Conclusions: Oleylethanolamide modulates motivation of intra-gastric feeding, possibly through normalization of PPAR-α-dependent vagal feedback to the brain in rodents. This supports its homeostatic function for regulating dietary fat intake via vagal-nigro-striatal pathways. Our study suggests that oleylethanolamide mediates reward-associated neural processes and this signaling plays an important role for hedonic regulation of food-craving and obesity in humans. It may be a valuable target for developing novel anti-obesity drugs.

EPILEPSY: PT601 – PT608

PT601
Evaluation of the behavioral and physiological roles of BRINP family genes in epileptic kindled mice
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Abstract
Objective: Induction of the BMP/RA-induced neural specific protein-1 (BRINP1) gene begins in the mouse nervous system from the early developmental stages, and it is highly expressed in various brain regions in adulthood. Studies have demonstrated that epileptic patients tend to have comorbid similar psychiatric symptoms to attention deficit hyperactivity disorder and autistic patients. In this study, the physiological role of BRINP1 was evaluated by conducting behavioral pharmacological tests in kindled BRINP1-deficient (KO) mice. Using immunohistochemistry, c-Fos expression levels in kindled mice were also studied.

Methods: To induce kindling, mice were intraperitoneally injected with pentylentetrazole at a dose of 35 mg/kg once every 48 h. After the final challenge, mice were tested.

Results: The development of kindled convulsions was not significantly different between wild-type and BRINP1-KO mice. BRINP1-KO mice showed less anxiety-like behavior than wild-type mice and the induction of kindling reduced anxiety-like behavior in both genotypes in the elevated plus maze test. In addition, c-Fos expression at steady state was significantly increased in the dentate gyrus of KO-kindled mice compared with wild-type mice. Furthermore, c-Fos expression was increased in the hippocampus, amygdala, and hypothalamus in both kindled and KO-kindled mice at 3 hours after pentylentetrazole injection, although this increase was similar in KO and wild-type mice.

Conclusion: These findings suggest that the BRINP1 gene is not directly involved in the epileptic behavior of kindling convulsions. However, elevated c-Fos expression in dentate granule neurons in BRINP1-KO mice at steady state implicated that BRINP1 involves regulation of neuronal excitability which is responsible for preventing onset of behavioral psychiatric symptoms.

PT602
The role of nitric oxide on the anticonvulsant activity of agmatine, valproic acid, gabapentin and phenytoin in mice
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Abstract
It was reported that nitric oxide, acting as a neuromodulator and neurotransmitter in central nervous system, has proconvulsant or anticonvulsant activities in different experimental convulsion models. The aim of the present study was to investigate the role of nitric oxide pathway on the anticonvulsant activities of valproic acid, gabapentin and phenytoin and also agmatine suggested as an anticonvulsant agent.

Swiss albino mice were used for the study. Seizures were induced by single intraperitoneal injection of 45mg/kg pentylentetrazole (PTZ). The existence of myoclonic jerk (MJ) and generalized tonic-clonic convulsions (GTCC) were recorded. Single doses of agmatine (10mg/kg), valproic acid (150mg/kg), gabapentin (20mg/kg) and phenytoin (20mg/kg) alone or with the precursor of nitric oxide, L-arginine (60mg/kg) or non-specific nitric oxide synthase inhibitor NG-nitro-L-arginine methyl ester (L-NAME) (5mg/kg) were injected intraperitoneally.

Agmatine and valproic acid significantly prevented but phenytoin and gabapentin did not prevent the GTCC and MJ. L-Arginine reduced the activity of agmatine on MJ but did not have any activity on GTCC. L-NAME did not affect the activity of agmatine on both MJ and GTCC. Both L-Arginine and L-NAME did not affect the activity of valproic acid and phenytoin on both MJ and GTCC. L-Arginine did not change the activity of gabapentin on both MJ and GTCC. L-NAME increased the activity of gabapentin on both MJ and GTCC.

This study suggested that nitric oxide may have a role on the anticonvulsant activity of agmatine and gabapentin but not those of valproic acid and phenytoin.
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 pentyleneetetrazole (PTZ) was administrated 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 by 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.