Arsenic-induces cognitive dysfunctyion through disruption of estrogen signalling: Resveratrol to the rescue?

Kamakshi Mehta
The University of New Mexico Health Sciences Center, USA

Prolonged inorganic arsenic (iAs) exposure induces deleterious effects on brain including oxidative stress, cognitive dysfunction and neurochemical changes. Little is known about the association between iAs and estrogen receptor regulation in brain areas. Owing to the neuroprotective and estrogenic activities of resveratrol (RES), we examined the combined effects of arsenic trioxide (As2O3) and RES on neurobehavioural functions, estrogen signalling and associated neurochemical alterations in mouse hippocampus. As2O3 alone (2 and 4 mg/kg bw) or along with RES (40 mg/kg bw) was administered orally for 45 days to adult female mice. From days 33 to 45, open field, elevated plus maze and Morris water maze tests were conducted to evaluate locomotion, anxiety and learning and memory. On day 46, animals were euthanized and brain tissue and hippocampi obtained therefrom were processed for atomic absorption spectrophotometry and western blotting respectively. As2O3 alone exposure resulted in enhanced anxiety levels, reduced locomotion and impaired learning and memory. As2O3 -induced behavioural deficits were accompanied by downregulation of estrogen receptor (ERα) expression with a concomitant reduction of BDNF and NMDAR 2B levels in the hippocampus. However, the behavioural alterations and expression of these markers were restored in RES-supplemented mice. Moreover, a dose-dependent iAs accumulation was observed in serum and brain tissues of mice receiving As2O3 alone whereas simultaneous administration of As2O3 with RES facilitated iAs efflux. Together, our findings indicate that reduced ERα expression with associated downregulation of BDNF and NMDAR 2B levels could be a potential mechanism by which iAs induces cognitive impairment; hence, the modulation of estrogen-NMDAR-BDNF pathway by RES represents a potential avenue to recover behavioural deficits induced by this neurotoxin.

Biography

Dr. Kamakshi has completed her PhD in the subject of Anatomy at the age of 28 years from All India Institute of Medical Sciences (New Delhi, India) and currently pursuing her postdoctoral fellowship from The University of New Mexico, School of Medicine. My current research work intends to understand the role of hyperhomocysteinemia in the progression of age-associated neurological diseases like stroke. Additionally, the research aims to determine how predisposition to hyperhomocysteinemia impacts the outcome of cerebral stroke and to develop potential therapeutic targets to mitigate ischemic brain injury under hyperhomocysteinemic condition. My previous work dealt with the arsenic-induced adverse effects in various brain regions and our lab made an attempt to explore the neuroprotective activities of plant-based polyphenols like curcumin and resveratrol agaisnt arsenic-induced neurotoxicity. I have published more than 5 manuscripts in reputed journals and my research work has been awarded by various prestigious associations of neuroscience and toxicology as well.

Received: January 20, 2022; **Accepted:** January 22, 2022; **Published:** March 25, 2022