CUMS groups, respectively. In immunohistochemical experiments, Iba-1 was overexpressed in CUMS group and BBG significantly reduced the overexpression of Iba-1.
Conclusion Our results suggest that chronic administration of BBG has an antidepressant-like activity supporting the notion of P2X7 receptors involvement in depression by modulating microglial activation.
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EW0754

Harmane suppresses microglial neuroinflammatory response and induce antidepressant-like effect in rats

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Objective Harmane is a beta-carboline, which binds to imidazoline receptors and it has been previously shown that it may have an antidepressant effect when administered acutely. This study is planned to investigate the effect of harmane on chronic unpredictable mild stress (CUMS) model and microglial (Iba-1) immunoreactivity in the same model as markers of neuroinflammation.
Methods Male Wistar Albino rats (290–360 g) were divided into groups such as control (saline), CUMS, CUMS + Imipramine (20 mg/kg; i.p.), CUMS + Harmane5 (5 mg/kg; i.p.), CUMS + Harmane10 (10 mg/kg; i.p.) groups (n = 10–12 in each). In CUMS model, various stressors were applied for 40 days. On day 20, harmane administration was started for 20 days. At the end, sucrose preference and forced swimming tests were performed. Then, brains were removed with paraformaldehyde perfusion for Iba-1 immunohistochemical analysis in hippocampus. One-way analysis of variance and Tukey's test were used for statistical analysis.
Results The time of immobility in forced swim test was significantly reduced while sucrose preference was increased in Imipramine and CUMS + harmane10 groups. In immunohistochemical experiments, Iba-1 were overexpressed in CUMS group and Harmane significantly reduced the overexpression of Iba-1.
Conclusion Our results suggest that chronic administration of harmane has an antidepressant-like activity in chronic stress model of depression. These results support the notion of imidazoline receptors involvement in depression by modulating neuroinflammation and at least a part of its antidepressant effect might be through modulating microglial activation as a reflection of neuroinflammation.
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EW0755

Investigation of chemical interactions of small peptides and vitamin substances at the developed dopamine D2 receptor models

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Introduction Dopamine receptors perform various functions essential to vertebrate central nervous systems and they are the major targets of antipsychotic drugs. Our recent studies pioneered to perform molecular modeling studies of the dopamine D2 receptor (D2R), describing the mechanism and binding affinities of marketed antipsychotics into the active sites of the $D2^{high}R$ and $D2^{Low}R$ [1]. Another study provided significant information about changes of binding cavity properties of D2R [2].
Objectives Since the marketed antipsychotics have serious side effects, we aim to explore ligands with better inhibition profiles on D2R with less unwanted outcomes. For this aim, we compare the effectiveness of the marketed drugs with small peptides and vitamin substances.
Aims The main goal of the research is to explore novel small molecules that inhibit D2R to be used in schizophrenia.
Methods In this study, we used a large number of endogen vitamins and peptides with dopamine D2R active-inactive forms in monomeric-dimeric patterns to understand their interactions at the active sites of targets. Nineteen of antipsychotic drugs, which are widely used in schizophrenia treatment are selected as reference molecules. Molecular docking, molecular screening and molecular modeling approaches were used.
Results Some of these endogen molecules showed similar or better inhibition profiles on D2R compared to the known standard inhibitors of the target.
Conclusions Proposed molecules may be potent for D2 receptor inhibition with less side effects for the use for schizophrenia.
Disclosure of interest The authors have not supplied their declaration of competing interest.
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EW0756

Pharmacodynamic targets of psychotic patients treated with a long-acting therapy

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Introduction Given the poor compliance of schizofrenic patients to antipsychotic therapies, are been developed drugs in long-acting formulation that for their pharmacokinetic ensures prolonged therapeutic activities. Currently, we consider that their efficacy depends on hereditary tracts, influencing both pharmacodynamic and pharmacokinetic parameters.

Objective Investigate relationships between clinical efficacy and genetic polymorphims of long-acting drugs' pharmacodynamic targets.
Methods Seventy-eight psychotic patients, treated with atypical long-acting antipsychotics (olanzapine pamoate, paliperidone palmitate, risperidon and aripiprazole), were examined. We carried out a blood sampling to evaluate dopaminergic DRD2 and glutamatergic GRM3 genetic receptors polymorphisms. PANSS and BPRS scales were used to assess clinical condition.
Results Regarding the *GRM3* genes, the study of rs2228595 and rs6465084 polymorphisms showed a prevalence of wild type genotypic frequency of 81.2% and 56.2%, respectively. The prevalence of the patients with mutated heterozygote genotype (rs6465084 polymorphisms) resulted high (40.6%). Considering rs1989796 e rs274622 polymorphisms, the sample showed a prevalence of mutated heterozygote genotype in the 53.1% e 45.3%, respectively, with a percentage of 43.7% of patients with a mutation in homozygosis. Considering the rs146812 polymorphism, the 53.1% of patients resulted with a wild type genotype. Finally, findings showed a prevalence of 56.2% for the mutated heterozygote genotype in the DRD2 rs6277 polymorphism. The genotypic categorization analysis demonstrated a significative association between the GRM3 rs274622 polymorphism and higher BPRS scores.
Conclusions The relationship between rs274622 polymorphism and worse clinical conditions could indicate a major resistance to long-acting antipsychotics in patients with genotypic frequency CT (mutated heterozygosis) for this polymorphism.
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EW0757

Prescribing patterns of psychiatric drugs in major depressive disorder – Findings from a large European multicenter, cross-sectional study

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Introduction The multicenter, cross-sectional survey summarizes the current prescription patterns of psychopharmacological medications in patients with major depressive disorder (MDD) treated in European university psychiatric centers.
Methods The study included a total of 1181 MDD patients who were recruited in 9 academic sites across 8 European countries. Socio-demographic, clinical, and psychopharmacological characteristics were collected within a detailed clinical interview and the current depressive symptom severity was measured by the Montgomery and Åsberg Depression Rating Scale (MADRS). Symptom reduction during the present MDD episode was analyzed by calculating retrospective MADRS scores. Descriptive statistics, analyses of variance (ANOVAs), and Spearman correlation analyses were performed to examine the impact of various features on the applied pharmacological strategies.
Results Regarding first-line antidepressant medication, the most frequently prescribed drug classes were selective serotonin reuptake inhibitors (SSRIs) (53.4%), serotonin-norepinephrine reuptake inhibitors (SNRIs) (23.6%), noradrenergic and specific serotonergic antidepressants (NaSSAs) (8.2%), tricyclic antidepressants (TCA) (5.1%), and the melatonergic antidepressant agomelatine (5.0%). The most commonly used individual antidepressants were escitalopram (18.4%), venlafaxine (15.2%), sertraline (12.9%), paroxetine (9.1%), mirtazapine (8.2%), duloxetine (7.0%), and fluoxetine (6.5%). Among the patients, 59.4% were treated with polypsychopharmaceutical medications (mean: 2 drugs) and for the number of individual drugs, we found a significant correlation with the present MADRS total score and the MADRS total score change during the current depressive episode.
Conclusion Consistent with surveys investigating primarily municipal psychiatric treatment centers, we could replicate the observation that SSRIs are the most commonly used antidepressants in MDD for the first time for European university centers.
Disclosure of interest The authors have not supplied their declaration of competing interest.

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EW0758

The regulation of orexins and their cognate receptors in two distinct rat models of depression and effects of treatments

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Introduction Depression has sleep disturbances as a key symptom and recently sleep has been suggested as a new area to optimize treatment in depression. Orexin is produced in the hypothalamus and projected throughout the brain innervating a number of structures important in depression. It controls a number of physiological processes including sleep, arousal, cognitive processes and stress, which are affected during depression.
Objective The study examines the possible implications for abnormalities in the orexinergic system in depression. We aim to determine whether treatment targeting this system relieves depressive symptoms.
Methods Using real-time qPCR and Western blotting optimal sampling time is determined by an assessment of the diurnal variation of orexin expression. Expression of orexin and its receptors are investigated in the hypothalamus, the hippocampus, and the prefrontal cortex of the Flinders Sensitive Line (FSL) and the Chronic Mild Stress model of depression. Behavioral and molecular response to treatment with a conventional antidepressant and an orexin receptor antagonist will be addressed in FSL rats. In addition, we will include exercise as a noninvasive treatment, which has shown positive effects on both sleep and depression in humans.
Results Real-time qPCR analysis showed increased expression of the orexin-1 receptor (40%) and the orexin-2 receptor (39%) in the prefrontal cortex of FSL rats compared to the control rats, the Flinders Resistant Line rats.
Conclusion This study may provide a platform for screening of drugs with effects on both sleep and depressive symptoms with perspectives for the development of novel strategies for treatment of depression.
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