World Academy of Science, Engineering and Technology
International Journal of Cognitive and Language Sciences
Vol:10, No:04, 2016

Effect of Toxic Metals Exposure on Rat Behavior and Brain Morphology: Arsenic, Manganese

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Abstract : Heavy metals remain one of serious environmental problems due to their toxic effects. The effect of arsenic and manganese compounds on rat behavior and neuromorphology was studied. Wistar rats were assigned to four groups: rats in control group were given regular water, while rats in other groups drank water with final manganese concentration of 10 mg/L (group A), 20 mg/L (group B) and final arsenic concentration 68 mg/L (group C), respectively, for a month. To study exploratory and anxiety behavior and also to evaluate aggressive performance in "home cage" rats were tested in "Open Field" and to estimate learning and memory status multi-branched maze was used. Statistically significant increase of motor and oriental-searching activity in experimental groups was revealed by an open field test, which was expressed in increase of number of lines crossed, rearing and hole reflexes. Obtained results indicated the suppression of fear in rats exposed to manganese. Specifically, this was estimated by the frequency of getting to the central part of the open field. Experiments revealed that 30-day exposure to 10 mg/ml manganese did not stimulate aggressive behavior in rats, while exposure to the higher dose (20 mg/ml), 37% of initially non-aggressive animals manifested aggressive behavior. Furthermore, 25% of rats were extremely aggressive. Obtained data support the hypothesis that excess manganese in the body is one of the immediate causes of enhancement of interspecific predatory aggressive and violent behavior in rats. It was also discovered that manganese intoxication produces non-reversible severe learning disability and insignificant, reversible memory disturbances. Studies of rodents exposed to arsenic also revealed changes in the learning process. As it is known, the distribution of metal ions differs in various brain regions. The principle manganese accumulation was observed in the hippocampus and in the neocortex, while arsenic was predominantly accumulated in nucleus accumbens, striatum, and cortex. These brain regions play an important role in the regulation of emotional state and motor activity. Histopathological analyzes of brain sections illustrated two morphologically distinct altered phenotypes of neurons: (1) shrunk cells with indications of apoptosis - nucleus and cytoplasm were very difficult to be distinguished, the integrity of neuronal cytoplasm was not disturbed; and (2) swollen cells - with indications of necrosis. Pyknotic nucleus, plasma membrane disruption and cytoplasmic vacuoles were observed in swollen neurons and they were surrounded by activated gliocytes. It's worth to mention that in the cortex the majority of damaged neurons were apoptotic while in subcortical nuclei –neurons were mainly necrotic. Ultrastructural analyses demonstrated that all cell types in the cortex and the nucleus caudatus represent destructed mitochondria, widened neurons' vacuolar system profiles, increased number of lysosomes and degeneration of axonal endings.

Keywords : arsenic, manganese, behavior, learning, neuron
Conference Title : ICBPCS 2016 : International Conference on Behavioral, Psychological and Cognitive Sciences
Conference Location : Paris, France
Conference Dates : April 25-26, 2016