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SPECTRAL CHANGES OF BRAIN ACTIVITY IN RAT OFFSPRING EXPOSED TO ALUMINIUM DURING GESTATION AND LACTATION

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Abstract – Exposure to aluminium during gestation causes changes in mammalian brain development and behavior. Our aim was to perform spectral analysis on electrocortical activity of Sprague Dawley male pups (30±3 days of age) whose mothers were treated with aluminium during gestation and lactation. There was a higher presence of power spectra in the delta range of parietal electrocortical activity, a lower presence in the theta range and increased values of the parameter DT as the ratio of delta to theta range in pups indirectly exposed to aluminium (whose mothers were drinking a 0.5% water solution of aluminium chloride during the gestation and lactation periods), compared to controls.

Key words: Maternal aluminium exposure**,** young rats**,** electrocortical activity, power spectra

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INTRODUCTION

Many studies have shown the association between oral aluminium exposure and brain development in early life and have pointed out the high toxicity of aluminium on the growth and development of fetuses and sucklings both in humans and experimental animals (Bishop et al., 1997; Yumoto et al., 2000; Colomina et al., 2005). Animal studies have documented central nervous system impairments following aluminium exposure, including neuropathological, neurochemical, neurophysiological and neurobehavioral changes (Wang et al., 2002; Walton, 2007; Ali et al., 2008).

MATERIALS AND METHODS

Experimental animals and aluminium treatment

Experiments were performed on young male *Sprague Dawley* rats after the lactation period. All procedures were done in accordance with the European Council Directive (86/609/EEC) and the rules for the care and use of laboratory animals at the Institute for Biological Research, University of Belgrade. All animals were maintained in a 12 h light-dark cycle and a temperature-controlled (22-25°C) animal room. Female rats were placed in cages for time mating with males. After two days, during the gestation and lactation periods, each female rat (at the time – with offspring) was housed in a separate cage. There were two feeding regimens of the female rats: the control and with aluminium. Thus, the control animals were exposed *ad libitum* to food and drinking water while the aluminium-treated rats were exposed *ad libitum* to the usual food and a solution of 0.5% aluminium-chloride ($AlCl_3{\cdot}6H_2O$) in their drinking water. The daily aluminium dose was about 45 mg/kg during gestation and about 160 mg/kg during lactation. For examination of acute exposure two groups of animals were used: the physiological control group of puppies whose mothers were under physiological treatment and the other group of puppies whose mothers were exposed to aluminium treatment. After 21 days of lactation the mothers were separated from their offspring. Thereafter, 2-4 young rats were kept per cage. The young rats were maintained on their mothers` regimen until electrocortical recordings.

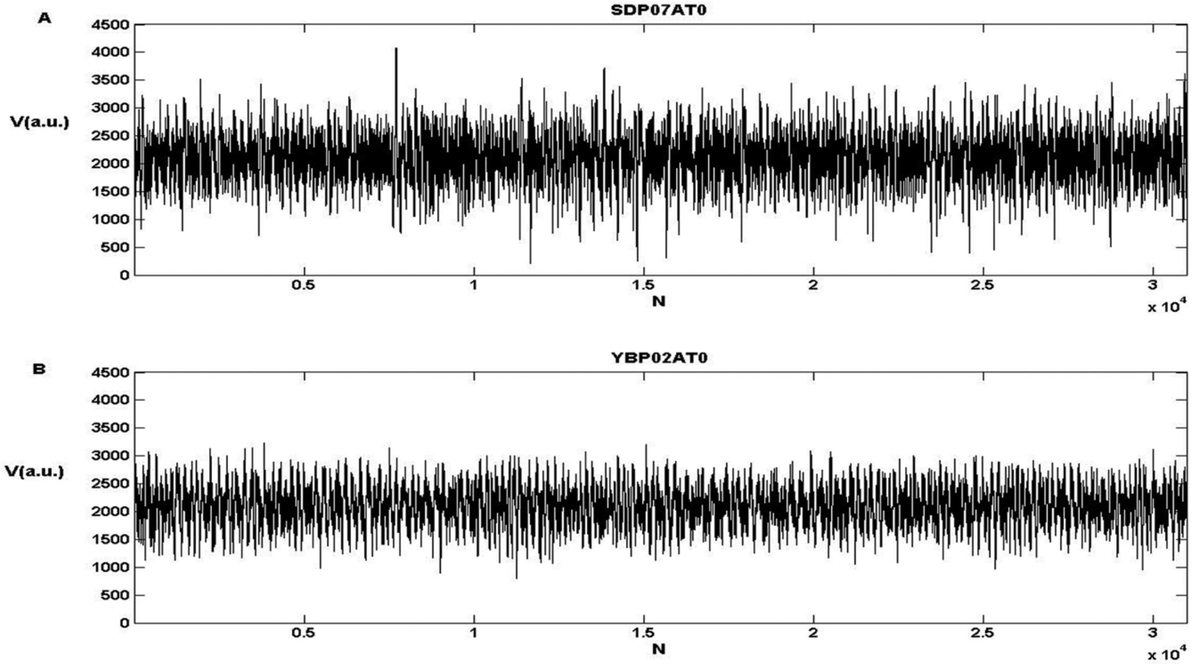

Fig. 1. Two typical biosignals: electrocortical activity in one control young rat (A) and one rat with maternal aluminium treatment (B).

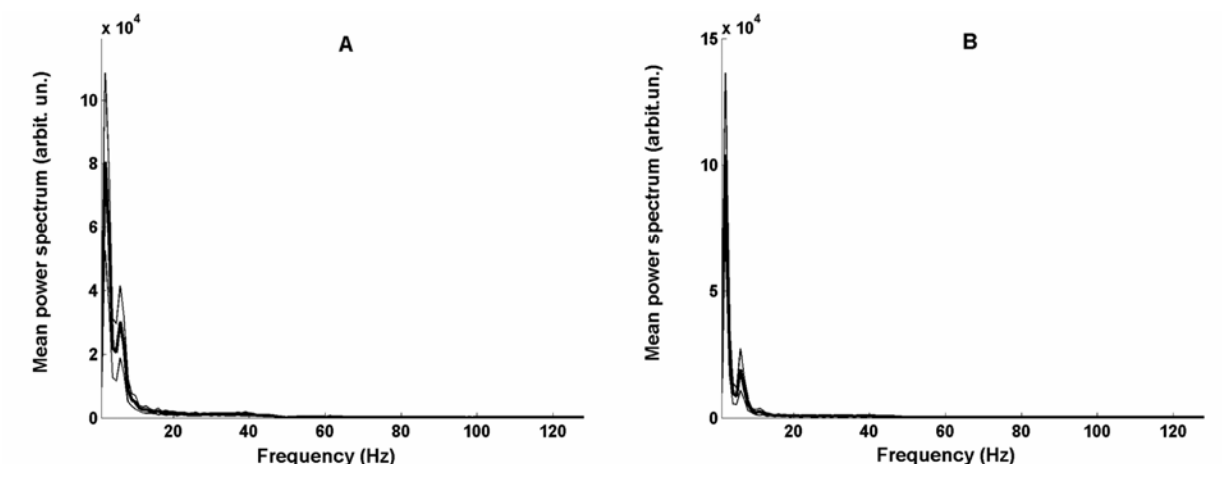

Fig. 2. Mean power spectra (±SD) of electrocortical activity from biosignals showed on Fig. 1.

Surgical procedure

Experiments examining acute exposure employed surgical procedures performed on young male rats at 30±3 days of age under *Zoletil* (Virbac S.A., Carros, France) anesthesia at an initial dose of 60 mg/kg and a subsequent supplement of ~15 mg/kg, when necessary to obtain stable anesthesia throughout the experiment. Each animal was mounted in a stereotaxic apparatus. Partial round-shaped craniotomies were made over the parietal cerebral cortex (P: 2-2.5mm; L/R: 2-2.5 mm).

Recording procedure and data acquisition

The local field potentials of the parietal cerebral cortex were monopolarly recorded by epidurally-positioned silver ball electrodes or intracortically superficially-positioned tungsten microelectrodes with a ground electrode laid over the frontal bone and temporal muscles. Electrocortical activity was amplified and filtered by a multi-channel processor (Alpha-Omega Eng, Nazareth) with high pass-DC, low-pass 150 Hz filters and a 50 Hz notch. Each recorded sequence lasted 121 s; there were at least 10 recorded sequences with interruptions of 5-10 min during 150 min of total acute experimentation. We analyzed digitized electrocortical signals at a sampling rate of 256 samples/s, filtered to avoid artifacts at 61, 107 and 121 Hz.

Data analysis

Spectral analysis of the recorded signals during sequences lasting 80 to 120 s (divided into epochs of 8 s), was obtained by Fast Fourier Transformation algorithm. Mean power spectra (of 10 to 15 epochs) of cerebrocortical activity were obtained in frequency ranges of 4 Hz up to 128 Hz. The parameter DT as the mean of at least five values of ratio of delta to theta power spectra of electro-cortical activity in each animal was established. Statistical t-test was used to test the difference of parameter DT between two groups of young animals.

RESULTS

The anesthetized state of the investigated young rats was characterized by a predominance of slow delta range (0.1- 4.0 Hz) in the mean total power spectra at the parietocortical level, as was the case in adult animals (Culic et al., 2005). However, the slower rhythms were more pronounced in young rats with maternal aluminium treatment. The typical activities (Fig. 1) and spectral characteristics of recorded signals in one control rat and one rat indirectly treated with aluminium are shown in Figs. 2, 3 and 4 (power spectra, frequency ranges histogram and the DT histogram of these two rats).

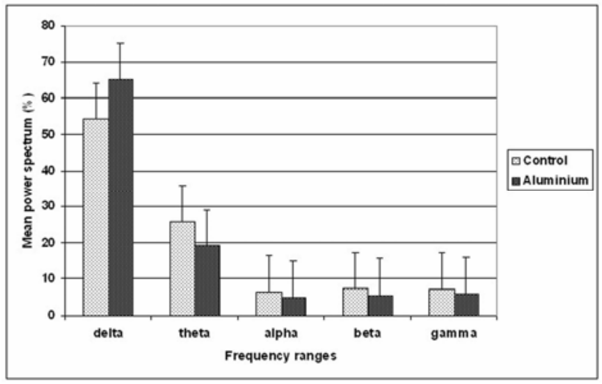

Fig. 3. Relative power spectra of two biosignals presented on Fig.1.

A statistical t-test showed that maternal aluminium treatment during gestation and lactation induced significant changes in the power spectral characteristics. The mean value of parameter DT was significantly increased ($p<0.002$) from 2.130 (control rats) to 3.348 (rats indirectly treated by aluminium) (Fig. 5).

DISCUSSION

Most behavioral studies have shown that chronic aluminium exposure at certain doses can cause behavioral morphological impairments in animals. In our study, results show that $AlCl_3$ consumption (even the values from 45 mg/kg/day during gestation to 160 mg/kg/day) during lactation, induce significant changes in the spectral characteristics of parietal cortical activity of offspring. There was an increase of power spectra in the delta range and a decrease in the theta range and particularly the established parameter DT as the ratio of delta and theta spectral powers was markedly greater in young rats with maternal consumption of aluminium during gestation and lactation, compared with the control rats. There could be some electrophysiological changes at some other level of the central nervous system but a greater sample should be studied, as we have already mentioned in our preliminary study (Podgorac et al., 2008) on young

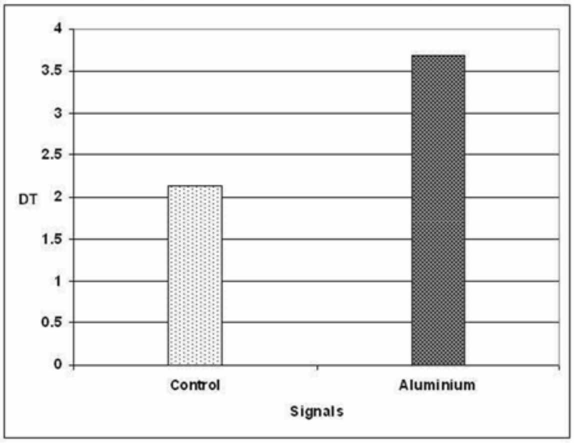

Fig. 4. The parameter DT (a ratio of delta to theta range) signals from Fig. 1.

rats with maternal aluminium treatment. The study on the relationship between aluminium exposure of female Wistar rats and the memory of their offspring showed that consumption of not less than 800 mg/kg/day of $AlCl_3$ during lactation can impair short-term and long-term memory of their offspring (Ali et al., 2008). It seems that changes in brain activity could denote aluminium neurotoxicity at lower doses than some behavioral tests. We have already shown that chronic aluminium chloride parenteral administration may induce an increase of slow power spectra of the electric brain activity in adult rats (Martac et al., 2006).

The evaluated parameter DT as the ratio of relative delta and theta spectral powers of brain activity increased in young rats indirectly treated by aluminium during maternal exposure to aluminium chloride in gestation and lactation.

These trends of growth intensity in the delta range and decrease in the theta band could be detected in brain disorders by wavelet analysis. According to recent experimental results from Berkeley (Barbaro et al., 2006), slow frequency ranges (delta and theta) have a key role in the coordination of activities between the various centers in the brain, which, roughly speaking, exchange information at higher frequencies. From this point of view, a decrease of activities in the

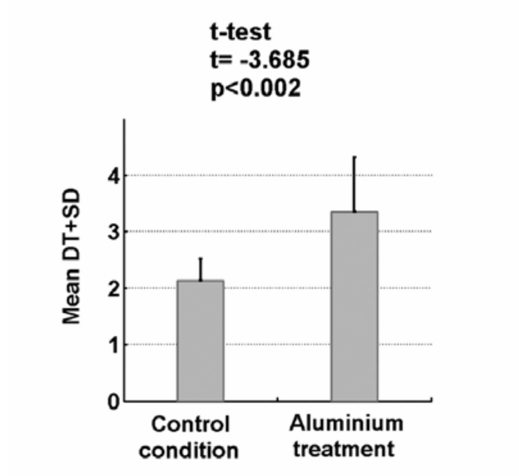

Fig. 5. The mean value of parameter DT in the group of control young rats (N=10) and the group of young rats with maternal aluminium treatment (N=10).

theta range may indicate a neurotoxic effect of aluminium.

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REFERENCES

Ali, M. A., Simin, E. V., and *C. Rahi* (2008). Effect of Oral Aluminium Chloride Administration During Lactation on Short- and Long-Term Memory of Their Offspring. J. Biol. Sciences 8, 767–772.

Barbaro, N.M., Berger, M.S., Canolty, R.T., Dalal, S.S., Edwards, E., Kirsh, H.E., Knight, R.T., Nagarajan, S.S., and *M.Soltani* (2006). High Gamma Power Is Phase-Locked to Theta Oscillations in Human Neocortex. *Science* **313**, 1626–1628.

Bishop, N. J., Morley, R., Chiz, B., Day, J. P., Lucas, A., and *N. Engl* (1997). Aluminium neurotoxicity in preterm infants receiving intravenous feeding solution. *Medicine* **336**, 1557–1562.

Colomina, M.T., Roig, J. L., Torrente, M., Vicens, P., and *J. L. Domingo* (2005). Concurrent exposure to aluminum and stress during pregnancy in rats: Effects on postnatal development and behavior of the offspring. *Neurotoxicology and Teratology*, **27**, 565–574.

Ćulić, M., Martać-Blanuša, Lj., Grbić, G., Spasić, S., Janković, B., and *A. Kalauzi* (2005). Spectral analysis of cerebellar activity after acute brain injury in anesthetized rats. *Acta Neurobiol. Exp*. **65**, 11–17.

Martać, Lj., Kesić, S., Ćulić, M., Grbić, G., Spasić, S., Sekulić, S., and *D. Lalošević* (2006). Effect of aluminium neurotoxicity on rat brain activity. *Acta Physiol. Pharmacol. Serbica*, **42**, 219–225.

Podgorac, J., Sekulić, S., Lalošević, D., Čapo, I., Grbić, G., Martać, Lj., and *M. Ćulić* (2008). Spektralne karakteristike moždane aktivnosti mladih pacova čije su majke pile vodeni rastvor $AlCl_3$, IV Kongres društva za neuronauke Srbije, 11 - 14. septembra 2008, Kragujevac, Zbornik sažetaka, str. 372–373.

Walton, J. R. (2007). An aluminum-based rat model for Alzheimer's disease exibits oxidative damage, inhibition of PP2A activity hyperphosphorylated tau and granulovacuolar degeneration. *Inorganic Biochem*., **101**, 275–284.

Wang, M., Chen, D.Y., and *Y.Z. Xu* (2002). The influence of developmental period of aluminium exposure on synaptic plasticity in the adult dentate girus in vivo. *Neurosociology* **113**, 411–419.

Yumoto, H., Nagai, H., Matzuzaki, T., Kobayashi, W., Tada, Y., Ohki, Y., Kakimi, S., and *K. Kobayashi* (2000). Transplacental passage of Al from pregnant rats to fetuses and Al transfer to suckling rats. *Nuclei Instrum*. Phys. **172**, 925–929.

СПЕКТРАЛНЕ ПРОМЕНЕ МОЖДАНЕ АКТИВНОСТИ КОД МЛАДУНАЦА ПАЦОВА ИЗЛОЖЕНИХ ДЕЈСТВУ АЛУМИНИЈУМА ТОКОМ ГЕСТАЦИЈЕ И ЛАКТАЦИЈЕ

Љ. МАРТАЋ[1], Г. ГРБИЋ[1], Г. КЕКОВИЋ[1], Ј. ПОДГОРАЦ[2], М. ЋУЛИЋ[1], С. СЕКУЛИЋ[3], Д. ЛАЛОШЕВИЋ[3], и И. ЧАПО[3]

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Излагање дејству алуминијума током гестације и лактације може довести до промена у развићу мозга и понашања код сисара. Наш циљ је био да се уради спектрална анализа електрокортикалне активности младих *Sprague Dawley* пацова мушког пола (старости 30±3 дана) чије су мајке биле третиране алуминијумом током гестације и лактације. У поређењу са контролом, код младих пацова који су били индиректно тровани алуминијумом (чије су мајке пиле 0,5 % водени раствор $AlCl_3$ током гестационог и лактационог периода) постоји већа заступљеност делта ритма активности коре великог мозга, мање присуство тета ритма, као и пораст параметра DT као однос између делта и тета опсега.