOTHALAMUS IS AN ATTRACTIVE TARGET FOR PREVENTION AND REPAIR OF HEAT STROKE

Chang CK

Department of surgery, Mackay Memorial Hospital, Taipei, Taiwan

Background-Oxidative and ischemic damage in the central nervous system has been associated with pathogenesis of many neurodegenerative disease models. Heat stroke is characterized by hyperthermia, central nervous system dysfunction, and multiorgan failure. We propose that oxidative and ischemic damage in the hypothalamus (the essential thermoregulatory center in the brain) may also be occurred during heat stroke.

Procedure-Heatstroke was induced by exposing the anesthetized rats to a high ambient temperature of 43°C until the moment at which mean arterial pressure decreased from its peak level and core temperature increased to a value of >42°C. The interval between the onset of heatstroke and animal death was defined as the survival time. In addition, unanesthetized and unrestrained mice were exposed to heat stress (42.4°C for 1 h) to induce heatstroke. Mice that survived on day of heat treatment were considered survivors. Results-In anesthetized rats, heatstroke induced hyperthermia, hypotension, and oxidative and ischemic damage to the hypothalamus. Heat shock preconditioning (40°C for 15 min) or regular, daily exercise for at least 3 weeks significantly induced overproduction of heat shock protein 72 and resulted in reduction of the heatstroke induced hyperthermia, hypotension, and hypothalamic oxidative and ischemic damage as well as prolongation of survival time. Free radical scavengers, brain cooling, or hypervolemic hemodilution is also found to be effective for prevention and repair of ischemic and oxidative damage in the hypothalamus during heatstroke. When transgenic mice that heterozygous for a porcine heat shock protein 72 gene ([+]HSP72) underwent heat, their fraction survival was found to be 12 of 12. However, transgenic negative littermate controls ([−]HSP72) had the fraction survival of 0/12 accompanied by thermoregulatory deficits and increment of ischemic and oxidative damage in their hypothalami. Conclusions-Our results indicate that oxidative and ischemic damage in the hypothalamus is an attractive target for prevention and repair of heatstroke.