Methods: Forty-five right-handed patients with PD who met the diagnostic criteria in Structured Clinical Interview for DSM-V and twenty-two healthy control were examined by means of MRI at 3 Tesla. We used the FreeSurfer software package to create a three-dimensional model of the cortical surface for estimating the cortical thickness. In order to test the effect of the gene polymorphism on the brain cortical thickness, we were evaluated their candidate gene polymorphisms of 5-HTTLPR, HTR1A, COMT, BDNF and RGS. We examined between-group differences in cortical thickness using a 2 x 2 analysis of covariance (ANCOVA) to control age, gender, and education.

Results: We found scores of cortical thickness of PD is significantly lower than those of HC in temporal pole (p=0.000) and insula (p=0.000). Furthermore, analyses of covariance controlling for age, gender and education showed an interaction effects of the genes polymorphisms-by-panic disorder on paralimbic area. 5-HTTLPR rs25531 (p=0.011, Lt, temporal pole; p=0.011, Lt, insula), HTR1A rs6295 (p=0.007, Lt, temporal pole; p=0.002; Lt, insula; p=0.031, Lt, rostral anterior cingulate), BDNF rs6265 (p=0.012, Lt, temporal pole; p=0.002; Lt, insula), COMT rs4680 (p=0.000, Lt, temporal pole; p=0.001; Lt, insula), RGS2 rs4606 (p=0.009, Lt, temporal pole; p=0.009; Lt, insula; p=0.034).

Key words: Panic Disorder, 5-HTTLPR Polymorphism, Treatment Response

PS249
White matter microstructural changes are associated with alcohol use in patients with panic disorder
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Abstract
Objective: A close relationship between panic disorder (PD) and alcohol use disorder (AUD) has been suggested. We aimed to investigate alterations in white matter (WM) volume or integrity in patients with PD comorbid with AUD.

Methods: Forty-nine patients with PD, free of comorbid AUD (PD–AUD), and 20 patients with PD comorbid with AUD (PD+AUD) were investigated. All subjects were assessed using the Panic Disorder Severity Scale, Anxiety Sensitivity Inventory-Revised (ASI-R), Beck Depression Inventory, and CAGE questionnaire. Voxel-based morphometry and tract-based spatial statistics were used for imaging analysis.

Results: Increased fractional anisotropy (FA), as well as decreased mean diffusivity and radial diffusivity were observed in multiple WM tracts, including the body and splenium of the corpus callosum and the retrolenticular part of the internal capsule, in the PD+AUD group compared to the PD–AUD group. CAGE scores in the PD+AUD group and ASI-R scores in the PD–AUD group were significantly correlated with FA values for the corpus callosum. No WM volume differences were found.

Conclusions: Our findings revealed microstructural changes in multiple WM tracts, including the corpus callosum and internal capsule, suggesting they could be significant neural correlates of AUD in patients with PD.

PS250
Appearance of atypical cortical rhythm during fear conditioning in rats
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Abstract
Specific electroencephalographic (EEG) activity occur during a certain behavior. To find a specific EEG marker during fear response, EEG was recorded from the frontal and parietal cortices and the hippocampus of Sprague-Dawley rats during and after fear conditioning. Fear response such as freezing behavior was evoked by a tone predicting the occurrence of electric shock through classical aversive conditioning. EEG activity was subjected to power spectrum analysis, and then they were compared to the EEG activity observed during other behavioral states, such as awake still, awake moving, and paralyzed. In awake state, 1.95–2.34 Hz peak was observed in the frontal cortex, while 7.03 Hz peak as well as 1.95–2.34 Hz peak was observed in both the parietal cortex and the hippocampus. In awake moving, there was a prominent 7.81 Hz peak in the hippocampus, though both 1.56 Hz and 7.81 Hz peaks were in all regions. In paralyzed state, both 1.56 Hz and 3.51 Hz peaks observed in all regions. In addition, 6.25 Hz peak observed in the hippocampus. In freezing, a prominent 3.12 Hz peak was observed in the frontal cortex, though both 3.12 Hz and 5.85 Hz peaks were observed in the hippocampus. These observations suggest that the characteristic rhythm could represent functional alteration of the brain region affected by a certain behavioral learning such as fear and could serve as a biomarker of fear.

POST TRAUMATIC STRESS DISORDERS: PS251 – PS267

PS251
Pharmacological suppression of the lateral habenula via the activation of mu opioid receptors ameliorate helpless behaviors in a rodent model of depression
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Abstract
Endogenous opioid systems are involved in stress response and emotion regulatory processes. Stressful events release endogenous opioids and activate three different types of opioid receptors. Among these, type opioid receptors (mOR) are G-protein coupled receptors and regulate presynaptic neurotransmitter release probability. mOR deficient mice exhibit reduced anxiety, reduced depressive-like behaviors and decreased corticosterone responses. However, whether this is due to the compensatory effect of constitutive genetic deficiency of mOR remains to be determined. The lateral habenula (LHB), a brain area involved in depressive disorders show the highest expression of mORs, however mOR in the LHB has not been investigated. To investigate the role of mOR in the LHB, we performed a whole-cell patch clamp recordings. We found that pharmacological mOR activation successfully decreases both excitatory and inhibitory neurotransmission in the LHB, while the net effect of mOR activation was reduction in synaptic transmission. Previous studies observed enhanced activity of the LHB in animal models of depression, thus reducing the activity of the LHB may contribute to reverse helpless behaviors. Surprisingly, mOR-induced decrease in synaptic transmission remains intact in the LHB obtained after exposure to an hour-long restraint plus tail-shock stress, raising the possibility of mOR activation as a pharmacological tool to reduce the activity of abnormally potentiated LHB after stress exposure. The selective activation of mOR in the LHB indeed ameliorate
helpless behaviors after stress exposure. Our observation is consistent with clinical reports of the interaction between mOR and depression. Therefore, we suggest that the selective activation of mORs in the LHb may serve as a possible therapeutic strategy for treating depressive disorders.

**PS252**

Effect of agmatine on behavioral changes over time in post-traumatic stress disorder

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**Abstract**

**Objective:** Post-traumatic stress disorder (PTSD) is a persistent mental and emotional condition after life-threatening events. A single prolonged stress (SPS) induced animal model has demonstrated to result in neurological dysregulation and behavior abnormalities observed in PTSD. However, agmatine which was proposed as antidepressant and anxiolytic endogenous molecule was investigated in a rat model of PTSD.

**Methods:** Rats (200–260 g) were divided into Control (saline), SPS, SPS+Imipramine (20 mg/kg), SPS+Agmatine (20, 40 and 80 mg/kg) groups. In SPS model, rats were restrained for 2 h, 20 min of group forced swim in water, allowed 15 min in home cages then placed in an empty cage with a wire mesh floor under which petri dishes filled with ether were placed until loss of consciousness. Control animals were only handled. Animals were housed for 1, 7 and 14 days without disturbance. Animals were tested in open field (OFT), forced swimming test (FST) and elevated plus maze (EPM).

**Results:** We found that the SPS rats spent less time than the control rats in the center. General locomotor behavior was measured as the total distance traveled during the OFT test, was significantly lower in SPS rats than in controls. SPS rats spent less time grooming, longer immobility time in the FST and the highest mean value were detected at day 7. All PTSD related findings significantly reversed by imipramine and agmatine treatment. In EPM, agmatine increased time spent and number of entries in open arm, in a dose-dependent manner. The effect is comparable to imipramine which induced increase in the occupancy in the open arm.

**Conclusion:** Our results indicate that SPS would trigger a constant anxiety-like behaviors, and significant depressive behavior which was reversed by agmatine. Since all anxiety-like behavior is reversed by Agmatine, as an endogenous molecule, might have a regulatory function in PTSD.

**PS253**

Establishing a fear extinction-impaired animal model of post-traumatic stress disorder

Establishing a fear extinction-impaired animal model of post-traumatic stress disorder

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**Abstract**

Post-traumatic stress disorder (PTSD), a common anxiety disorder, occurs less than 10% of individuals after experiencing one or more terrifying accidents. One of key symptoms reported in PTSD patients is repeatedly and persistently re-experiencing the traumatic event due to the recurrent visits of fearful memory. The estimated lifetime prevalence of PTSD among adult Americans is 7.8% while ~60% of adults reported to have experienced at least one traumatic event. Currently available animal models include physical and social stress models, however stressor models cannot distinguish general trauma coping responses from persistent and selective PTSD symptoms. Therefore, we took advantage of a genetic strain of mouse, 129S1/SvImJ (129S1) to establish a convincing animal model for PTSD. 129S1 has been reported to have a trouble with fear memory forgetting or fear extinction after fear conditioning. Here, we evaluated 129S1 as a bona-fide, fear extinction-impaired animal model for PTSD at cellular, synaptic and behavioral levels. 129S1 shows reduced immediate early gene, c-Fos expression in infralimbic cortex of medial prefrontal cortex and basolateral amygdala compared to C57BL/6, both of which are parts of fear extinction circuitry. We found that 129S1 had no problem in fear memory formation while having impaired fear extinction in both auditory and contextual fear conditioning protocols. 129S1 exhibited comparable hippocampal dependent spatial memory in Morris water maze following contextual fear conditioning compared to C57BL/6, suggesting that fear memory impairment is only selective to fear extinction in 129S1. Therefore we propose that 129S1 could serve as a useful animal model for PTSD to study the etiology and pathophysiology underlying PTSD.

**PS254**

Enhancement of forgetting remote contextual fear memory through increase in adult hippocampal neurogenesis in combination with reactivation of hippocampus by long-time memory recall

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**Abstract**

Approaches to develop treatment for PTSD using rodents have been targeted on extinction and reconsolidation of recent memory although traumatic memories associated with PTSD are remote. Recent study has shown that forgetting of recent fear memory is promoted by the treatment with memantine (MEM) that increases in hippocampal neurogenesis. Here we show that forgetting of remote contextual fear memory is enhanced by the MEM treatment only after long-time memory recall. Treatment with MEM for 4 weeks after contextual fear conditioning enhances forgetting but this treatment fails to enhance forgetting of remote fear memory. Interestingly, the same treatment promotes forgetting of remote memory only after long-time recall by the re-exposure to the conditioned stimulus (CS) for 10 min, but not 3 min. Similarly, exercise, another hippocampal-neurogenesis enhancer, also promotes forgetting of remote memory after the prolonged recall. As a possible mechanism by which long-time recall allows remote memory forgetting, we found that long-, but not short-, time recall of remote memory activates gene expression of hippocampus and induces hippocampus-dependent reconsolidation. More importantly, retrieval of remote contextual fear memory becomes hippocampus-dependent after the long-time recall. These observations suggest that remote fear memory returns into a hippocampus-dependent state after long-time retrieval, thereby allowing enhance forgetting by increased hippocampal neurogenesis. Our findings may contribute to develop a method for the PTSD treatment by enhancing forgetting of traumatic memory.