Iron and oxidative stress in AD

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Iron is a potent source of the highly reactive hydroxyl radical generated by the Haber-Weiss reaction with H2O2, which in turn is produced by the enzyme superoxide dismutase from superoxide and water. Increasing evidence indicates that reactive oxygen species (ROS), including superoxide and hydroxyl radicals, play a critical role in the alterations in brain function observed in AD. Because iron is important for the formation of hydroxyl radicals, this metal is thought to be involved in the mechanisms of oxidative damage in AD. Cerebral blood vessels are particularly susceptible to oxidative damage and cerebrovascular dysfunction is emerging as a critical pathogenic factor in the mechanisms of AD. An important source of ROS in AD is the enzyme NADPH oxidase, a multiunit enzyme originally discovered in neutrophils, but enriched in cerebral blood vessels. Mice lacking the NADPH oxidase subunit NOX2 are resistant to the cerebrovascular dysfunction induced by amyloid beta and genetic deletion of NOX2 is markedly beneficial in mouse models of AD. Collectively, these observations highlight the critical role that iron and related oxidative stress play in the mechanisms of AD.