

# Animal model of neurodegeneration and stress cause by aluminum toxicity

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**Abstract:** Electro cortical group neuron activity describe changes in neurotransmission cause by different factors. Such changes could be qualitatively described by spectral analysis of electro cortical activity as a variation of relative spectral power in different frequency ranges. We used fractal dimension to compare treated animals with control to quantitatively describe degree of pathophysiological state. The aim of this study was to qualitatively and quantitatively evaluate effect of the stress and the neurodegeneration in animal model of chronic intoxication by aluminum. This animal model is comparable with Alzheimer's disease and Parkinson disease. By spectral and fractal analysis we described changes in electro cortical activity of aluminum intoxication compare to physiological control. We used adult animals, during 6 weeks intraperitoneally treated with aluminum. Stress was caused by experimental treatment and immobilization. Neurodegeneration was observed histologically. Results show that decrease in delta range of spectral power and fractal dimension might be used for evaluation of pathophysiological state of stress and neurodegeneration.

**Keywords:** Aluminium, Neurotoxicity, Neurodegeneration, Stress

## 1. Introduction

Stress events and neurodegeneration are factors which determine pathophysiological state and might be used for diagnosis and prognosis of Alzheimer's dementia and Parkinson diseases. We used animal model of aluminum intoxication to describe these events. Stress was caused with aluminum accumulation in brain through the blood brain barrier. Secondary events are change in ion homeostasis and neuron transmission. Progress in disease is neurodegeneration caused by metabolic change in neuron. All these events could be qualitatively described by changes in electro cortical activity and quantitatively described by fractal dimension.

## 2. Materials and methods

Experiments were done in accordance with approval of the Ethical committee of IBISS. Wistar rats were exposed to aluminum for 6 weeks and the first reaction was noticed in 2 weeks. First group of animals were intraperitoneally injected with doses of 2 mg/kg of aluminum daily and

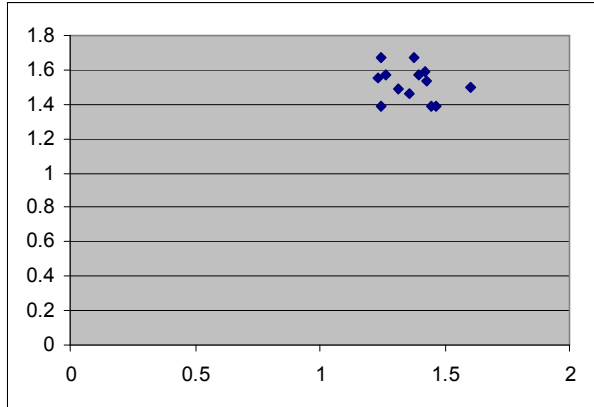
exposed to stress. Previous investigation showed neurotoxic effect in animal model (Lj. Martać, 2006). Rats were during the experiment anesthetized with 40mg/kg Nembutal anesthesia and after surgical procedure we added 15mg/kg of anesthetics. After treatment we recorded electro cortical activity. Rats were during the experiment lightly anesthetized and immobile. Under this condition we recorded activity of parietal cortex (P:2.5, L:2mm in respect to bregma) and cerebellum cortex (P:10.5, L:1.5 in respect to bregma) with tungsten electrodes. Recordings were done for 121s in intervals of 5 min with sampling rate 256Hz. Fractal analysis was made by applying Higuchi algorithm.

## 3. Results

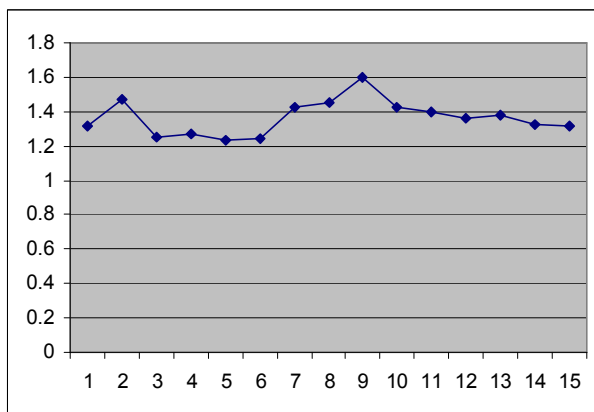
Spectral analysis qualitatively describes changes in ECoG electro cortical brain activity. Quantitatively fractal analysis is used as a measure of changes in ECoG activity compared to control.

As the histogram shows we can notice that effect of stress and neurodegeneration causes changes in fractal

dimension. This results shows that in different pathophysiological state cause by intoxication we have increase in fractal dimension. Aldo the experiments were done under anesthesia this effect was eliminate as change in relative spectral power in delta range.



**His 1.** Fractal dimenson in group of treated animals with aluminum (2mg/kg)

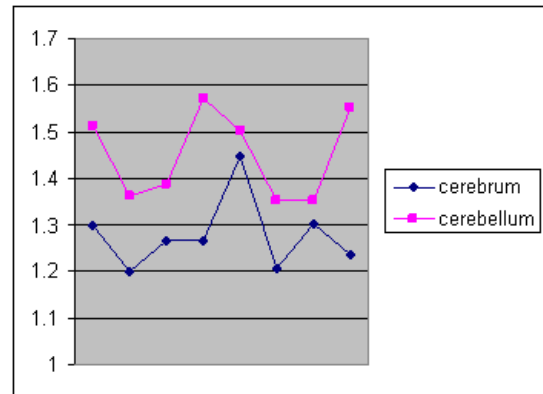


**His 2.** Linearisation of fractal dimension which corespond effect of stress and neurodegeneration

Effect of stress and neurodegeneration cause by aluminum intoxication have different symptoms in different brain structures. We used cerebral and cerebellar activity which has largest and lowest acumulation of aluminum and done linearisation to describe change in fractal dimension in this experimental model. Animal model is comparable with state of some diseases and might be used in prognosis of Alzheimer's disease and Parkinson disease. However for the state of conditions of patient should be consider mental state of disruption.

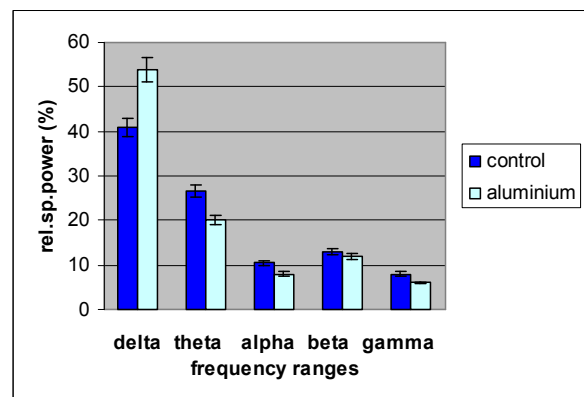
This results shows that decrease in fractal dimension of cerebrum and increase in fractal dimension of cerebellum can be measure of stress and neurodegeneration due to aluminum intoxication. However this changes are different for brain structures due to mechanisms of plasticity and acumulation. In evaluation of this effects we include all events which affect neurotransmission such as changes in neuron metabolic activity disruption of ion homeostasis and excitatory and inhibitory effects on synapses. This

results were calculated with respect to control group of anesthetised animals so we exclude effect of anesthesia.



**His 3.** Fractal dimension in animal model of stress and neurodegeneration in Alzheimers demention and Parkinson disease

In the group of animals with neurofibrillary tangles and beta amiloid or changes in dopamine and serotonin neurotransmission we have differences in fractal dimension in cerebrum and cerebellum. Alzheimers demention effects mostly cerebrum and Parkinson disease effects cerebellum. This to oposite effects have variation because conectivity between this brain structures. This two pathophysiological state have similarity with stress and neurodegeneration evants so it can be observed in comparison. We calculate change in fractal dimension for animal model and adjust it with a stete of illness in Alzheimer's demention and Parkinson disease and propouse fiu states of pathophysiological condition. This changes in cerebral and cerebellar activity can not be lineariste due to different effects of disruption of neurotransmission and conectivity.



**His 4.** Changes in frequently ranges in aluminum model of neurotoxicity

In the model of neurotoxicity as an indicator of changes in the rhythm of the delta was observed spectrum registered rat brain activity that is correlated with all of the aforementioned changes. This is accomplished by varying the dose of the anesthetic and maintain the state of suppressing pain. In this model, the extent of the registered spectrum sigma brain activity of rats corresponding to the alpha rhythm in humans, which comprises a cognitive and

intellectual abilities, while the beta rhythm refers to the ability of the chain (Ćulić M., 2007). Gamma rhythm rule is observed in accordance with the previously developed model tissue lesions when registering (Ćulić M., 2005).

Our previous work and spectral analysis shows that events of stress and neurodegeneration causes increase in spectral power in delta range. Also under anesthesia we have increase of relative spectral power in delta range. In this cause we eliminate effect of anesthesia and present changes in frequency domain booth for animal model and patient state of stress and neurodegeneration. This increase is comparable with decrease in higher frequency domain due to different mechanisms of disruption. Also in Alzheimer's dementia and Parkinson disease spectral analysis shows increase in lower frequently ranges.

## 4. Discussion

The aim of this study was to present the results of fractal analysis based on spectral analysis of electrocortical activity of rats brain and to do the extrapolation of results to animal model in diseases. This animal model is convenient because stress and neurodegeneration have synergistic effect in diagnosis and prognosis of Alzheimer's dementia and also causes Parkinsonism. In adult types of intoxication is accompanied by reduced apoptosis and neurodegeneration (P. Bharathi, 2008). Due to the accumulation of aluminum in the brain leads to oxidative stress and inflammation of the brain tissue, which results in the development of neurodegeneration (A. Campbell, 2000). This animal model is comparable with Alzheimer's and Parkinson disease (M.Kawahara, 2005). Increase in delta, a decrease in alpha and beta spectral power have diagnostic and prognostic significance. Delta 45% above described oxidative stress, inflammation and neurodegeneration, as the alpha and the beta rhythm of the related motor behaviors of rats, ie. the more psychological, cognitive and memory function in human patients.

Results shows decrease fractal dimension as measure of pathophysiological state. Due to mechanisms of recovery which are still unknown we can observed increase in fractal dimension which is in animal model different compare to humans so this results should be observed as the mean value which describes typical pathophysiological state and might be used in diagnosis. Lower value compare to mean value could be estimate as progression of disease. Higher values compare to control are due to mechanisms of adaptation in animal and can not be used for humans. However the degree of max adaptation compare to mean value could be indicator of tolerancy because in experiments all animals survive treatment. Comparison shows that fractal dimension in the group of animals with neurofibrillary tangles and beta amyloid compare to disruption in dopamine and serotonin transmission have opposite effects on cerebro-cerebellar connections. Molecular mechanisms which might effect pathophysiological state are described particularly (Gupta 2005; Adler 1999).

## 5. Conclusion

Previous results shows that decrease in fractal dimension can be measure of stress and neurodegeneration due to aluminum intoxication. However this changes are different for brain structures due to mechanisms of plasticity and accumulation. Linearisation shows changes in fractal dimension which correspond effect of stress and neurodegeneration in animal model of aluminum intoxication. Both in animals and humans increase in delta spectral range could be reliable for pathophysiological state of disease.

Decrease in fractal dimension in this animal model of stress and neurodegeneration could be used for diagnosis and prognosis of Alzheimer's dementia and Parkinson disease. This work describe changes in group neuronal activity and in prognosis of disease should be consider a state of dementia and mental activity which is described as a neural network modeling (Y. He, 2009) or oscillatory activity in brain (J.L.W. Bosboom, 2006).

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