Temporal window of metabolic brain vulnerability to concussions: oxidative and nitrosative stresses--part II.


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Abstract

OBJECTIVE: In the present study, we investigated the occurrence of oxidative and nitrosative stresses in rats undergoing repeat mild traumatic brain injury (mTBI) delivered with increasing time intervals.

METHODS: Rats were subjected to two diffuse mTBIs (450 g/1 m height), with the second mTBI delivered after 1 (n = 6), 2 (n = 6), 3 (n = 6), 4 (n = 6), or 5 days (n = 6). The rats were sacrificed 48 hours after the last mTBI. Sham-operated animals were used as controls (n = 6). Concentrations of biochemical indices of oxidative stress (malondialdehyde, ascorbic acid, reduced and oxidized glutathione) and nitrosative stress (nitrite, nitrate) were synchronously measured by high-performance liquid chromatography in deproteinized tissue extracts (three right + three left hemispheres for each group of animals).

RESULTS: Increase of malondialdehyde, reduced/oxidized glutathione ratio, nitrite, nitrate, and decrease of ascorbic acid and glutathione were dependent on the interval between impacts with maximal changes recorded when mTBIs were spaced by 3 days. Biochemical markers of oxidative and nitrosative stresses were near control levels only in animals receiving mTBIs 5 days apart.

CONCLUSION: This study shows the remarkable negative contribution of reactive oxygen species overproduction and activation of inducible nitric oxide synthase in repeat mTBI. Because these effects were maximal when mTBIs were spaced by 3 days, it can be inferred that occurrence of a second mTBI within the temporal window of brain vulnerability not only causes profound derangement of mitochondrial functions, but also induces sustained oxidative and nitrosative stresses. Both phenomena certainly play a major role in the overall brain tissue damage occurring under these pathological conditions.

PMID: 17806141 [PubMed - indexed for MEDLINE]