

EVALUATION OF THE NEUROTOXICAL EFFECT OF ALUMINUM ON THE WISTAR RAT

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Abstract - Our previous investigations on an animal model of neurotoxicity show that increased power in the delta range is connected with the neurotoxic effect of aluminum exposure. In this study we used several aluminum-treated animals as a reliable model for the evaluation of the neurotoxic effects of aluminum on neurons, and compared it with a control group. We conclude that spectral analysis and the ratio between the delta and theta ranges might be reliable for a qualitative description of the neurotoxic effect of aluminum, and that the t test might be used to evaluate the change in brain activity between the treated and control groups of animals. The animal model under anesthesia was used to describe the state of brain activity with neurotoxicity with suppressed functional connectivity in the brain structure. We also performed fractal analysis to quantitatively describe neurotoxic effect in different pathophysiological states of animals treated with different doses of aluminum. A decrease in the fractal dimension is an indicator of neurodegeneration in the state of stress. This animal model is suitable for evaluation of the neurodegenerative processes in Alzheimer's dementia and Parkinson's disease.

Keywords: Aluminum, neurotoxicity, Wistar rats

INTRODUCTION

Aluminum is recognized as a neurotoxic element with wide distribution in the environment. Studies show that aluminum is a risk factor in the development of neurodegenerative disorders such as Alzheimer's and Parkinson's disease. However, epidemiological studies show a high variety of critical doses and tolerance. Also, the toxic effects of aluminum can cause different changes in development, metabolism and accumulation. This animal model is suitable for the description of group neuronal activity without the functional connectivity of brain structures. Also, this model describes change in neuronal activity and can be used for the evaluation of neurodegenerative processes and stress.

MATERIALS AND METHODS

Wistar male rats were exposed to aluminum for 6 weeks. The first reaction was noticed in 2 weeks. The animals were intraperitoneally injected with

doses of 2, 3, 4 and 6 mg/kg of aluminum ($\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$) daily. After treatment we recorded their electrocortical activity. During the experiment, the rats were anesthetized with 80mg/kg of Zoletil (VIRBAC, Carros, France). The activities of the parietal cortex (P:2.5, L:2mm with respect to the bregma) and the cerebellar cortex (P:10.5, L:1.5 in respect to the bregma) were recorded at 121 s in intervals for 5 min at a sampling rate of 256 Hz, using tungsten electrodes.

The recorded signals were analyzed by spectral power analysis and the ratio between delta (1-4Hz) and theta (5-8Hz) activity was used to evaluate the neurotoxic effect of neuronal group activity. Calculations were performed for three animals which exhibited median increases in delta power range which served as a sign of the neurotoxic effect.

We used the fractal dimension Hqutchi algorithm to describe neurodegeneration as a secondary effect of aluminum neurotoxicity. Fractal dimension quantitatively describes all changes in neuronal

activity that might occur in this animal model as a result of the toxic effect of aluminum. A group of 10 pups was exposed to aluminum during gestation and lactation. In the group of pups the effect of aluminum was the same as in the adult group of rats, but the mechanisms of brain plasticity suppressed the neurotoxicity. This result was compared with the result obtained from adult animals. It can be an indicator of tolerance to aluminum.

Three groups of animals were used. The first group consisted of 3 animals that exhibited the typical effects of neurotoxicity and stable anesthesia and immobility. The second group of 9 animals described fluctuations in toxic events that might occur during the experiment. The third group consisted of 10 pups exposed to a uniform neurotoxic regime. The first group of animals was used for the evaluation of neurotoxicity of neurons using the delta-theta ratio as a measure of change in activity. This group was compared to control animals on which recordings were performed under the same conditions but without aluminum exposure. The second group of animals showed fluctuations of neurotoxicity that might have occurred in the experiment due to stress, and functional connectivity transmission changes. The third group of 10 pups was used for evaluation of mechanisms of repair and plasticity of neuronal circuits. This group and the previous group described all of the events in neuronal group activity caused by the toxic effect of aluminum.

RESULTS

As can be seen from Table 1, both the cerebrum and cerebellum had higher values of delta-theta ratio in the group of animals treated with aluminum. The t-test shows a statistical change of 0.129 in the cerebrum and 0.081 in the cerebellum.

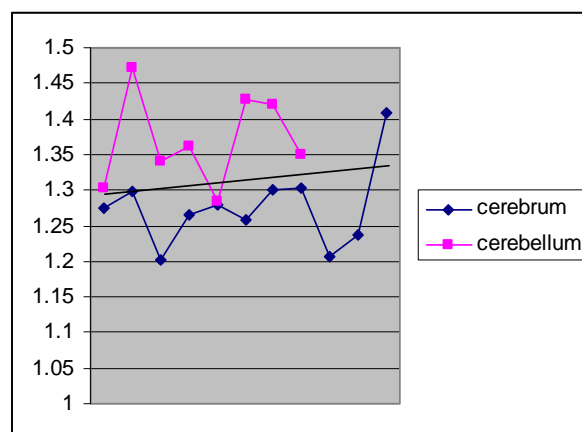
These data were calculated and compared to the average control value. They show opposite changes in the cerebrum and cerebellum. The real contribution (changes in neurotransmission) of aluminum neurotoxicity in the measure of the power spectra range (increase in delta and decrease in theta range) is an effect.

Table 1. Delta-theta ratio in group of 3 control and 3 aluminum treated rats

	control	aluminum treated
cerebrum	2.59	4.84
cerebrum	1.83	2.98
cerebrum	2.02	2.69
	control	aluminum treated
cerebellum	2.82	4.61
cerebellum	0.81	5.74
cerebellum	3.45	3.66

Table 2. Effect of aluminum in cerebrum and cerebellum

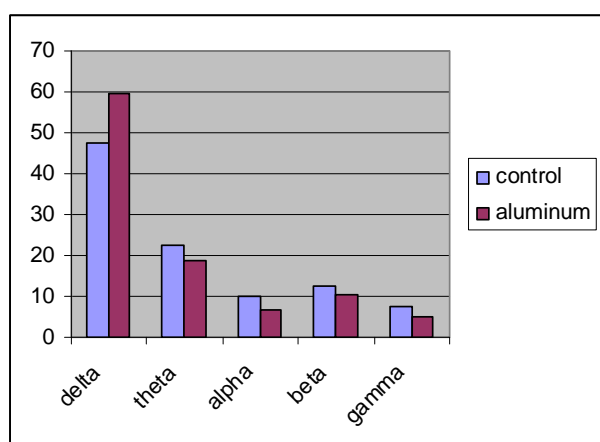
	1-4Hz	5-8Hz	1-4Hz	5-8Hz
effect	0.74	0.38	1.18	1.01



Graph 1. Linearisation of fractal dimension which corresponds to the effect of stress and neurodegeneration with a pathological state

The presented data show changes in the group of aluminum-treated animals, depending on the physiological state of an animal in comparison to the effect of stress and neurodegeneration.

In the group of young pups treated with aluminum we observed a change in the delta range. This change was statistically significant. The changes in the delta range were connected to a decrease



His. 1. Changes in delta power spectra in group of 10 pups

in other frequency ranges, and indicates a state of neurotoxicity.

DISCUSSION

Aluminum is recognized as a neurotoxic element in animals and humans. However, the mechanisms of aluminum neurotoxicity are not known (Goncavales et al., 2007). In this study, using spectral and fractal analysis, we describe changes in an animal model of intoxication by aluminum. Aluminum disrupts ion homeostasis and in higher doses causes neurodegeneration. However, these changes can be described as changes in group neuron activity. Spectral analysis is convenient for qualitative analysis of neuronal activity (Martać et al., 2007), and fractal analysis quantitatively describes changes connected with neuron activity.

Our results show that the delta-theta ratio is a reliable diagnostic tool for neurotoxicity. Neurotoxicity-related changes in neurotransmission are due to the disruption of ion homeostasis at the cerebellar level. Brain plasticity has an effect on changes caused by neurotoxicity in young pups. A secondary event is neurodegeneration which is evaluated by using average value in the estimation of the toxic effect in the first and second group of animals.

This study can be used to define the pathophysiological state of neurotoxicity or neurodegeneration in humans. As our previous work shows, an increase in the delta range could be an indicator of neurotoxicity. The theta range contributes to secondary events, such as neuronal loss. The fractal dimension was calculated for different pathophysiological states of neurotoxicity. The animals were treated with different doses of aluminum (2, 3, 4, 6mg/kg aluminum). The results show that a decrease in the value of the fractal dimension might be an indicator of toxicity only for the cerebrum. The cerebellar fractal dimension does not show a significant decrease. In the group of young rats, the increase in delta range was an expression of the toxic effect in young rats. In adult rats, we registered an effect because of different actions of aluminum.

CONCLUSION

This animal model is comparable to neurotoxic changes in neurotransmission and neurodegeneration due to exposure to aluminum. Spectral changes in the delta power range are an indicator of neurotoxicity. The fractal dimension is comparable to the pathophysiological state. The results are comparable to human models of neurotoxicity and neurodegeneration, as presented in Alzheimer's and Parkinson's diseases.

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PROCENA NEUROTOKSIČNOG EFEKTA ALUMINIJUMA U ANIMALNOM MODELU WISTAR PACOVA

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Претходна истраживања на анималном моделу неуротоксичности алуминијума показују да повећање спектралне снаге у делта опсегу је индикатор неуротоксичности. У овој студији смо користили неколико животиња које су погодне за процену неуротоксичног ефекта алуминијума у поређењу са контролом. За квалитативни опис неуротоксичности користили смо доднос делта и тета опсега и т тест за опис промене између третираних и контролних пацова. Коришћен је анимални модел у усло-

вима анестезије је опис мождане активности са супримираним функционалним везама између можданих структура. Користили смо и фракталну димензију за квантитативни опис неуротоксичног ефекта у различитим патофизиолошким стањима. Смањење фракталне димензије је израз неуродегенерације у условима стреса. Овај модел је компарабилан са неуродегенеративним и неуротрансмитерским променама у Алцхејмеровој болести и Паркинсоновој болести.