(DHB), which irreversibly inhibit CYP3A4, potentially increasing drug plasma concentrations and the risk of adverse effects (Bailey et al. CPT 1998, 64(3) 248-256; de Castro et al. J. Agric. Food Chem 2006, 54(7) 2498-2503; Row et al. J. Med. Chem 2005, 49(20), 6139-6146).
Objectives: This review aims to quantify the impact of grapefruit juice on the plasma concentrations of buspirone, carbamazepine, and diazepam and to understand the duration of these effects to better manage patient safety.
Methods: A comprehensive review of existing pharmacokinetic studies (Furukori et al. BJCP 2003, 55(3), 307-311; Lane et al. Psychopharm 2001, 155(3), 356-359; Tanaka et al. Clin. Pharm 2013, 52(5), 397-420; Wang et al. CPT 1993, 65(3), 314-321; Yasui et al. Psychopharm, 145(1), 84-87) was conducted to gather data on the effects of grapefruit juice on CYP3A4 substrate psychiatric medications. Quantitative increases in plasma concentration metrics (AUC and Cmax) were extracted, and the duration of the inhibition effect was analyzed.
Results: Buspirone plasma concentrations increased by 4.3-fold, with effects lasting 24 hours. Carbamazepine showed a 1.4-fold increase in AUC and a 1.2-fold increase in Cmax, with effects persisting up to 24 hours. Diazepam concentrations increased by 3-fold in AUC and 2-fold in Cmax, with an effect duration of 24 hours. No significant interaction was observed for clozapine and haloperidol.
Conclusions: Grapefruit juice significantly increases the plasma concentrations of buspirone, carbamazepine, and diazepam by inhibiting CYP3A4, with effects lasting up to 24 hours. Clinicians should educate patients on avoiding grapefruit consumption while on these medications and monitor for potential toxicity. Further research is needed to develop guidelines for managing these interactions and to explore genetic variations in response to grapefruit consumption.

Disclosure of Interest: None Declared

Psychoneuroimmunology

EPP503

Immune4Plasticity: do non-pharmacological interventions modulate the inflammatory pattern of major depressive disorder? A study protocol

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Introduction: Major depressive disorder (MDD) is a severe mental disorder with a prevalence rate of 10%. Approximately 30-40% of patients suffering from MDD show higher levels of proinflammatory cytokines, associated to low response to pharmacotherapy. Thus, modulation of immune system might have a key role in the management of MDD.
Objectives: This study is aimed to: 1) assess the interrelation between immune hyperactivation and neuronal plasticity; 2) assess how non-pharmacological treatments impact on the immune hyperactivity in patients suffering from MDD; 3) identify biological makers able to predict the course of MDD and the effectiveness of treatments.
Methods: Immune4Plasticity is a longitudinal, multisite trial funded by Italian Ministry of Health. Preclinical analyses aimed at investigating the interrelation between immune hyperactivation and neuroplasticity as well as the identification of biological markers of MDD will be carried out at National Institute of Health in Rome. Clinical part of the study will be performed at the Department of Psychiatry of University of Campania, Naples, and at the Vita-Salute San Raffaele University, Milan. Seventy patients aging 18-65, with a diagnosis of MDD according to the DMS-5 criteria without psychotic symptoms, scoring more than 14 at the 17-item Hamilton Depression Rating Scale and able to release informed consent will be included. Thirty-five participants will attend a lifestyle psychosocial intervention in Naples; thirty-five will undergo light-therapy sessions in Milan. Assessments of both groups will be performed at recruitment (T0), after 3 months (T1) and after 6 months (T2), by using standardized psychometric tools and blood samples. The project will be carried out for 24 months.
Results: This multidisciplinary, translational study will shed more light on the complex interrelationship between MDD, immune system and neuroplasticity by investigating the role of psychosocial intervention and light therapy as 'modulators'. This will make it possible to develop innovative therapeutic strategies by integrating non-pharmacological approaches with anti-inflammatory drugs and to identify new peripheral markers to assess the response to treatment of patients with MDD.
Conclusions: MDD is a complex mental disorder associated with higher expression of inflammation. Sometimes, it is not adequately responsive to pharmacotherapy. Understanding the effect of non-pharmacological treatments as "modulators" of the inflammatory pattern of MDD may be an important strategy to optimize clinical management of this disorder.

Disclosure of Interest: None Declared

Psychopharmacology and Pharmacoeconomics

EPP504

Lipopolysaccharide induced acute inflammation leads to a higher systemic and brain exposure to olanzapine in mice

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Introduction: Pro-inflammatory mediators inhibit drug metabolism and transport. Detailed knowledge is lacking on the mechanism and extent of alterations in olanzapine pharmacokinetics during acute inflammatory states accompanying infections.
Objectives: To quantify the extent of systemic and brain exposure to olanzapine in a murine model of endotoxemia compared to a non-endotoxemia model.

Methods: Acute endotoxemia model was established in C57BL/6N mice intraperitonealy injected with 5 mg/kg *Escherichia coli* lipopolysaccharide (LPS). On Day 2 following LPS administration, LPS-injected mice and saline-treated controls were given single doses of olanzapine orally (p.o.) or intravenously (i.v.) or desmethylolanzapine (DMO) i.v. Concentrations and unbound fractions of olanzapine and DMO were measured in plasma samples and brain homogenates. Moreover, plasma biochemistry parameters and mRNA expression patterns were evaluated of pro-inflammatory cytokines, selected phase I and II drug-metabolizing enzymes and transporters in the liver, ileum and brain.
Results: Following p.o. olanzapine, the areas under the concentration-time curve (AUC) for olanzapine and DMO in the plasma were increased 3.8-fold and 2.6-fold ($P<0.05$) in LPS-injected mice vs. controls. The AUC for olanzapine in the brain homogenate was 5.2-fold higher ($P<0.05$). Brain DMO was hardly detectable in both groups. The penetration ratios ($K_{p,brain}$) of 8.5 and 6.3 confirmed that LPS increased the passage of olanzapine into the brain. Expression of mRNAs was decreased in the liver of CYP1A2 and UGT1a1/1a5 enzymes and Abcb1a, Bsep and Ntcp transporters and of ileal Abcb1a, whereas Abcb1a and Abcb1b in the brain and inflammatory cytokines and chemokines mRNAs in the liver were upregulated.
Conclusions: Investigation of olanzapine pharmacokinetics in endotoxemia mice clearly indicates a considerable increase in systemic and brain concentrations of the drug after oral administration. Further studies should clarify whether or not the inflammation-induced inhibition of metabolism and efflux transport results in brain overexposure to the drug and adverse effects in accutely infected patients treated with oral olanzapine.

Disclosure of Interest: None Declared

Psychoneuroimmunology

EPP505

Immune/inflammatory parameters as potential predictors of high-lethality suicidal behavior in individuals with/without psychiatric conditions: a retrospective single-center study

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Introduction: Accumulating research has suggested a possible role of the immune/inflammatory response system in the pathophysiology of suicidal behavior, more specifically of specifically high-lethality suicide attempts (SA). To count with reliable and affordable biological markers of high-lethality SA to complement clinical assessment for early detection of individuals at a high risk of committing suicide is thus mandatory.
Objectives: To assess if immune/inflammatory parameters may differ between suicide attempters with and without SA, taking into account the type of suicide method. The odds of repeating a high-lethality SA in the future will also be explored.
Methods: In this retrospective observational single center study, medical records of suicide attempters admitted to the Emergency Department at Vall d'Hebron University Hospital (Barcelona, Spain) between 2017-2021, will be reviewed. The following immune/inflammatory parameters (i.e., total and differential white blood cell count, platelet counts, C-reactive protein levels) will be extracted for comparisons between subjects without a history of previous suicide attempt (SA), and those with a history of previous SA. Additionally, the following ratios/indexes will be calculated as a proxy of subject's inflammatory status: neutrophil-to-lymphocyte ratio (NLR), basophil-to-lymphocyte-ratio (BLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), systemic inflammatory response index (SIRI). Analyses will be controlled for clinical and sociodemographic variables, such as age, gender and/or primary psychiatric diagnosis. Analyses will be also stratified according to the attempt method. Moreover, the capability of the previously mentioned parameters to predict a high lethality SA or to commit suicide in the coming two years will also be evaluated.
Results: Results from the interim analysis will be presented at the congress.
Conclusions: Peripheral immune/inflammatory parameters may allow us to discriminate subjects at risk of committing suicide. In case of positive findings, immune/inflammatory parameters could be incorporated in the comprehensive evaluation of high-lethality SA in individuals admitted to the emergency setting, contributing to improve early detection of suicide risk.

Disclosure of Interest: L. Martorell Mensua Shareolder of: First authorship, W. Vidal Cachay Shareolder of: First authorship, M. Quesada Franco: None Declared, A. Beneria Gonzalez: None Declared, J. Ramos Quiroga: None Declared, A. Motger Albertí: None Declared, G. Arteaga-Henriquez Shareolder of: Last authorship, D. Braquehais Conesa Shareolder of: Last authorship.

Psychosurgery and Stimulation Methods (ECT, TMS, VNS, DBS)

EPP507

Optimizing Pulse Frequency in Electroconvulsive Therapy

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Introduction: Effective seizure induction with minimal adverse effects in Electroconvulsive Therapy (ECT) are influenced by administered electrical pulse frequency. Optimized pulse frequency is key to ensure therapeutic efficacy and reduce side effects.
Objectives: This study examines electrical pulse frequency impact on neuronal excitability and seizure quality in ECT, guided by chronaxie and refractory periods.
Methods: A comprehensive literature review was conducted to assess neurophysiological properties affected by ECT and how different frequencies influence treatment outcomes.
Results: Neurons fire action potentials when membrane potentials reach a -55 mV threshold. Lower frequencies (20-32 Hz) balance depolarization and repolarization to trigger seizures without excessive neuronal firing. The neuronal absolute refractory period is 1-2 msec,