and anxiolytic properties in several studies. However there is limited data showing the beneficial effect of linalool following exposure to chronic stress. The aim of the present study was to investigate the effect of linalool in chronic stress rats on behaviour related depressive disorder and BDNF protein in hippocampus. Male Wistar rats were randomly divided into 5 groups, 1) Tween 80 + home cage (HC) 2) Tween 80 + restraint stress (RS) 3) linalool 50 mg/kg + RS 4) linalool 160 mg/kg + RS and 5) linalool 500 mg/kg + RS. Either Tween 80 or linalool was intraperitoneally injected to rats daily for two weeks. Some rats were housed in home cage but the others induced chronic restrained stress (15 min daily) for two weeks. At the end of the treatment, rats were assessed for depressive-like behavior using the forced swimming test. Then, the rats were immediately decapitated and hippocampus was removed for the measurement of BDNF protein by ELISA. Restricted rats injected with linalool 500 mg/kg for two weeks significantly reduced immobility time (p<0.05) and increased climbing time (p<0.05) compared their controls, suggesting that this dose produced antidepressant activity. Linalool had no effect on the level of BDNF protein in hippocampus. Therefore, these findings suggest that linalool decreases behaviour related depressive disorder but has no effect on hippocampal BDNF in chronic restrained stress.

**PS121**

**Evaluation of extrapyramidal side effects in the treatment of behavioral and psychological symptoms of dementia (BPSD): Interactions between anti-Alzheimer drugs and antidepressants**

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**Abstract**

**Background/Objectives:** Antidepressants are often used in conjunction with anti-Alzheimer drugs to treat the behavioral and psychological symptoms of dementia (BPSD). Here, we studied the interactions between anti-Alzheimer drugs, cholinesterase inhibitors (ChEIs), and antidepressants in inducing extrapyramidal side effects (EPS).

**Methods:** Male ddY mice were used. Using the pole test, we examined the actions of serotonin reuptake inhibitors (SSRIs), fluoxetine and paroxetine, a serotonin and noradrenaline reuptake inhibitor (SNRI) milnacipran, a noradrenergic and specific serotonergic antidepressant (NaSSA) mirtazapine in modulating the ChEIs (galantamine and donepezil)-induced bradykinesia.

**Results:** Both fluoxetine and paroxetine significantly potentiated galantamine-induced bradykinesia in a synergistic manner. The EPS augmentation by fluoxetine was antagonized by ketanserin (5-HT, antagonist) and SB-258585 (5-HT, antagonist), but not by ondansetron (5-HT, antagonist). In contrast to SSRIs, milnacipran and mirtazapine failed to augment galantamine-induced EPS. In addition, combined treatment of prazosin (α antagonist), but not yohimbine (α antagonists), with milnacipran significantly potentiated galantamine-induced EPS.

**Conclusion:** The present results indicate that SSRIs and ChEIs synergistically facilitate the EPS induction; the activation of 5-HT, and 5-HT, receptors, in the treatment of BPSD. The combination of ChEIs with SNRIs (or NaSSA) is recommended in terms of EPS liability for the BPSD therapy, where the activation of α receptors by SNRIs seems to reduce EPS.

**PS122**

**Overexpression of N-acetyltransferase Shati/Nat8l in the dorsal striatum induces depression-like behaviors in mice.**

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**Abstract**

Depression is one of the most serious psychological disorders, but its pathogenesis remains unclear and the current medical treatment is mainly restrictive effect. We have identified Shati/Nat8l, which is containing a well-conserved N-acetyltransferase sequence, in the brain of psychosis animal model. Shati/Nat8l synthesizes N-acetylaspartate (NAA) from L-aspartate and acetyl-CoA, and NAA is subsequently converted into N-acetylaspartylglutamate (NAAG) by being condensed with glutamate. It is reported that NAA and NAAG abundantly exist in human brains and those both or one quantity change in the postmortem brain of patients with psychological disorders including depression. In the present study, to clarify the functional roles of Shati/Nat8l in depression, we investigated various behavioral analyses in Shati/Nat8l-overexpressed mice.

Firstly, the expression levels of Shati/Nat8l mRNA were assessed in the brain of depressed C57BL/6J mouse model, which was exposed repeated social defeat stress for 10 days following procedure as physical stress for 10 min and sensory stress for 24 hrs by aggressor ICR mice. And, Shati/Nat8l mRNA in the dorsal striatum of the depression mice significantly increased compared with that of control mice. Therefore, mice were microinjected Shati/Nat8l-inserted or non-inserted (Mock) adeno-associated virus vectors into the dorsal striatum. The Shati/Nat8l-overexpressed mice exhibited decreased social interaction and sucrose preference after subthreshold social defeat stress as the exposure to aggressor ICR mice for 5 min x3 on only one day, which showed normal behaviors in the Mock mice. These two phenotypical impairments in the Shati/Nat8l-overexpressed mice were ameliorated by treatment with a selective serotonin reuptake inhibitor fluvoxamine at the dose of 10 mg/kg i.p., which has no effect in the Mock mice.

**Results:** Both Shati/Nat8l mRNA and protein expression levels were significantly increased in Shati/Nat8l-overexpressed mice.

These findings suggest that Shati/Nat8l in the striatum plays an important role in depression-like behaviors including diminished sociability and pleasure by regulating the serotonergic neuronal system.

**PS123**

**Altered peptide ligands of myelin basic protein produce persistent antidepressant-like effects**

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**Abstract**

Cytokine levels were generally changed in both depressed patients and animal models. Altered peptide ligand (APL) of myelin basic protein (MBP) regulates levels of various cytokines,
and MBP_{A91, A96} exerted significant antidepressant-like effects which was more effective than imipramine. And also bupropion (40 mg/kg) exerted significant antidepressant-like effects which was more effective than imipramine. Again, desipramine, venlafaxine and bupropion (20 mg/kg) exerted significant anxiolytic-like effects which was as effective as diazepam. And also bupropion (40 mg/kg) exerted significant anxiolytic-like effects which was more effective than diazepam.

**Conclusions reached:** desipramine, venlafaxine and bupropion (20 mg/kg) exerted significant antidepressant-like effects which was as effective as imipramine. And also bupropion (40 mg/kg) exerted significant antidepressant-like effects which was more effective than imipramine. Again, desipramine, venlafaxine and bupropion (20 mg/kg) exerted significant anxiolytic-like effects which was as effective as diazepam. And also bupropion (40 mg/kg) exerted significant anxiolytic-like effects which was more effective than diazepam.

**PS125**

Functional and morphological changes induced by ketamine in the hippocampus

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**Abstract**

**Introduction:** Depressive disorders constitute a major burden for society in terms of productivity and years lost to disability. However, despite decades of research, the neurobiology of depressive disorders is largely unknown. Recently it was shown that ketamine (KET), a non-competitive NMDA receptor antagonist, originally introduced as a dissociative anesthetic, induces a rapid (within hours) and sustained (up to 1 week) antidepressant effect in patients with treatment-resistant depression. The mechanism by which KET ameliorates depressive symptoms is still unclear. Therefore, the aim of the current study is to provide a morphological and functional characterization of the effect of ketamine in the hippocampus (HPC) of naïve rats.

**Objective:** To measure changes in basal and depolarization-evoked endogenous glutamate (Glu) release in parallel with assessment of alterations in synaptic morphology induced by acute KET in the HPC of naïve rats.

**Methods:** Glu release experiments were assessed using purified synaptosomes in superfusion. Purified HPC synaptosomes were layered on microporous filters in parallel superfusion chambers and superfused with standard medium. A 90-sec period of stimulation with KCl was applied. Fractions collected were analyzed for endogenous Glu content by HPLC.

For morphological analysis, one hemisphere per animal was processed for Golgi staining. The areas of interest were delineated using a light microscope (Olympus BX50). Collapsed Z-stacks were analyzed with IMARIS 7.6.

**Results:** Our preliminary results show that a single injection of KET modulates evoked Glu release. We are currently investigating morphological correlates in terms of dendritic morphology, spine types and spine density.