

Effects of Oral Administration of Aluminium Chloride on the Histology of the Hippocampus of Wistar Rats

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Abstract: The study of the effects of oral administration of aluminium chloride on the Hippocampus of wistar rats was designed in order to ascertain whether the small daily amount of aluminium that gain access to the body produce any damage to the hippocampus. This investigation was carried out using 50 female adult wistar rats. The animals were divided into five groups; 10 rats per group (cage). Stock solution of aluminium chloride was prepared (2 g/L or 2 mg/mL). Different concentrations of aluminium were administered to different groups orally. Group I was control, while Groups II-V were given 0.4, 1, 2, and 3 mg, respectively per each rat with an average weight of between 150-200 g for duration of twelve (12) weeks. The animals were humanly sacrificed using chloroform and then the brain tissues were fixed immediately in Bouin's fluid. The brain sections (hippocampus) were processed through the routine tissue processor. The stained samples were examined by means of light microscope for histological changes. Histological examinations showed clumpy of cell neurons, or reduced pyramidal cells and scanty neurofibrillary tangle which was an indication of neurodegeneration in the treated groups when compared to the control. It was however, concluded that the oral administration of aluminium chloride could induce brain damage which may impair memory and learning as seen in Alzheimer disease.

Key words: Aluminium chloride, effects, hippocampus, oral administration, wistar rats

INTRODUCTION

Aluminium is present in small amounts in mammalian tissues, yet it has no recognized physical role. On the contrary, its neurotoxic effect on living organisms is becoming clear, aluminium being implicated as interfering with a variety of cellular metabolic processes in the nervous system and in other systems. Although molecular mechanisms by which aluminium exerts its neurotoxicity remain to be established, several pieces of evidence suggest that Aluminium can interfere with cellular metabolism in terms of biological stimulation, inhibition, or metal accumulation and compartmentation (Zattal *et al.*, 1991).

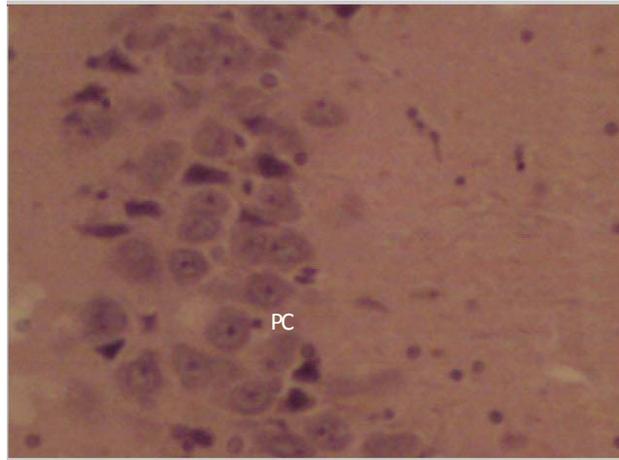
Aluminium, (Al), is ubiquitous in the environment and its extensive industrial utilization has stimulated considerable interest in the possible environmental toxicity of this metal. However, little is known about possible effects of Al as a trace element in animals and humans in normal conditions. It has recently become clear that when Al is mobilized from soil by acid rain, it poses a hazard to all exposed organisms (Beavon, 2004; Birchall *et al.*, 1989)

Williams (1992): Aluminium compound have been used for 30 years to control phosphate levels in patients

undergoing haemodialysis. The toxic effect arising from the absorption and accumulation of aluminium have well been documented and include a progressive encephalopathy which eventually leads to dementia. The hippocampus is a major component of the brains of human and other mammals. It belongs to the limbic system and plays important roles in long-term memory and spatial navigation. In humans and primates, the hippocampus is located inside the medial temporal lobe, beneath the cortical surface (Bradbury, 1992).

Al contributes to a variety of cognitive impairments in mice, rabbits, and rat pups (Muller *et al.*, 1990; Yokel, 1985; Bilkei-Gorzo, 1993; Mari, 2001). Studies on workers exposed to Al dust in industrial environments demonstrate similar effects (Rifat *et al.*, 1990; Bast-pettersen *et al.*, 1994; White *et al.*, 1992; Akila *et al.*, 1999). Many researchers have found elevated Al levels to be associated with a decline in visual memory, attention, concentration, frontal lobe function and lower vocabulary scores in hemodialysis patients (Bolla *et al.*, 1992).

The hippocampus as a whole has the shape of a curved tube, which has been analogized variously to a seahorse, a ram's horn (*Cornu Ammonis*, hence the subdivisions CA1 through CA4), or a banana. It can be



PC=Pyramidal cells
NC=Neuroglial cells

Plate 1: Showing the normal histology of the Pyramidal cell layers of the brain (Hippocampus) of wistar rat. Control section stained with H and E; mag. X 250

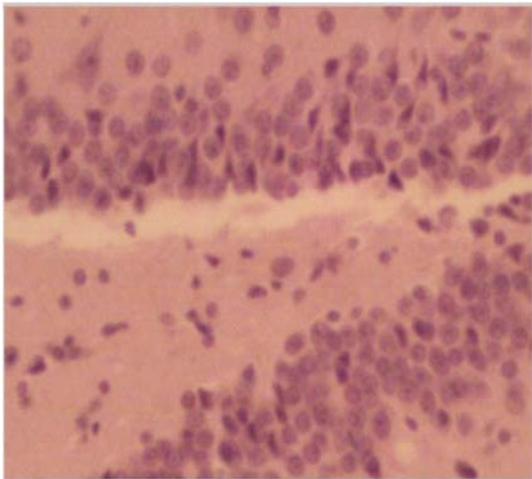


Plate 2: Section of the normal Histology of granular cells of dentate gyrus of the hippocampus of the control group stained with H and E; mag. X 250

distinguished as a zone where the cortex narrows into a single layer of densely packed pyramidal neurons 3-6 cells deep in rats, which curl into a tight U shape; one edge of the "U," field CA4, is embedded into a backward facing strongly flexed V-shaped cortex, the dentate gyrus. (Amaral and Lavenex, 2006; Moser and Moser, 1998).

The hippocampus is a major component of the brains of humans and other mammals. It belongs to the limbic system and plays important roles in the consolidation of information from short-term memory to long-term memory and spatial navigation. Like the cerebral cortex, with which it is closely associated, it is a paired structure, with mirror-image halves in the left and right sides of the brain. In humans and other primates, the hippocampus is located inside the medial temporal lobe beneath the

cortical surface. It contains two main interlocking parts: Ammon's horn and the dentate gyrus. There is now almost universal agreement that the hippocampus plays some sort of important role in memory; however, the precise nature of this role remains widely debated (Eichenbaum and Cohen, 1993; Eichenbaum *et al.*, 2007; Moser *et al.*, 2008)

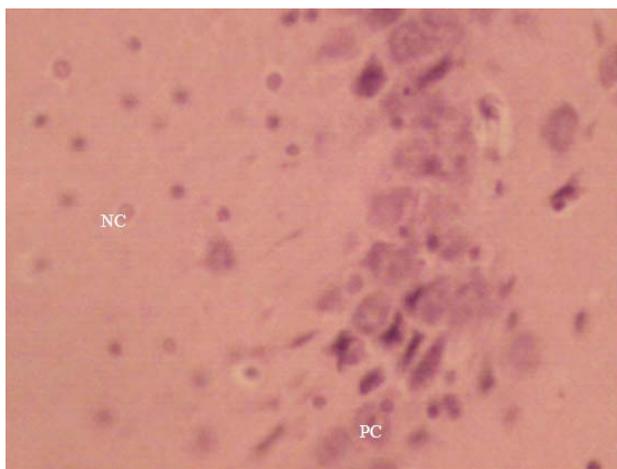
Aim and objective: This study was designed in order to assess the effects that aluminium could have on the histology of the hippocampus of wistar rats.

MATERIALS AND METHODS

This experiment was conducted in the Department of Human Anatomy, Faculty of Medicine, Ahmadu Bello University, Zaria, and Kaduna State, Nigeria

Experimental animals: The subjects used in this research work were 50 female adult wistar rats. The rats were purchased from the Faculty of Vet. Medicine A.B.U. Zaria with an average weight of between 150-200 g at the beginning of the research study. They were kept in the animal house of Dept of Human Anatomy, Ahmadu Bello University, Zaria for three weeks under (normal) standard environmental conditions (relative humidity of 60%, 12h-12h light-dark cycle with light on at 08:00h) with sufficient food, water and under a good ventilation in order for the animals (wistar rats) to acclimatized. The animals were all fed with grower's mash obtained from Nassara Feeds, Kaduna.

Experimental design: Stock solution of Aluminium Chloride used was 2 g/L (2 mg/mL). The animals (wistar rats) were divided into five groups of 10 rats per cage (group). Different concentration of Aluminium chloride was administered to different groups as stated below:



PC = Pyramidal cells
NC = Neuroglial cells

Plate 3: Section showing the histology of the pyramidal cell layers of the Hippocampus of Group II with slight distortion of cells stained with H and E; mag. X 250

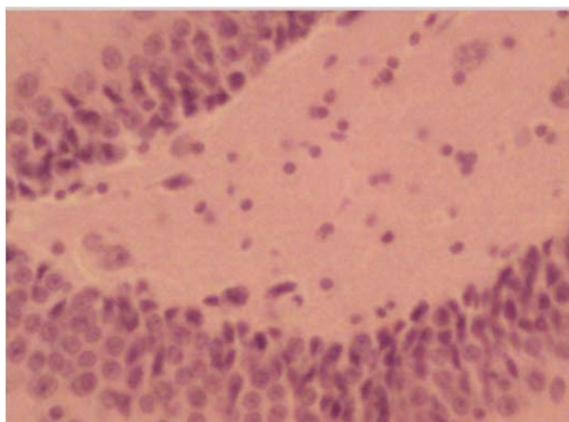
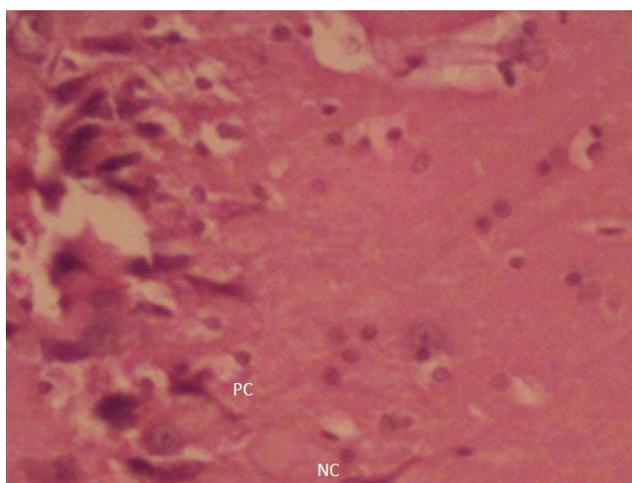
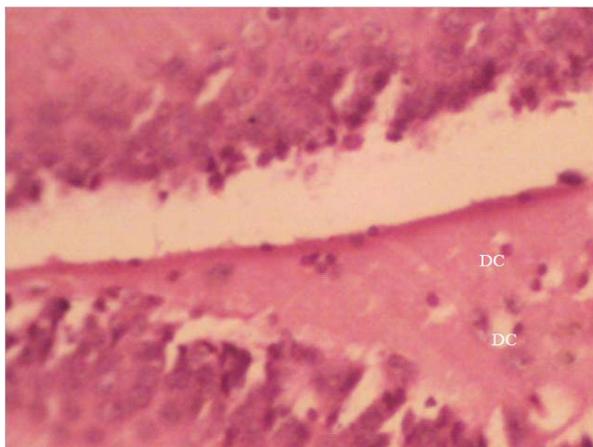


Plate 4: Showing the Histology of the granular cells of Dentate gyrus (DG) of the brain (Hippocampus) of Group II stained with H and E; mag. X 250



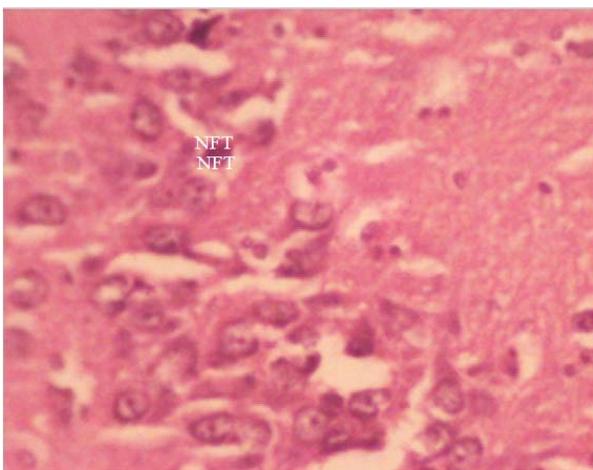
PC = Pyramidal cells
NC = Neuroglial cells

Plate 5: Showing the Histology of pyramidal cell layers of the brain (Hippocampus) of group III with reduced pyramidal cells (PC) stained with H and E; mag X 250



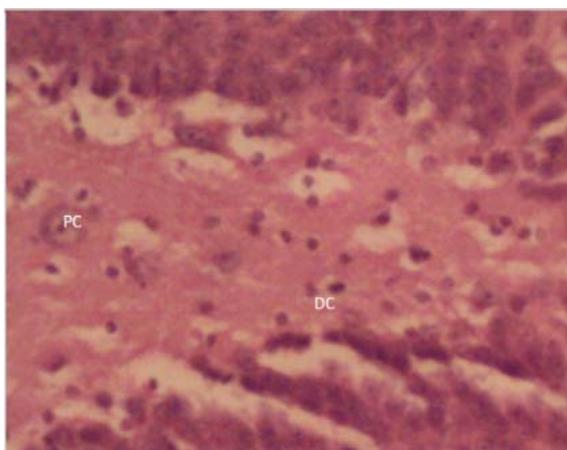
Distorted cells

Plate 6: Showing the Histology of the granular cell layers of the brain (Hippocampus) of group III with some level of Neurodegeneration. mag. X 250



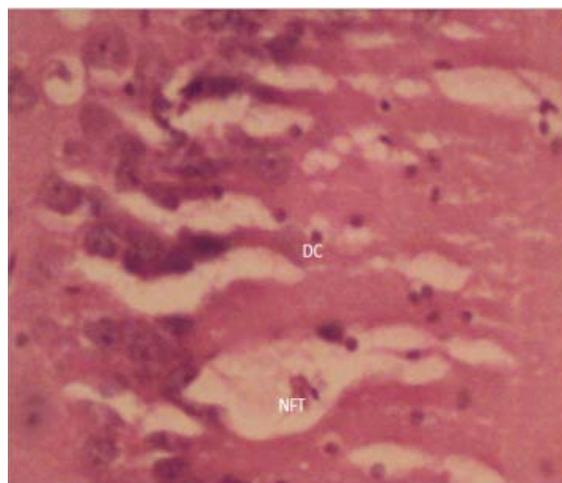
NFT= Neurofibrillary Tangle

Plate 7: Showing Histology of the pyramidal cell layers of the brain (Hippocampus) of group IV with Degenerating cells; Neurofibrillary tangle (NFT). Mag X250



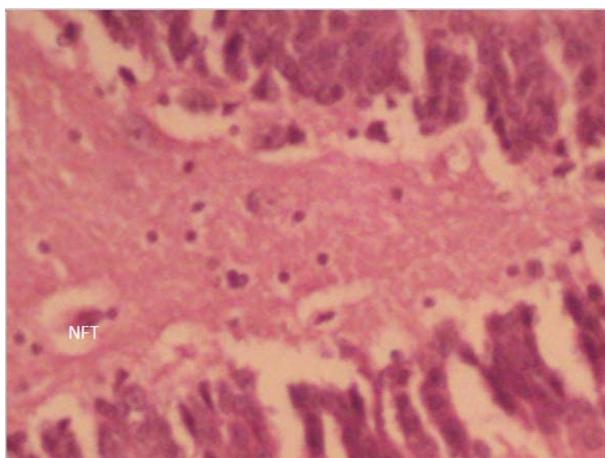
DC= Distorted cells

Plate 8: Showing Histology of granular cell of dentate gyrus of brain (Hippocampus) of group IV with cells distortion (Neurodegeneration). mag. X 250



DC = Distorted cells

Plate 9: Showing Histology of pyramidal cell layers of brain (Hippocampus) of group V with cell degenerations; reduced pyramidal cells and few neurofibrillary tangle. mag. X 250



NFT = Neurofibrillary tangle

Plate 10: Showing Histology of granular cells of the Dentate gyrus of brain (Hippocampus) with cell distortion and few Neurofibrillary tangle. mag.X.250

Group I was the control
Group II was 0.4 mg
Group III was 1 mg
Group IV was 2 mg
Group V was 3 mg
Duration of administration was 12 weeks

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

The stained sections of the hippocampus were examined under the light microscope.

RESULTS AND DISCUSSION

Experimental procedure: After oral administration of various concentration of Aluminum chloride to each group of the animals except group I (control) (Plate 1, 2); the animals were sacrifice with the use of chloroform in a closed tight box. Section of the brain was dissected and then fixed in Bouin's solution immediately in order to prevent enzymatic and other postmortem changes that could degrade tissue and also to harden the brain so that it can be sectioned (cut into thin slices) without tearing.

According to Brodal (1992), the functions of certain learning and memory have been associated with different areas of the brain like the hippocampus and cerebellum. While the hippocampus is associated with memory of new words, faces, place and event, cerebellum has been associated with memory of learning new skills like playing an instrument etc.

Group II treated showed slight sign of degeneration with slight cell distortion (Plate 3, 4). However, groups

III, IV and V (Plate 5, 6, 7, 8, 9 and 10) showed marked cell distortion with high level of degeneration in the cell as you proceed from group III to V. This supports a hypothetical statement by Yokel (1983) that Aluminium exposure has neuro-degenerating effect resulting in learning deficits and also the documentation compiled by Frank (2006) who stated that in human aluminium inhibits learning. There were also few neurofibrillary tangles in groups IV and V which suggested the possible effects of acute oral administration of aluminium chloride on the brain of the animals (rats). This is in line with Muller *et al.* (1990), who suggested that aluminium might have a role in the aetio pathogenesis of Alzheimer's disease although based on circumstantial evidence.

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 and the neurofibrillary changes observed in Alzheimer's disease were found mostly within the cortical and hippocampal neurons: this suggests why there were clumpy of neurons in the pyramidal layer of the groups III, IV and V respectively. This is an indication of neurodegeneration as could be found in Alzheimer.

Aluminium injection significantly impaired the acquisition and performance of a variety of other behaviour tasks. For example when aluminium was injected directly into the hippocampus of cats, there was an increase in density of the neurofibrillary tangle that correlated with impaired performance in acquisition of a conditioned avoidance task (Crapper *et al.*, 1980; Beal *et al.*, 1989). The neurofibrillary tangles observed on the treated group was very scanty which do not totally agree with what Crapper *et al.* (1980) observed. The scanty neurofibrillary tangle observed in this experiment could be as a result of the fact that the aluminium was administered orally unlike Crapper *et al.* (1980), who injected directly into the hippocampus. However, our results showed that there was a correlation between drinking water containing aluminium and brain (hippocampus) damage as observed from the photomicrographs of the treated groups when compared with the control. This supports the works of Cowling *et al.* (1991). From careful observation of the photomicrograph of the slides, The chronic oral administration of Aluminium chloride in the experimental groups have shown some level of neurodegeneration (or granulovacuolar) on the hippocampus of the treated rats (Plate 5-10) when compared with the control group I (Plate 1 and 2).

We therefore concluded that oral administration of aluminium chloride has a neurodegenerating effects (damage) on the hippocampus of wistar rats as shown in Plate 3-10.

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