Aluminum Mediated Changes in Rat Brain Using MRI/ MTC Imaging

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INTRODUCTION:

Aluminium is the third most abundant element in the earth crust. Aluminium exposure occurs mainly through food, drinking water, aluminium containers and cooking utensils. The increased level of Al^{3+} in living organisms may also increase the risk of several neurological disorders such as Alzheimer's disease (AD). Four independent lines of evidences implicate the Al^{3+} as a toxic environmental factor[1].1) Al^{3+} treated rats showed marked effect on the neurobehavioral status of rat. 2) Al^{3+} induced neurochemical changes in the brain 3) Clinical progression of AD after removal of brain Aluminium. 4) Epidemiological evidences. However, this remains controversial. The present MRI studies have therefore been carried out on male albino rats' model using MTC imaging in order to gain better insight into Al^{3+} neurotoxicity and its effect on simultaneous treatment with Bacoside extracted from Brahmi and is responsible for strengthening memory and cognition[2] and Donepezil (a known potential neuroprotective drug used for treatment of AD) in Al^{3+} exposed rats. The results may reveal the possible mechanism of the role of Al^{3+} in the neurological disorders.

MATERIALS AND METHODS

24 Male albino rats of three month age having weight range 100-120 ± 10 g were taken. One group of rats (n = 6) were treated with oral dose of $AlCl_3$ 100 mg / kg body weight given per day for 90 days. B & D (n = 6) group of rats were treated with Bacoside and Donepezil along with $AlCl_3$ respectively. Finally C group of rats (n = 6) were taken as positive controls. These rats were treated with similar volume of physiological saline in order to minimize the time dependent changes. For intra-ventricular injection the animals were anesthetized by intra-peritoneal injection of Ketamine (200 mg/kg body weight) and Xylazine (16 mg/kg body weight). All the images were recorded using 9.4 T Bruker Biospin NMR wide bore (80mm) spectrometer and a 35mm proton volume resonator was used for the study. The T_1 weighted axial section images were recorded by using following imaging parameters.TR = 500 ms, TE = 13 ms, Fov = 4cm, Matrix size = 256 X 256, Slice Thickness = 2mm, NEX = 4, Total Scan Time = 8min. Similarly MT images of same rats were also recorded using the following MT parameters. Length = 3ms, RF Power = 6 µT, Pulse Gain = 10 dB, Irradiation Offset = -3000 Hz, Pulse No = 10.MTR was calculated in percentage by using the standard formula.

RESULTS:

The typical T_1 weighted MT images of rat brain showing hippocampal ROI'S 1, 2, 3, 4, 5 and 6 for four group of rats i.e. C, Al^{3+}, B and D of third month are shown in Fig 1. Table 1 shows MTR % Mean ±SD value of all four groups of rats for 1, 2 and 3 month in all 6 hippocampal ROI'S. MTR value was found to be increased in second month and then decreased during third month in Al^{3+} and B treated group of rat as compared to control and D treated group, where it successively decreases from one to third month. Besides this, paired t-test shows significant difference in MTR of second and third month in Al^{3+} treated group and in MTR of Al^{3+} and B treated group during third month in all 6 ROI'S. No significant differences are seen in Donepezil treated group of rat. Paired t-test also shows significant difference in MTR of first and third month in Al^{3+}treated group and in MTR of Al^{3+}& C group during third month in two ROI'S of frontal cortex of rat brain.

Table 1: Hippocampus MTR % Mean ±SD

R	M	C	Al^{3+}	p-value(Al^{3+})	B	p-value (Al^{3+}& B)	D
1	3	33.6 ±6.2	26.0 ±9.8	a= 0.16	39.3 ±8.1	0.02	32.7 ±15.2
	2	38.9 ±8.7	39 ±10.9	b=0.05	44.7 ±19.3	0.47	39.4 ±12.1
	1	44.6 ±12.1	30.8 ±12.5	c=0.41	29.6 ±13.3	0.83	44.9 ±9.3
2	3	33.6 ±6.3	25.7 ±8.3	a=0.07	38.7 ±6.5	0.01	33.9 ±14.5
	2	38.8 ±9.7	40.2 ±7.4	b=0.04	43.4 ±18.6	0.67	38.6 ±12.5
	1	45.5 ±9.7	29.3 ±12.5	c=0.56	30.5 ±11.9	0.83	45.9 ±10.8
3	3	35.3 ±6.8	27.2 ±7.7	a=0.05	38.1 ±7.3	0.02	35.3 ±15.9
	2	39.4 ±7.1	43.2 ±7.3	b=0.02	44.4 ±17.6	0.85	39.3 ±14.1
	1	46.3 ±9.4	33.0 ±11.0	c=0.36	31.8 ±10.4	0.81	47.7 ±9.9
4	3	32.5 ±6.7	24.8 ±7.2	a=0.14	40.1 ±7.1	0.01	31.7 ±15.9
	2	38.3 ±8.2	38.5 ±9.3	b=0.04	44.9 ±18.5	0.47	37.4 ±13.1
	1	43.7 ±10.5	28.0 ±12.7	c=0.65	28.8 ±11.3	0.85	46.2 ±8.5
5	3	30.9 ±8.6	23.7 ±8.4	a=0.08	38.4 ±5.0	0.01	33.4 ±13.6
	2	36.8 ±9.6	38.6 ±8.1	b=0.03	46.5 ±21.2	0.42	38.5 ±11.8
	1	43.8 ±9.4	24.7 ±14.3	c=0.89	25.5 ±12.7	0.89	45.6 ±9.05
6	3	33.4 ±9.6	26.0 ±6.1	a=0.07	37.8 ±4.8	0.01	34.5 ±15.4
	2	37.0 ±7.1	40.3 ±5.5	b=0.003	47.6 ±19.1	0.33	37.0 ±15.6
	1	45.0 ±10.2	28.3 ±12.4	c=0.68	31.2 ±10.9	0.53	46.0 ±8.3

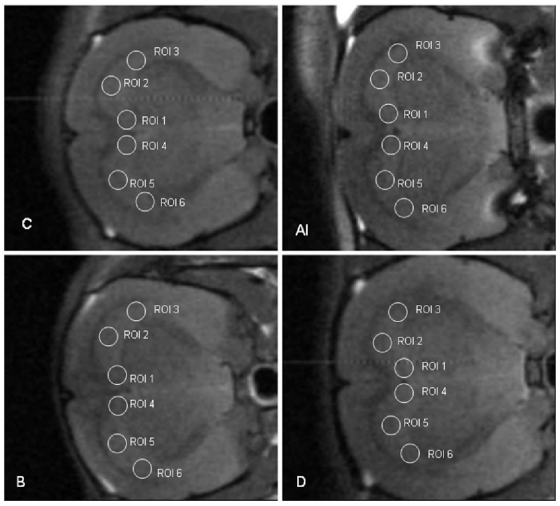

Figure 1

a= (1-2 month), b= (2-3 month), c= (3-1 month), R= ROI, M= month.

DISCUSSION & CONCLUSIONS:

Three dimensional structure of protein maintains its hydrophilicity around it i. e. bound water is present on its outer surface which gives rise to MT effect. Decreased values of MTR during third month in Al^{3+} treated group of rats clearly demonstrate the amyloid protein precipitation or the formation of plaques during third month which could be explained as an effect of Al^{3+} neurotoxicity in hippocampus, brain's seat of memory. Therefore, we propose that Al^{3+} neurotoxicity may play a role in neurodegenerative diseases such as AD and therefore minimizing Al^{3+} exposure may provide significant public health benefits. Similarity between the C and D groups of rats shows that Donepezil can act as antidote to Al^{3+} neurotoxicity but significant difference between Al^{3+} and B group of rats and increased value of MTR of B group as compared to Al^{3+} treated group of rat during third month shows that Bacoside is not compensating the damage caused by Al^{3+} neurotoxicity but it help to repair damaged neurons by adding muscle to kinase, the protein involved in the synthesis of new neurons to replace the old ones [2]. Significant difference in MTR of first & third month in Al^{3+} treated group of rat in only two regions of frontal cortex is attributed to non –uniform distribution of lipofusion granules in the frontal cortex region of Al^{3+} treated rat of third month which was confirmed by histopathological examination. Our findings were further substantiated by the behavioral studies on these rats' model as carried out earlier[3]. To the best of our knowledge it is first non-invasive *in vivo* findings of Aluminium overload and its treatment with Donepezil and Bacoside.

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