Neuronal Damage Induced by Perinatal Asphyxia Is Attenuated by Postinjury Glutaredoxin-2 Administration

Romero J.I.

Holubiec M.I.

Tornatore T.L.

Rivière S.

Hanschmann E.-M.

Kölliker-Frers R.A.

Tau J.

Blanco E.

Galeano P.

Rodríguez De Fonseca F.

Lillig C.H.

Capani F.

The general disruption of redox signaling following an ischemia-reperfusion episode has been proposed as a crucial component in neuronal death and consequently brain damage. Thioredoxin (Trx) family proteins control redox reactions and ensure protein regulation via specific, oxidative posttranslational modifications as part of cellular signaling processes. Trx proteins function in the manifestation, progression, and recovery following hypoxic/ischemic damage. Here, we analyzed the neuroprotective effects of postinjury, exogenous administration of Grx2 and Trx1 in a neonatal hypoxia/ischemia model. P7 Sprague-Dawley rats were subjected to right common carotid ligation or sham surgery, followed by an exposure to nitrogen. 1 h later, animals were injected i.p. with saline solution, 10 mg/kg recombinant Grx2 or Trx1, and euthanized 72 h postinjury. Results showed that Grx2 administration, and to some extent Trx1, attenuated part of the neuronal damage associated with a perinatal hypoxic/ischemic damage, such as glutamate excitotoxicity, axonal integrity, and astrogliosis. Moreover, these treatments also prevented some of the consequences of the induced

neural injury, such as the delay of neurobehavioral development. To our knowledge, this is the first study demonstrating neuroprotective effects of recombinant Trx proteins on the outcome of neonatal hypoxia/ischemia, implying clinical potential as neuroprotective agents that might counteract neonatal hypoxia/ischemia injury.