Introduction: Olanzapine (OL) represents one of the main chooses for the treatment of psychosis. However, OL increase the risk of metabolic syndrome (MS). Previous literature proposes the "Leptin resistance" as a possible hypothalamic pathogenesis of OL induced MS because of the occurrence of weight gain with increased Leptin blood level.
Objectives: The aim of our study is to investigate in a murine model of full-MS phenotype induced by Olanzapine the hypothalamic gene expression of the pathways involved in Leptin receptor signalling to clarify if a Leptin resistance occurs.
Methods: For the experiment C57BL/6Jfemale mice are used.The OL group (n=15) received pure Olanzapine compounded into chow (54 mg/kg of diet). The vehicle group (n=15)is fed with the same chow without OL. Weight gain is measured every 5 days. After 4 weeks of treatment, mice are sacrificed by rapid cervical dislocation. Blood is collected for Glucose, Insulin and Leptin evaluation. Hypothalamus is dissected and RNA-seq is performed.
Results: The OL group shows a significantweight gain compared to Control (p= 0.02). Likewise blood glucose, Insulin and Leptin levels appear increased (p= 0,0089, p= 0,01, p= 0,0012). From the analysis of RNA-seq hypothalamic differentially expressed genes the anorexigenic POMC pathway downstream to the Leptin Receptor shows a 4-fold increased compared to control.
Conclusions: In our study the "Leptin resistance" involvement in OL induced MS is not confirmed. In fact, although there is an increase in blood Leptin, the expression of Leptin receptor downstream pathways shows a significant increase. This could suggest a possible "POMC resistance" mechanism for OL induced MS.

Disclosure: No significant relationships.
Keywords: Translational medicine; Metabolic syndrome; Hypothalamic RNAseq analysis; Psychopharmacology

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Predicting the risk of drug-drug interactions in psychiatric hospitals

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Introduction: The most common medical decision is the prescription of medicines. More than 130 different drugs with proven efficacy are currently available for the treatment of patients with mental disorders.
Objectives: The aim was to use routine data available at a patient's admission to the hospital to predict polypharmacy and drug-drug interactions (DDI).
Methods: The study used data obtained from a large clinical pharmacovigilance study sponsored by the Innovations Funds of the German Federal Joint Committee. It included all inpatient episodes admitted to eight psychiatric hospitals in Hesse, Germany, over two years. We used gradient boosting to predict respective outcomes. We tested the performance of our final models in unseen patients from another calendar year and separated the study sites used for training from the study sites used for performance testing.
Results: A total of 53,909 episodes were included in the study. The models' performance, as measured by the area under the ROC, was "excellent" (0.83) and "acceptable" (0.72) compared to common benchmarks for the prediction of polypharmacy and DDI, respectively. Both models were substantially better than a naive prediction based solely on basic diagnostic grouping.
Conclusions: This study has shown that polypharmacy and DDI at a psychiatric hospital can be predicted from routine data at patient admission. These predictions could support an efficient management of benefits and risks of hospital prescriptions, for instance by including pharmaceutical supervision early after admission for patients at risk before pharmacological treatment is established

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Keywords: Drug Prescriptions; Medication Therapy Management; machine learning; psychiatry

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Safety of esketamine nasal spray: Analysis of post-marketing reports submitted to the FDA adverse event reporting system in the first year on the market

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Introduction: The approval of the esketamine nasal spray for treatment-resistant depression in March 2019 by the Food and Drug Administration (FDA), and few months later by the European Medicine Agency, triggered a vivid debate and many concerns, mainly because of the lack of convincing evidence on its efficacy and safety, based on the development programs, approval trials and few post-marketing trials.
Objectives: We aimed to detect and characterize safety signals for esketamine, by analyzing relevant adverse events (AEs) reports in the FDA Adverse Event Reporting System (FAERS) database (March 2019-March 2020).
Methods: We performed disproportionality analysis through the case/non-case approach: reporting odds ratios (ROR) and information components (IC) with 95% confidence intervals (95%CI) were estimated for esketamine-related AEs with at least four counts. We compared serious and non-serious AEs using non-parametrical tests.
Results: The FAERS database registered 962 reports of esketamine-related AEs in one year. Signals (i.e., statistically significant disproportionality) were detected for several AEs, such as dissociation, sedation, feeling drunk, suicidal ideation and completed suicide. Signals for suicidal ideation, but not suicide attempt and completed