

Objective Investigate relationships between clinical efficacy and genetic polymorphisms of long-acting drugs' pharmacodynamic targets.

Methods Seventy-eight psychotic patients, treated with atypical long-acting antipsychotics (olanzapine pamoate, paliperidone palmitate, risperidone 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 polypharmaceutical 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.

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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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