

Cholinergic system: a new target of uranium after chronic exposure

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Memory, learning and sensorimotor are govern by cerebral cortex which is a cholinergic widespread structure. Previous studies showed that sleep/wake cycle, spatial memory and locomotion were impaired after a chronic exposure to depleted uranium (DU) and enriched uranium (EU). The aim of this study was to establish if these physiological disruptions came from a cholinergic system alteration. Rats ingested DU or EU by drinking water at 40 mg/L during 1.5 or 9 months. Cortex was removed then gene expression and protein level were analysed to assess potential changes in acetylcholine, acetylcholinesterase (AChE), butyrylcholinesterase (BuChE), and cholinergic receptors. After short term exposure, Ach levels decreased significantly after DU (-22%) and EU (-25%). Concerning AChE, its gene expression (-70%) and activity (-7%) decreased after EU but not after DU. However, the other breakdown enzyme, BuChE, was decreased (-40%) after DU only. Any variation has been observed on cholinergic receptors. After long term exposure, Ach levels increased significantly (+9%) after EU but not DU. AChE was not affected by DU or EU exposure except gene expression (+28%) after DU. Concerning gene expression of cholinergic receptors, muscarinic type 1 increase after DU (X10) and nicotinic receptors increased after EU (X2.5). These results demonstrate for the first time that cholinergic system is a target of uranium. However, isotopic components of uranium and exposure time induced different responses which must be explained. These cholinergic disturbances could be a track to understand how uranium acts on the rats' behaviour, notably on spatial memory and sleeping.