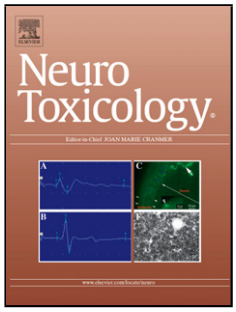

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Inhibition of NRF2 signaling and increased reactive oxygen species during embryogenesis in a rat model of retinoic acid-induced neural tube defects

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Highlights

- Oxidative stress is induced and NRF2 signaling is inhibited in atRA-induced NTDs.
- NRF2 inhibition weakens cellular defenses against atRA-induced oxidative stress.
- NRF2 signaling plays an important role in the occurrence of atRA-induced NTDs.
- NRF2 activation should be considered for NTD prevention and treatment.

ABSTRACT

Exposure to retinoic acid (RA) during pregnancy increases the risk of serious neural tube defects (NTDs) in the developing fetus. The precise molecular mechanism for this process is unclear; however, RA is associated with oxidative stress mediated by reactive oxygen species. Nuclear factor erythroid 2-related factor 2 (NRF2) is a master regulator of oxidative stress that directs the expression of antioxidant genes and detoxifying proteins to maintain redox homeostasis. We established a rat model of NTDs in which pregnant dams were administered all-