



Synergistic interaction between zinc and reactive oxygen species (ROS) amplifies ischemic brain injury in rats. This study delineates an ordered sequence and dynamic relationship between zinc and ROS that leads to dramatic neuronal death after cerebral ischemia. Cerebral ischemia causes zinc release, which in turn both activates neuronal NADPH oxidase and increases mitochondrial ROS production. ROS produced by NADPH oxidase leads to further increased zinc accumulation, thus creating “zinc-ROS-zinc” feedback loop that causes greater brain injury. These findings provide a novel mechanism explaining cerebral ischemia damage and an effective and viable new target for treating ischemic stroke.