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Original Research

Flash Visual Evoked Potentials (FVEP) in Newborn Rats after Pre- and Postnatal Exposure to Zinc

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Abstract

The aim of this paper was to find any alterations in flash visual evoked potentials (FVEP) after pre- and postnatal exposure to Zn in rats.

18 white adult Wistar rats drank tap water containing 50ppm of $ZnSO_4$ x $7H_2O$ and ate pelleted food during 21 days of pregnancy. 14 pregnant rats of the control group drank only tap water. 10 newborn rats from pure (without prenatal Zn exposure) breeding had the oral Zn supplementation with the same dose of Zn for 21 postnatal days. The fluid consumption of each dam and each offspring rat was monitored daily. Every rat during the whole period consumed about 66.15mg of pure Zn. The offsprings were divided into three groups: prenatal Zn group (18 rats), postnatal Zn group (10 rats) and control group (14 rats). The FVEP recordings were made using the UTAS 1000 LKC electrophysiologically interfaced personal computer system (USA), with Ganzfield stimulation in all groups every 5 min for 30 min. The decrease in the latencies and increase in the amplitudes of N_1 and P_1 waves were observed in both Zn groups in comparison to the control, but only in the prenatal Zn group were the changes statistically significant. The maternal Zn supplementation may have a beneficial influence on visual cortical responses in newborn rats.

Keywords: zinc, visually evoked potentials, rats

Introduction

Zn is a nutritional trace element essential, among others things, for good eye metabolism. Zn is present in high concentrations in ocular tissue, particularly in retina and choroid [1]. Zn plays an important role in the immune and neurological response and is required by metalloenzymes such as superoxide dimutase and alcohol dehydrogenase. The administration of Zn supplementation is a response aimed at maintaining antioxidant status. Even a moderate Zn deficiency increases oxidative stress to the retina [2]. Leure-duPree et al. describe the ultrastructural alterations of the retinal pigment epithelium (RPE). The deepening of the basal infoldings of the cells of the RPE, the vesiculation and degeneration of the photoreceptor of outer segments were observed [3]. Zn deficiency may contribute to age-related macular degeneration [1, 4-6]. Tate et al. found that peripheral RPE contained significantly more metallothionein and Zn than macular RPE [7]. Exposure to high doses of Zn can be harmful; stomach cramps, anemia and cholesterol level changes have been described [1]. The zinc deficiency and disorders in

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its metabolism caused behavioral changes, developmental and memory retardation and stunt growth in offsprings [8, 9]. Wallwork concluded that there is a strong relationship between abnormal Zn homeostasis and central nervous system disorders [10].

The aim of this paper is to obtain information on the impact of Zn administered in the form of aqueous solutions for pregnant rats and their offspring on the ability to perceive visual sensations in the form of cortical response to evoke flash in rats.

Material and Methods

The study was performed on white rats Wistar, weighing from 280 to350g, between 3-4 months of age. Three groups of animals were formed:

- group I – offspring of mothers drinking only distilled water during pregnancy (control n=14)
- group II – offspring of mothers drinking within a period of 3 weeks during pregnancy 50ppm $ZnSO_4$ x $7H_2O$ (group preZn n=18)
- group III – offspring coming from a pure breed drinking within a period of postnatal 3 week$_s$ 50 ppm $ZnSO_4$ x $7H_2O$ (group postZn n$_=$ 10)

The liquid consumptions by each rat was monitored daily, each rat consumed a dose of 66.15mg of pure zinc.

Rats were provided with electrodes implanted in the laboratory of the Department of Pharmacology in Zabrze.

Following intraperitoneal anesthesia with a solution of pentobarbital (Tiopental) in a dose of 10mg/kg of body weight, each animal was located in a stereotaxic frame. After properly setting its head, the skin was cut at the length of 1.5cm to uncover the bones of the skull base. An active electrode was placed on pachymeninx through a hole (L=1mm, A=1mm from lambda) above visual cortex and passive electrode was placed on a skull cover bone in the interorbital region. The electrodes were fixed to the bones with Duracryl glue (manufactured by Z. Ch. Oświęcim, Chemical Works). After tighting it with the glue, the postoperative wound was sewn up with a plane suture. After the procedure the animal was kept 6-7 days in animal quarters for convalescence. Then, in the Department of Ophtalmology in Bytom electrophysiological tests with the use of UTAS 1000 (LKC,USA) apparatus were performed. For the purpose of the above-mentioned test animals were anesthetized by intraperitoneal administration of 10% solution of chloral hydrate in the dose of 0.03/100g of body weight. (The remedy was selected because of its low neurotoxicity and no influence on evoked potentials of brain cortex). Pupils were dilated with 1% drops of Tropicamidum or with 1% Atropinum sulfuricum (Polfa), whereas the eyelids were kept open using single sutures applied to their edges. FVEP was measured for 30 minutes after a period of adaptation to test conditions lasting approx. 20-30 minutes. Rats were stimulated with 150 flashes of light every 5 minutes at a frequency of 1.9 Hz. Signals went through low and high-frequency filters, respectively (0.3 and 100 Hz). The responses were time-averaged and saved. Six FVEPs were obtained from each animal. Latencies and amplitudes of the first negative N_1 and positive P_1 peaks of FVEP wave in relationship to izoelectric line were subject to assessment (Fig.1). The results obtained in each tested group were subject to the statistical T-Student test in relation to the control group.

The significance level for the results was assumed at $p < 0.05$.

The study was approved by the Ethics Committee of the Medical University of Silesia in Katowice and was supported by grant No. NN-2-110/99 from the Medical University of Silesia.

Results

The results are presented in Table 1. In the control group the average value of latencies of N_1 was 50 ms (100%) and of P_1 71ms. The prenatal exposure to Zn led to a statistically significant ($p<0.05$) shortening of both latencies.

N_1 to 46 ms (92%) and P_1 to 67 ms (92%). In the postZn group the shortening of latencies, N_1 to 49 ms (98%) and P_1 to 70 ms (98%) did not differ significantly statistically in comparison with control.The mean value of N_1amplitude in control rats was 36μV (100%), in preZn group 60 μV (166%) and in the postZn group 41μV (111%). It means that the increase of N_1 amplitude in both groups was of 66% and of 11%, respectively, and showed the highly statistical significance ($p<0.01$). Significant differences ($p<0.05$) also occured between the value of amplitude of P_1, in the preZn group it was 38 μV (180%), in the postZn group 25 μV (118%) compared to the control group 21 μV (100%).

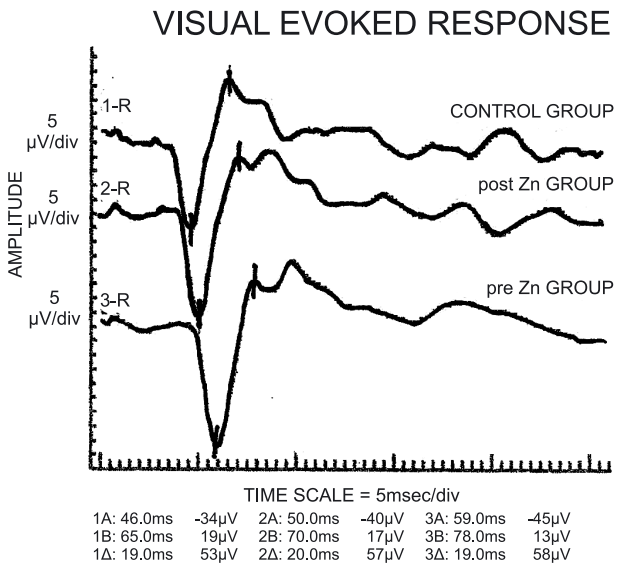

Fig.1. The FVEP wave in control, postZn and preZn groups. The registration was obtain in 20 min of examination in every group.

Table 1. The mean values of the latencies and amplitudes of the first deep negative peak (N_1) and the next positive one (P_1) of flash visual evoked potentials (FVEP) in prenatal (preZn) and postnatal (postZn) exposed for zinc rats and in the control group.

	N_1 latency [ms]	SD d.f. t(calc)	p≤	P_1 latency [ms]	SD d.f. t(calc)	p≤	N_1 amplitude [μV]	SD d.f. t(calc)	p≤	P_1 amplitude [μV]	SD d.f. t(calc)	p≤
CONTROL GROUP n=14	50 100%	0.8		71 100%	1.1		36 100%	2.3		21 100%	2.8	
preZn GROUP n=18	46 92%	2.4 30 2.435	0.05	67 94%	0.7 30 2.287	0.05	60 166%	3.5 30 3.255	0.01	38 180%	4.2 30 5.135	0.01
postZn GROUP n=10	49 98%	1.8	NS	70 98%	0.5	NS	41 111%	7.2 22 2.125	0.05	25 118%	5.6 22 2.095	0.05

n – the number of rats in the group; N_1, P_1 – values are presented as arithmetic mean ±SD; p ≤ – versus the control

Discussion

For many years our department has been performing investigations on the impact of environmental pollutants on the eyes. Among others the influence of such pollutants as cadmium [11], lead, manganium, mercury [12, 13] and selenium to visual potentials of optical cortex have been studied. All metals tested in our department except for selenium, to a different extent, made changes in the FVEP wave, which is typical for toxic damages to the optical pathway, expressed by lengthened latencies and the decrease in the amplitude of FVEP response. Our own studies [14] and those from other laboratories [15, 16], prove that pattern visual evoked potentials (PVEP) usually faithfully correspond to the visual acuity; moreover, the FVEP wave in rats is very similar to the PVEP in humans and it differs only in shorter latency because of shorter distance from the eye to the optical cortex. The results obtained in this study might show the beneficial role of Zn supplementation on visual cortical responses, especially in the prenatal period. Such electrophysiological studies were not described earlier in the available literature. Paterson et al. showed that marginal Zn deficiency in the postnatal rat model produced the morphologic ocular changes with depression of the electroretinogram and oscillatory potentials [17]. The results we obtained allowed us to assess the influence of Zn on optical nerve and pathway function, we cannot draw any conclusions about its impact on retina. Our results were consistent with those of Labus et al.[18], who showed that the behavioral changes in the same rat model were greater after prenatal exposure to Zn only. Nowak et al. also observed that pre- and postnatal exposure to Zn increased the dopamine concentration and its synthesis in rat's brain. The increase concerned to a larger extent the rats from postZn group [19]. Behavioral changes and altered morphology in brain, which were associated with Zn deficiency, also were reported by Wallwork [10]. Zn is involved in the metabolism of some neurotransmitters and indirectly affects dopamine metabolism [20]. Colvin et al. [21] assumed that Zn could play an important neuromodulatory role at glutamatergic synapses. Zn-induced neurotoxicity showed sensitivity to NMDA channel antagonists, suggesting that the Zn influx can also occur across glutamate-activated channels. Chowanadisai et al. observed that prenatal and early postnatal Zn deficiency impairs learning and memory and these deficits persist into adulthood. The key modulator in this process may be the NMDA receptor; however, effects of Zn deficiency on the regulation of NMDA receptor activity are still not well understood [22].

It's also known that Zn blocks the $GABA_A$ receptor, glutamate and the dopamine transporter [21].

Conclusion

Maternal zinc supplementation increased the sensitivity of visual systems to light in newborns, so it may have a beneficial influence on visual cortical responses.

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