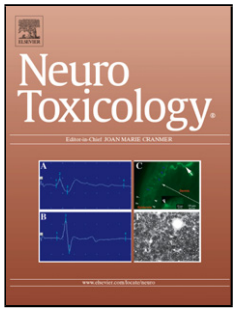

Title: Sex modulated effects of sarin exposure in rats: toxicity, hypothermia and inflammatory markers

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Sex modulated effects of sarin exposure in rats: toxicity, hypothermia and inflammatory markers.

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Highlights

- Sex modulates toxicity of sarin exposure in rats.
- Sarin induced deeper acute hypothermia in males but slower recovery in females.
- Sex modulates sarin-induced increase in plasma and brain inflammatory markers.

Abstract

This work focused on sex differences in rats exposed to sarin. Females were found to be more sensitive to sarin toxicity (LD50 67µg/kg) than males (88µg/kg), showed less acute hypothermic effects than males **(**at 120 min post sarin, 3.1±1.1 and 4.5±1ºC decrease, respectively), but with a significant slower recovery over days. Females' temperature response to the cholinergic agonist oxotremorine (0.25 mg/kg, im) was more pronounced than that of males (at 30 min, 3.13±0.27 and 2.13±0.19ºC decrease, respectively) and both sexes recovered within 2h of exposure. 24h after sarin exposure (80 µg/kg followed 1 min later by TA treatment (TMB4 7.5 mg/kg and atropine 5 mg/kg)) a 255% increase in plasma MCP-1 in males but not in females was recorded. In the brain, TIMP-1 increased 43 fold in females and 25 fold in males, compared to control rats. MCP-1 increased 8 fold in females only. TNFα increased in both sexes, but the increase in female brain was higher than that recorded in males. IL-6 increased in females but not in males. IL-1β increased in both sexes. This work clearly demonstrates significant sex modulation effects on measures of toxicity, hypothermia and inflammatory markers in brain and plasma 24 h following exposure to sarin. In general, females seem to be more sensitive to the toxicity of sarin, but may be better protected against