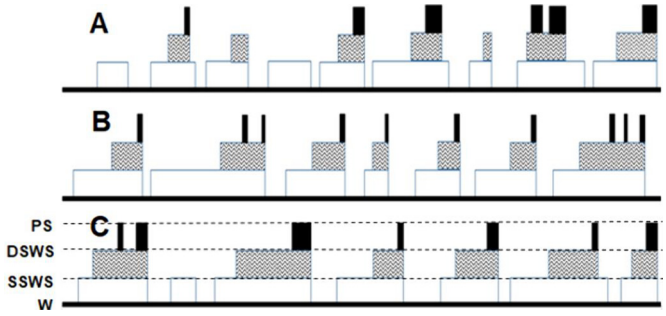

Fig.1. Time-course of sleep-wakefulness cycles registration in control (A), kindled rat (B) and kindled rat treated with pitolisant (C) registration. Data is presented during the third hour from the moment registration starts. DSWS – deep SWS, and SSWS – superficial slow wave sleep.

Results

In control rats, the wake (W) state occupied 27.4% of the total time of observation, while paradoxal sleep (PS) – was 12.5%, and slow wave sleep (SWS) – was 60.1% (Fig.1, A). The number of full SW cycles was 12.33 ± 3.56. In kindled rats, W state occupied 21.8% ($P > 0.05$), PS – 7.1% ($P < 0.05$), and SWS – 71.1% ($P > 0.05$) (Fig.1, C). The number of full SW cycles exceeded that one in control by 39.7% ($P < 0.05$). In kindled rats treated with pitolisant W state occupied 29.0% ($P > 0.05$), PS – 11.6% ($P > 0.05$), and SWS – 71.0% ($P > 0.05$). The number of cycles exceeded the control data by 17.2% ($P > 0.05$).

Conclusions

PTZ kindled SW disturbances – shortage of PS and its fragmentation are blocked with the pitolisant. **Financial support:** Ministry of Health Care of Ukraine (N0121U114510).

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Comparative effectiveness of niacin-oxietilyden-di-phosphonste germanat (MIGU-4) and diazepam upon neuronal loss in the retina of rats with pentylenetetrazol (PTZ)

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Background and aims

Epilepsy is accompanied by neuronal loss, which is observed in the retina as well. **The work aimed** to study the density of neurons in retina layers of rats with pentylenetetrazol (PTZ)-kindled seizures and compare neuroprotective effects of niacin-oxyethylene-di-phosphonate-germanate (MIGU-4) with diazepam.

Methods

The fully kindled seizures were induced in Wistar rats by administration of PTZ at a dose of 35.0 mg/kg, i.p., for three weeks. Fully kindled rats were administered with MIGU-4 (25.0 mg/kg, i.p.), and diazepam (1.5 mg/kg, i.p.) for four weeks. After euthanasia, the morphology of the retina was examined.

Results

Gained data revealed that the cell density in the ganglion layer in kindled rats was 2.14 times lower ($P < 0.05$). It was 41.0% and 19.0% lower in the inner and outer nuclear layers, respectively ($P < 0.05$) compared to the control. Under conditions of MIGU-4 treatment ganglion layer neurons, density exceeded the control value by 38.0% ($P < 0.05$), while in diazepam-treated rats, density was higher by 29.5% ($P < 0.05$). The density of cells in MIGU-4 treated rats in the inner nuclear layer exceeded that in control by 30.5% ($P < 0.05$). Diazepam administration was also characterized by an increased density of neurons by 22.7% ($P < 0.05$). In the outer nuclear layer density of neurons in kindled rats was not differ from the control group ($P > 0.05$).

Conclusions

The level of the neuroprotective effect of four weeks of administration of niacin-oxyethylene-di-phosphonate-germanate (MIGU-4) in a dosage of 25.0 mg/kg corresponds to such one induced with diazepam in a dosage of 1.5 mg/kg.

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121571

Synergy of antiseizure and anxiolytic action of rapamycin and histamine H_3 inverse agonist pitolisant on the PTZ-kindled seizures

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Background and aims

Neuroinflammatory contribution is principal for developing chronic epileptic seizures. The work aimed to investigate chronic seizures and anxious behavior in pentylenetetrazole (PTZ)-kindled rats under combined treatment with the histamine H_3 blocker pitolisant and mTOR blocker rapamycin.

Methods

Kindling was produced in Wistar male rats by administration of three-week PTZ (Sigma Aldrich, 35.0 mg/kg, i.p.). Rats with generalized seizures were chosen for observation. Treatment with rapamycin (Pfizer, 0.5 mg/kg, i.p.) and pitolisant (Selleck, 5.0 mg/kg, i.p.) was performed for ten days in fully kindled rats. Anxiety was investigated in the open field test.

Results

Combined administration of rapamycin and pitolisant prevented generalized seizures in 7 out of 8 rats ($P < 0.025$), while separate administrations failed to reduce seizures. The number of crossed central squares of the kindled animals was 4.1 times less, pertained to control ($P < 0.01$). Combined treatment abolished the reduction, which did not differ from control ($P > 0.05$), while under the condition of separate drug administration, the decline was 2.2 times for rapamycin ($P < 0.01$) and 2.7 for pitolisant ($P < 0.01$). The number of rearings was reduced in the kindled rats by 3.0 times compared to the control ($P < 0.001$). The number of rearings remained less compared with the control by 2.2