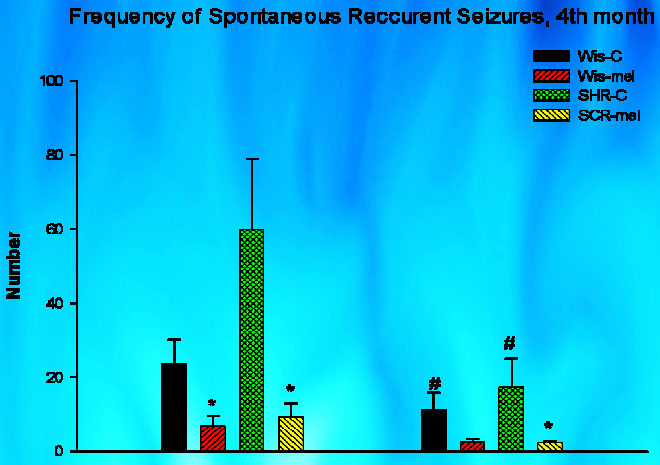
Effects of chronic melatonin treatment on diurnal variations of spontaneous recurrent seizures and behavioral changes in kainate model of temporal lobe epilepsy

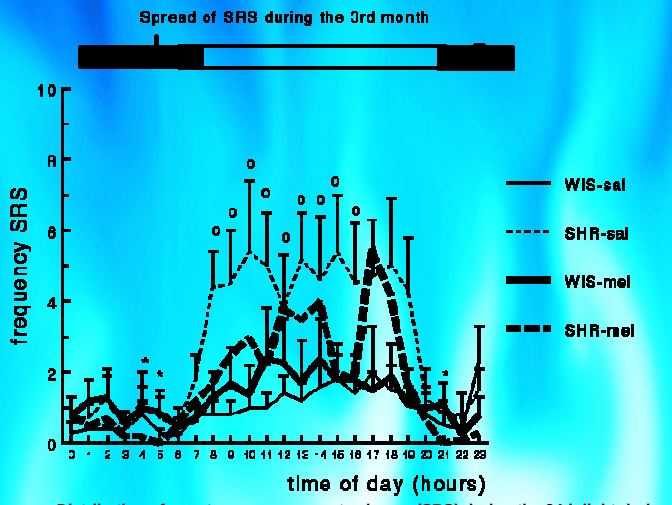
Zlatina Petkova, Daniela Pechlivanova, Jane Tchekalarova

Institute of Neurobiology, Acad. G. Bonchev Str., Bl. 23, Bulgarian Academy of Sciences, Sofia 1113, Bulgaria.

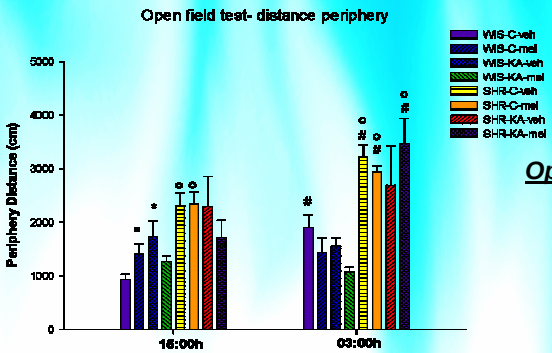
Temporal lobe epilepsy which is the most common type of acquired epilepsy in adults can be associated with neurobehavioural deficits, including anxiety, psychoses and memory impairment. The hormone melatonin exerts an inhibitory function in central nervous system and possesses anticonvulsant, sedative, hypnotic and anxiolytic activity in rodent models (Sugden, 1983). Besides its primary function as a synchronizer of the biological clock, melatonin is a powerful antioxidant that can easily cross cell membranes and blood brain barrier. The aim of the present study was to analyze the effect of chronic melatonin treatment during epileptogenesis on diurnal rhythms of spontaneous recurrent seizures (SRS) and behavioral activity in Wistar (WIS) and spontaneously hypertensive rats (SHRs).



The frequency of SRS was assessed by video-monitoring over twelve weeks. Spontaneous reccurent seizures occurred in all WIS and SHRs with either vehicle or melatonin treatment, respectively. Melatonin significantly alleviated the seizure frequency in WIS rats during the light phase while in SHRs melatonin decreased the seizure frequency during the light and the dark phase at the 4rd month after KA-induced status epilepticus (t-test: $p<0.05$).

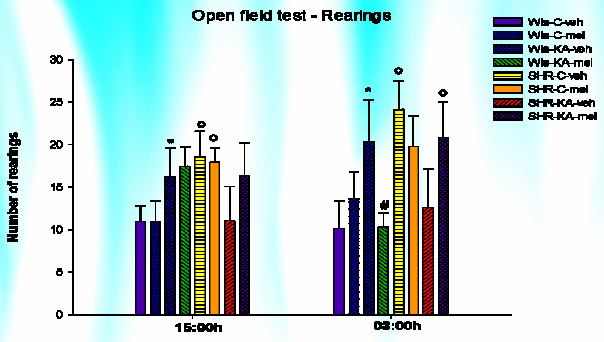


Distribution of spontaneous reccurent seizures (SRS) during the 24-h light-dark cycle at the 3rd month after KA-induced status epilepticus is demonstrated in Fig. 2. We have found a circadian distribution in the appearance of SRS with a prevalence of seizures when lights were on (between 8 a.m. and 8 p.m.) in both saline-treated and melatonin-treated rats, respectively. Epileptic SHRs (SHR-sal) showed higher seizure frequency than Wis rats (WIS-sal) during the chronic phase of epilepsy.

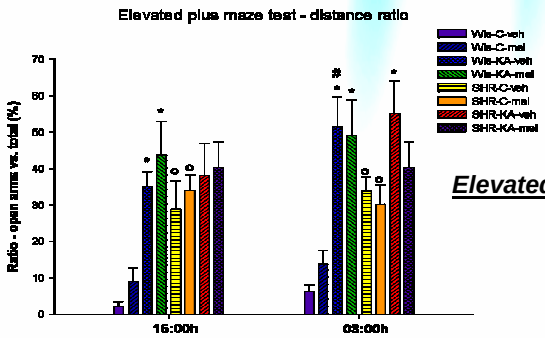


Open field test

Effect of chronic melatonin treatment (10 mg/kg in drinking water, 8 weeks) on distance in periphery (cm) in the open field test. The test was performed between 12 and 16 weeks after status epilepticus. Data are presented as means ± SEM (n = 9-13); *p < 0.05 controls vs epileptic rats; °p < 0.05 WIS vs SHRs, # 15:00 h vs 03:00 h.

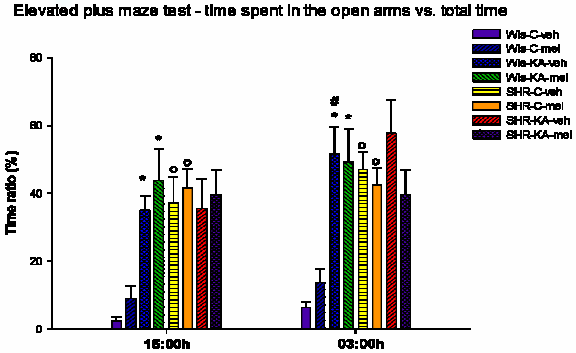


Effect of chronic melatonin treatment (10 mg/kg in drinking water, 8 weeks) on number of rearings in the open field test. The test was performed between 12 and 16 weeks after status epilepticus. Data are presented as means ± SEM (n = 9-13); *p < 0.05 controls vs epileptic rats; °p < 0.05 WIS vs SHRs, # 15:00 h vs 03:00 h.



Elevated plus maze-test

Effect of chronic melatonin treatment (10 mg/kg in drinking water, 8 weeks) on ratio distance open/distance total in the elevated-plus maze test. The test was performed between 12 and 16 weeks after status epilepticus. Data are presented as means ± SEM (n = 9-13); *p < 0.05 controls vs epileptic rats; op < 0.05 WIS vs SHRs, # 15:00 h vs 03:00 h.



Effect of chronic melatonin treatment (10 mg/kg in drinking water, 8 weeks) on time ratio open/ total in the elevated-plus maze test. The test was performed between 12 and 16 weeks after status epilepticus. Data are presented as means ± SEM (n = 9-13); *p < 0.05 controls vs epileptic rats; op < 0.05 WIS vs SHRs, # 15:00 h vs 03:00 h.

Conclusion: Epileptic rats treated with either vehicle or melatonin showed circadian distribution of SRS and were hyperactive, with lower anxiety level and abolished diurnal rhythms of locomotor activity. Melatonin decreased the frequency of SRS in Wis and SHRs. The hormone exerted a diurnal rhythms of locomotion in epileptic SHRs and rearings in epileptic Wis rats, respectively. Melatonin abolished the diurnal variations of anxiety level in epileptic Wis rats.

The poster is financially supported by the National Science Fund contract No DTK 02/56, 2009-2012.

No potential conflict of interest.