Studies of Al metabolism in animal by accelerator mass spectrometry*

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Abstract The correlation between Al metabolism and senile dementia in animal has been studied by AMS (accelerator mass spectrometry). Three groups of laboratory rats were fed with normal food, food with high Al content, and with enriched Ca and Mg together with high Al, respectively for six to eight months. Mapping test was made to record the degree of wisdom degeneration. Half of the rats were sacrificed and Al contents in various organs were measured by atomic absorption spectroscopy. The rest were injected with ^{26}Al, killed after 5, 10, 15, 25, and 35 d and ^{26}Al contents measured by AMS. The distribution of Al as well as the correlation among the accumulation of ^{26}Al, and the existed Al content and dementia was studied.

Keywords Accelerator mass spectrometry(AMS), ^{26}Al, Senile dementia, Rats

1 Introduction

Senile dementia can seriously deteriorate the quality of life of aged people. A survey shows that in Shanghai area, 0.046 of the population over 65 ages are afflicted with dementia. Although the causes of senile dementia are still unknown, people believe some trace elements play an important role both in the physiology and pathology of central nervous system. It has been hypothesized that Al might be implicated as a potential cofactor in the etiopatho-genesis of this disease. In 1978 Crapper *et al*[1] reported that the Al content in brains of Alzheimer's patients is 10 to 30 times higher than that of healthy people, and most of the Al is accumulated in neurofibrillary tangle-bearing neurons. On the other hand, in 1983 Shore and Wyratt[2] suggested that the Al accumulation in brain tissue is the result instead of the cause of dementia disease. Another report indicated that in the places where drinking water had high Al and low Ca and Mg contents, the incidences of Alzheimer's and its related diseases are higher. Therefore great attention has been paid to investigate the effect of Al toxicity on senile dementia in the last years. However, researches into its mechanism, especially the kinetic metabolism of Al in humans and the possible measures to interfere the Al burden have been severely limited by the absence of a suitable Al isotope for conventional tracer studies. The recently developed accelerator mass spectrometry (AMS) can detect the long-lived isotope ^{26}Al ($T_{1/2}$=740 ka) with extremely high sensitivity and makes the tracer measurement of ^{26}Al possible. Meirav *et al*[3] have applied AMS to make a preliminary investigation of Al kinetics in rats. Their results demonstrated the advantage of this technique for isotope tracer studies in animal as well as in human.

Animal tests have been performed in this study by AMS technique. The Al kinetics in rat's brain is investigated, the correlation between Al accumulation in brain and the existed Al content, and the possible relationship between Al accumulation in brain and wisdom degeneration are studied.

2 Experimental methods

For experimental studies 120 Wistar rats were divided into three groups and fed for 6 to 8 months. For control group the rats were fed with normal food; for high Al group 0.3mg Al was added to the drinking water per day

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for each rat; for interfering group enriched Ca (20 mg/d) and Mg (3 mg/d) were added to the drinking water in addition to Al to study the interfering effect.

At the end of six months, the "mapping test" was performed for the rats to record the training time required for them to be able to choose a correct route to reach the safety zone in the mapping cage, which reflect the extent of wisdom degeneration. Then 30 rats in each group were sacrificed and the Al contents in their brains and other organs were analyzed by atomic absorption spectroscopy (Al distribution and kinetics in kidney and liver will be published in another paper). The rest of the rats were given intraperitoneal injection of ^{26}Al solution. Each rat was received 0.5 ng ^{26}Al and 1mg ^{27}Al. They were killed on the 5 th, 10 th, 15 th, 25 th, and 35 th day after the injection, respectively. The ^{26}Al contents in their brains and other organs were measured with AMS on the 6 MV tandem accelerator in Shanghai. The main features and operation of the AMS facility can be found in Ref.[4]. Here only some points pertaining to this experiment are mentioned. The accelerator was operated at 4 MV and Al^{5+} ions were selected and counted at the particle identification system. An off-set Faraday cup located at the exit of the analyzing magnet intercepts the $^{14}N^{3+}$ beam while the $^{26}Al^{5+}$ beam is analyzed. The error signal derived from the $^{14}N^{3+}$ beam spot off its center position is used to stabilize the terminal voltage.

Table 1 Al content in brain samples measured by AMS

Group	Sample No.	Days after injection	$^{26}Al/^{27}Al$ (10^{-12})	Al adsorbed in brain /ng·g^{-1}	Average Al content before injection /μg·g^{-1}	Mapping test result/d
Control	1	5	9.9	54	1.19	5
	2	10	2.4	11		
	3	15	–	–		
	4	25	8.8	42		
	5	35	5. 1	33		
High Al	1	5	12.5	70	4.16	8
	2	10	15.5	71		
	3	15	8.2	44		
	4	25	16.0	76		
	5	35	14.0	120		
Interfering	1	5	8.2	46	1.31	4
	2	10	8.7	48		
	3	15	4.6	29		
	4	25	5.2	26		
	5	35	2.2	11		

3 Results and discussion

The time variation of injected Al adsorbed in brain is shown in Table 1. Each experimental datum in Table 1 is an average of two rats. The total error is ~20%, which is mainly from the statistical fluctuations. The amount of Al adsorbed in rat's brain becomes relatively stable within 5 d after injection, which indicates the biological half-life is of the order of months or longer. The Al content of high Al group is significantly higher than that of controls. The rats fed with high Al together with enriched Ca and Mg have lower Al content than the high Al group, which shows that enriched Ca and Mg are helpful in reducing Al accumulation in brain. It is worth while to mention that there is a possible positive correlation between the accumulation of injected Al and the existed Al content in brain. Another interesting point can be drawn from the mapping test results. There is an indication that the more rat's wisdom degenerates, the more Al is accumulated.

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