

14,3% and 0% respectively. The rates were determined as 77,8%, 85,7% and 42,9% in RES, GBP10mg/kg and DZ0,01mg/kg groups respectively and as 71,4% and 57,1% for RES+GBP10mg/kg and RES+DZ0,01mg/kg combination groups respectively. The seizure severity score was 0 in GBP20mg/kg and DZ0,2mg/kg groups. The scores in RES, GBP10mg/kg and DZ0,01mg/kg groups or in combinations of RES with GBP and DZ were determined as 4 and 5. There was no significant difference between groups in terms of the mortality rates. There were acidophylic neurons indicating acute neuronal injury and gliosis in hippocampal CA1, CA3, H, DG regions and cerebellar hemorrhagia in all groups except GBP 20 and DZ 0,2mg/kg groups.

GBP 20mg/kg and DZ 0,2mg/kg significantly decreased the seizure severity and provided protection against PTZ-induced seizures. Any preventive effect or any reduction in seizure severity were not observed when RES used alone or in combinations with subeffective doses of GBP and DZ. Histopathological evaluations also supported the behavioral results.

Keywords: diazepam, gabapentin, pentylenetetrazole, resveratrol, seizure

PT604

Attenuation of PTZ-induced epileptic seizure by deficiency in the gene encoding solute carrier OCTN1/SLC22A4

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Abstract

Identification of novel molecular targets for treatment of epilepsy is required to solve the problems in its pharmacotherapy including side effects and tolerance in currently used antiepileptic drugs. Carnitine/organic cation transporter OCTN1 is functionally expressed in brain neurons, and transports various organic cations including the food-derived antioxidant ergothioneine and the neurotransmitter acetylcholine. The aim of the present study is to examine possible involvement of OCTN1 in epilepsy to find a target for its treatment. The γ -aminobutyric acid (GABA) receptor antagonist pentylenetetrazole (PTZ) was administered to wild-type or *octn1* gene knockout (*octn1*^{-/-}) mice, and then severity of seizure and PTZ concentration in the body were evaluated by behavioral observation and LC-MS/MS, respectively. *octn1*^{-/-} mice showed lower seizure score and higher survival rate compared to wild-type mice, whereas tissue concentrations of PTZ was almost the same between the two strains. To clarify the mechanism underlying the attenuation of PTZ-induced seizure in *octn1*^{-/-} mice, we examined the difference in expression of GABA receptor subunits, efficacy of the GABA receptor agonist pentobarbital or diazepam, and release of GABA into the synaptic cleft, between wild-type and *octn1*^{-/-} mice. Expression of GABA receptor subunits mRNA in cerebral cortex and hippocampus, and sleep latency and sleeping time induced by the GABA agonists were almost the same between the two strains. The measurement of GABA concentration in brain interstitial fluid with microdialysis showed no significant difference at steady-state between the two strains, whereas the increase in GABA by treatment with high potassium in *octn1*^{-/-} mice tended to be more rapid than that in wild-type mice. These results suggest that OCTN1 may positively regulate PTZ-induced seizure via the mechanism different from pharmacokinetic regulation or modulation of GABA receptor function, supporting necessity of further studies to establish OCTN1 as a target molecule of anticonvulsant.

PT605

Alterations of functional connectivity in pilocarpine-induced mouse model of temporal lobe epilepsy in latent period

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Abstract

Temporal lobe epilepsy is a neurological disorders that characterize abnormal electrical activities in hippocampus as epileptic foci. During epileptogenesis, spontaneous recurrent seizures (SRSs) occurred and introduce to a chronic stage. Seizure-free period with no SRSs during epileptogenesis is important to early diagnosis and medication of epilepsy. However, researches related to latent period of temporal lobe epilepsy are not well understood. Although few reports have been investigated this period in epilepsy mouse model, there is one previous study indicated that social behavior deficits and abnormal cortical activity appear in latent period. We could have questions about this underlying mechanisms that how can the epileptic mice show disruptions of social behavior similar to chronic stage even though SRSs were not occurred in latent period. Patients with temporal lobe epilepsy suffered from psychiatric comorbidities including depression, anxiety, psychotic disorders, cognitive and personality changes and many human fMRI studies suggested that altered resting-state functional connectivity is associated with these symptoms and psychiatric comorbidities. Therefore, we could hypothesize that resting-state functional connectivity is altered in several brain regions which has been associated various deficits of behavior. Furthermore, the resting-state functional connectivity mapping with optical intrinsic signal imaging (fOIS) recently reported that could investigate the large-scale brain networks in mice. Using this functional neuroimaging, we observed the changes of intrinsic functional connectivity in latent period of chronic epilepsy mouse model by seed-based functional connectivity analysis. We demonstrated that there were significant decreased interhemispheric functional connectivity in frontal, temporal and visual cortex regions. Moreover, we detected two clusters centered on the left frontal and cingulate cortex regions using connectivity matrix and these two clusters showed persistently reduced functional connectivity with several brain regions. Interestingly, there were significantly differences in spectral features over the functional connectivity band in latent phase. These results suggest that the psychopathology of epilepsy might be involved with the altered intrinsic functional connectivity and could help to understand about latent period that is important to early diagnosis of temporal lobe epilepsy.

PT606

Effects of Chronic Ethosuximide Treatment on Cardiovascular Changes in Genetic Absence Epileptic WAG/Rij Rats

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Abstract

Objective: There is limited evidence about the cardiovascular changes in absence epilepsy (AE). Ethosuximide (ETX), a T-type calcium channel blocker, is one of the most commonly used drug in AE treatment. But its effects on cardiovascular functions in AE also has not been investigated. This study aimed to