



Neurotoxicity of heavy metals (aluminum chloride) studies performed on rats wistar

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Abstract

Every day we are exposed to toxic heavy metals that pose a health risk, in an invisible way. All heavy metals are naturally present in trace amounts in our environment such as Aluminum chloride (AlCl₃). Heavy metals are a metal element characterized by a high density greater than 5g per cm³. They are present everywhere in the environment most often in very small quantities; They accumulate in living organisms and disturb balances and biological mechanisms accumulate in the body and cause toxic effects. They can affect the nervous system, kidney, liver, respiratory or other functions. The aim of this study was to reveal the effects of aluminum chloride (AlCl₃) on the architecture of Cerebral Cortex. In our study, twenty healthy female rats were intraperitoneally administered of aluminum chloride (ALCL₃) at 10 mg / kg body weight with consecutively for 5 days, 10 day, 15 day. The results showed a significant reduction in body weight. This is because aluminum has an anorectic effect. The histological study present the alterations in the brain marked tissue necrosis and cytoplasmic vacuolations and karyopyknosis of neuronal cells of the Cerebral Cortex.

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Introduction

Heavy metal is a metal element characterized by a high density greater than 5g per cm³. They are present everywhere in the environment most often in very small quantities. One of the most commonly toxic metals studied, aluminum (Al). Al is a highly abundant and ubiquitously distributed as environmental and industrial toxicant and is also contained in many food products, (S. Han *et al.* 2013), medicines, it is also added to drinking water for purification purposes (Newairy *et al.* 2009). And is widely used in antacid drugs, as well as, tooth paste (Abbasali *et al.* 2005). It has been shown clearly that aluminum accumulates in various tissues including brain, bone, kidneys, muscle, and heart such as brain, bone, liver (Wills *et al.* 1993; Sahin *et al.* 1994, Anthony *et al.* 1986; Nayak. 2002).

The brain is one of the largest and most complex organs in the human body. It is made up of more than 100 billion nerves that communicate in trillions of connections called synapses.

The cerebral cortex is the biggest part of the brain. This large and complicated neural circuit is involved in most of the brain's highest functions, such as memory, language and sight. In man and higher animals, modifications of behaviour are due to cortical activity. (Pavlov. 1927). The brain regions particularly affected by Al neurotoxicity include those involved in memory and learning. This may be due to the specific distribution of transferrin receptors (tfrs) and neuroanatomical connections between brain regions important for cognitive processes (Veer Bala Gupta *et al.* 2005). Brain is a preferential site of Al accumulation in both gray and white matter, mainly at some cortical regions and hippocampus (Kawahara. 2005; Miu *et al.* 2003; Walton, 2009). Although chronic intoxications are closer to the situation in which humans are contaminated in the polluted environment it has been shown that acute Al intoxication causes encephalopathy in humans (Perazella and Brown. 1993; Berend *et al.* 2001) and neuropathological changes (Forrester and Yokel, 1985; Kumar, 1998) as well as damage to other organs

(El-Sayed *et al.*, 2011) in experimental animals. The neurotoxic effects of Al compounds are related to a preferential tropism of this metal for CNS structures (Oteiza *et al.* 1993; Zatta *et al.* 1993) In the CNS, Al can interfere with several physiological processes, inducing damage by oxidative stress, membrane biophysics alterations, deregulation of cell signaling, and impairment of neurotransmission (Pohl *et al.* 2011; Verstraeten *et al.* 2008).

Materials and methods

The ground-breaking studies on Al neurotoxicity in experimental animals were initially described in 1886 by Siem and Dollken (Terry R. D, 1965).

Twenty (20) female wistar rats were selected for this experiment.

The wistar rats were housed in a stainless steel cages maintained at standard environmental conditions (12h-12h light-dark cycle with light on at AM) with sufficient food, water and under good ventilation.

All the rats were acclimatized for 1 week before the test, and randomly divided into four equal groups:

Control group I was given NaCl 0.9.

Group II received 10mg/Kg body weight ALCL₃ for five days (5D).

Group III received 10mg/Kg body weight ALCL₃ ten days (10D).

Group IV received 10mg/Kg body weight ALCL₃ five teen days (15D).

Aluminum chloride administered to female rats via injection intraperitoneally.

The wistar rats were humanely sacrificed by anesthetizing them in a suffocating chamber using chloroform, after the end of the experiment, animals were sacrificed by decapitation and brain were immediately removed and immediately fixed in 10% formalin. After fixation, the tissues were transferred

into an automatic processor where they went through a process of dehydration in ascending grades of alcohol (ethanol) 70%, 80%, 95% and absolute alcohol for 2 changes each. The tissues were then cleared in xylene and embedded in paraffin wax. Serial sections of 5 micron thick were obtained using a rotary microtome. The tissue sections were deparaffinised, hydrated and stained using the routine haematoxylin and eosin staining method (H&E). The stained sections were examined under the light microscope fitted to a digital camera and lap top. The histological sections of the gonads were made in the pathology laboratory of hospital Abdelkader Hassani in Sidi Belabbes.algeria

Result

The tissue was processed and stained with Haematoxylin and eosin (H&E).

The stained sections of cerebral cortex were examined under the light microscope. No rats died during the experiment.

Photomicrographs of rat brain sections stained with haematoxylin and eosin (bar=25 μ m). The normal histological structure of Cerebral Cortex in rats brain with intact neurons and glial cell were seen in control animals. (Fig. 01- Fig. 02).

Group II treated showed slight sign of degeneration with slight cell distortion karyopyknosis of neuronal cells (pyramidal cell) Fig. 03

Photomicrographs of rat brain sections $AlCl_3$ intoxication (group 03) resulted in severe necrosis and vacuolation of the cerebral cortex. (Fig. 04-p Fig. 05)

Our results show that The sub chronic administration of Aluminum chloride in the experimental groups have shown some level of neurodegeneraion (necrosis) on the hippocampus of the treated rats (Fig. 3-4-5) when compared with the control group I (Fig. 1 and 2).

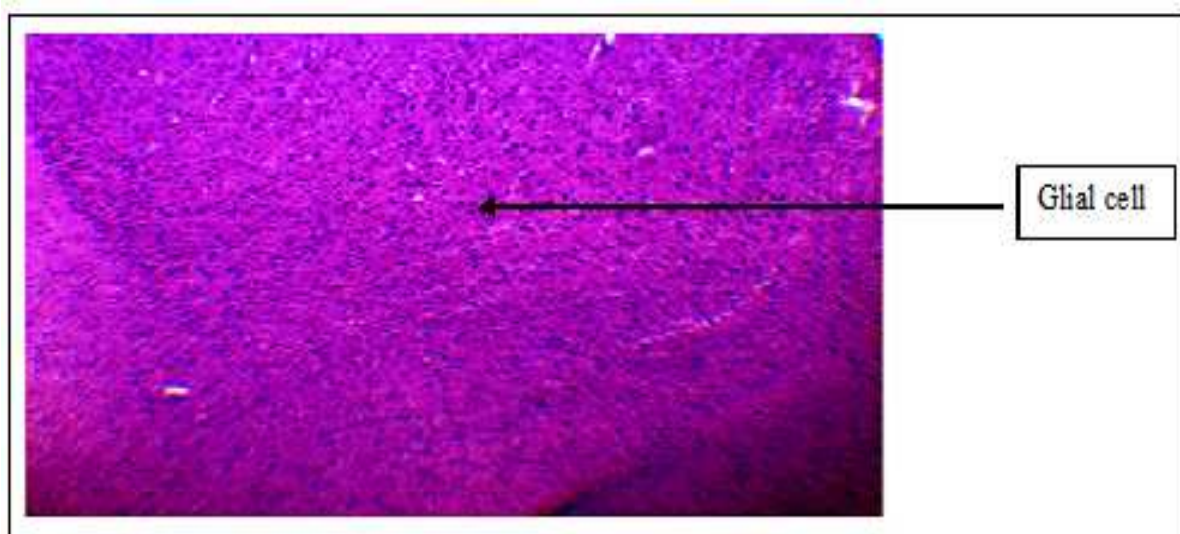


Fig. 1. Histological sections of Cerebral Cortex tissue in rats brain stained with H&E (control group).x10.

In the present study, $AlCl_3$ exposure caused brain histopathological lesions

Discussion

Toxic metals, pesticides, and phenols are considered major environmental pollutants. The cerebral cortex is the key structures of memory formation. It also integrates higher mental functions, general

movement, visceral functions, and behavioral reactions. (Brodal .1977; Cauller . 1995).

In this study, we have investigated neuropathological effects of the sub chronic experimental intoxication of adult rats with $AlCl_3$. a variety of changes were observed in the brains of Al-infused animals compared with controls.

Histological sections of the cerebral cortex in group II and group III illustrate that there is a cell degeneration, vacuolation and a necrosis

characterized by fibrosis (Fig. 03-05) compared to control lot who present a large number of normal neurons accompanied by glial cells.

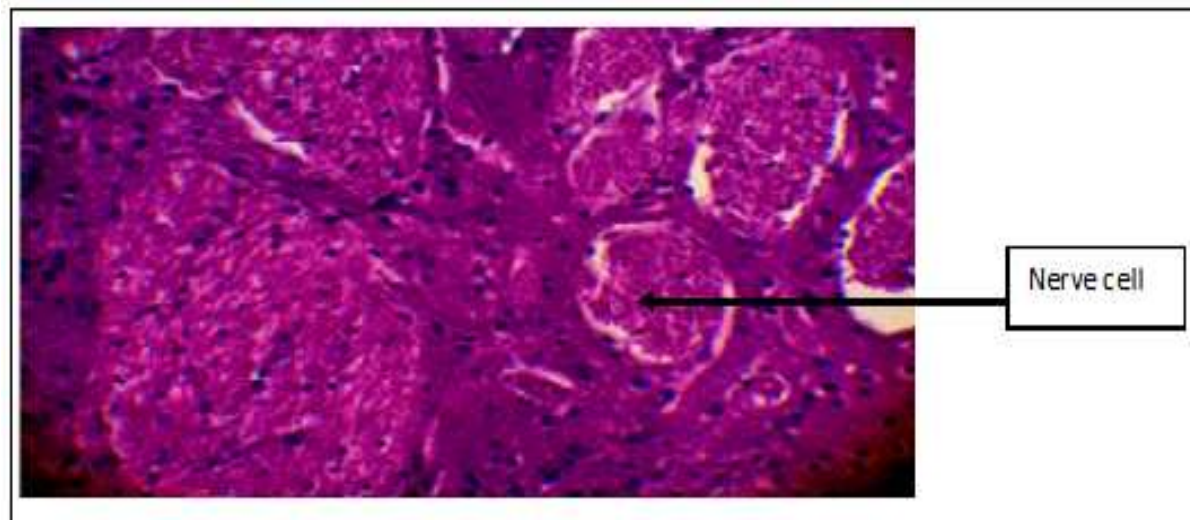


Fig. 2. Histological sections of Cerebral Cortex in rats' brain stained with H&E (control group).x100.

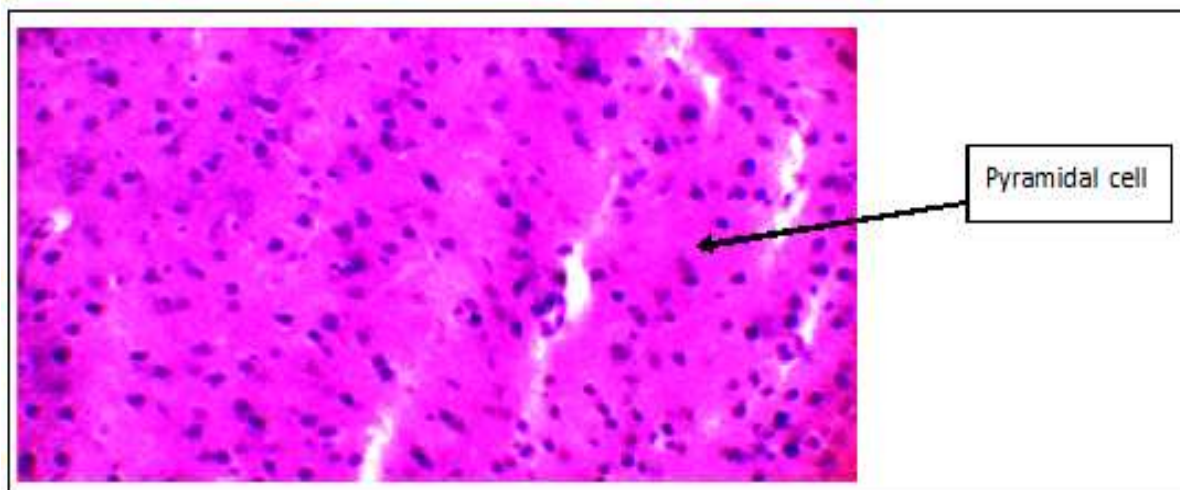


Fig. 3. Histological sections in rats brain showing slight neuronal fibrosis *karyopyknosis of neuronal cells* of the Cerebral Cortex of wistar rats of group I, stained with H&E. X40.

Microscopic observation of histological sections in the brain of rats and their offspring reveals the effect action of aluminum chloride.

This effect is reflected in tissue architecture by neuronal vacuolation and necrosis of the brain our results are similar to those of Buraimohet *al* (2012b) who demonstrated that exposure of rats to AlCl₃ for eight weeks would induce severe neurodegeneration at the level of the hippocampus demonstrated by histological studies. According to Crapper *et al.*

(1980) aluminium concentration was elevated in neurons containing neurofibrillary tangles and perhaps within senile plaques, however, aluminium might accumulate in neurons.

Secondarily to intracellular degenerating changes and the neuropathological and behavioural changes following the aluminium exposure were similar to those observed in Alzheimer's disease,

This is in line with Muller *et al.* (1990), who suggested

that aluminium might have a role in the pathogenesis of Alzheimer's disease although based on circumstantial evidence. We therefore concluded that

administration of aluminium chloride has a neurodegenerating effects (damage) on the hippocampus of wistar rats as shown in Fig. 3-5.

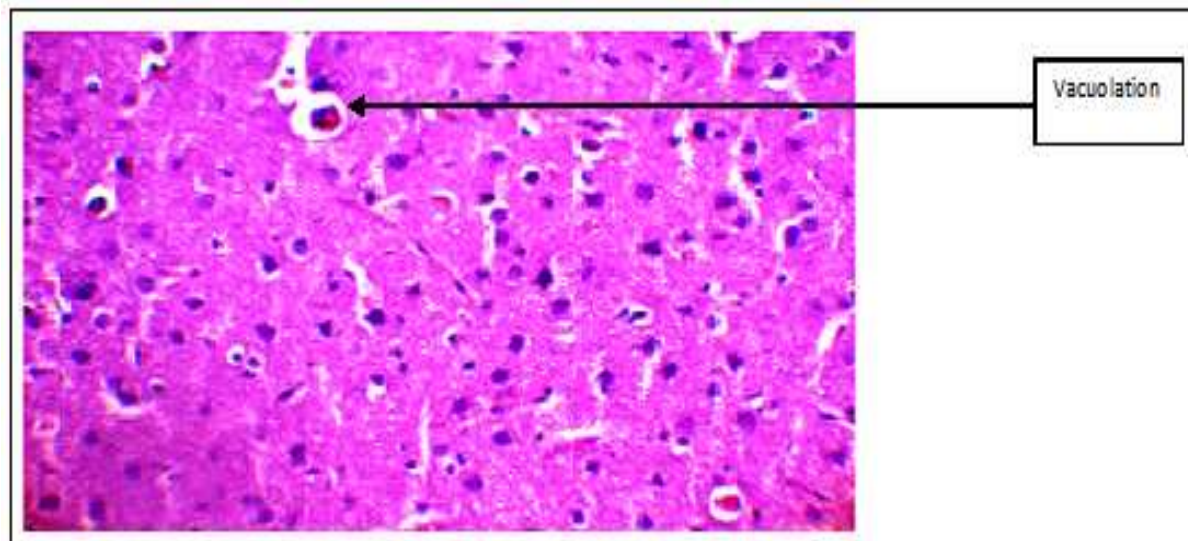


Fig. 4. Histological sections in rats brain showing slight neuronal vacuolation of the Cerebral Cortex of wistar rats of group II, stained with H&E. X40.

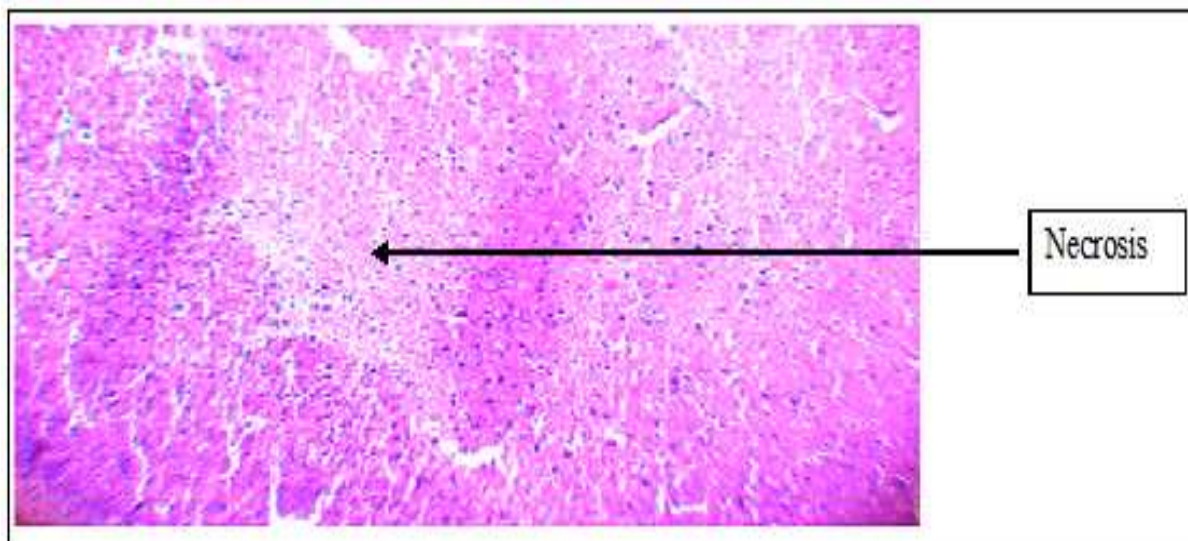


Fig. 5. Histological sections showing necrosis of the Cerebral Cortex in rats' brain of group III stained with H&E.X10.

Conclusion

The omnipresence of heavy metals in our environment at higher and higher concentrations and their significant toxicity to human health makes this source of pollution an increasingly important public health problem in our society. Toxic metals are classified as non-biodegradable substances, as well as plastics and detergents, because they are not

degraded by microorganisms. Among these heavy metals there are Aluminum which is a highly reactive element and ubiquitous environmental contaminant has been associated with some diseases. Such as Alzheimer's and Parkinson's Disorders (Miguel *et al.* 2015). We have reviewed the neurotoxicology of one common environmental neurotoxicants, with chloride aluminum our results reported that

aluminum chloride (AlCl₃) 10 mg/pc capable of caused marked alterations in most complex organs in the human body (brain). Shown some level of neurodegeneraion in cortex cerebral Toxic metals represent a global health risk because of their ability to contribute to a variety of diseases Aluminum Involvement in Neurotoxicity the effects of metals on brain development have only recently drawn attention. Unfortunately, it appears that excess metal exposure may be a common source of neurotoxicity in multiple populations around the world.

Potential conflict of interest

There are no conflicts of interest, all authors are in agreement with the content of the manuscript. The authors confirm that our work does not violate the policies established by the journal The Author(s) warrants and affirms that:

The Manuscript is an original work and sole property of the Author(s) and that the manuscript has not been published elsewhere nor it is currently under consideration for publication by another journal.

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