During the pandemic period, for all the three cohorts, patients with mental illness had 10% lower probability of being adherent to the recommended drug therapies.
The association between SMI and discontinuation was significant and varied among the three cohorts, with HR (95% CI): 1.27 (1.21; 1.33) for antihypertensives users, 1.16 (1.07; 1.26) for antidiabetics users and 1.08 (1.01; 1.16) for statins users.
Compared with 2019 the gap remained similar, except for discontinuation of antidiabetics, where the gap diminished from 34% in 2019 to 16% in 2020.
No differences between the two mental disorders were found.
Conclusions: Results show that suffering from a mental disorder in people with chronic physical conditions affects their adherence to recommended drug therapies. During the pandemic period, the restrictive measures adopted may have led to a better care by family members, counteracting any increase in the gap.
The healthcare gap in patients suffering from mental illness remains an unsolved problem of primary importance for public health.

Disclosure of Interest: None Declared

Depressive Disorders

O0094

N-acetylcysteine counteracts increased brain excitatory/inhibitory balance following maternal high-fat diet and restores emotional and cognitive profiles in adult mouse offspring

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Introduction: High-fat diet (HFD) consumption during pregnancy can shape fetal brain development, increasing susceptibility to mental disorders. Nevertheless, the mechanisms underlying these negative outcomes remain unclear.
Objectives: We hypothesize that mHFD induces inflammation and oxidative stress (OS) in the fetal brain, disrupting excitatory/inhibitory (E/I) balance in the adult brain. This results in altered hypothalamic-pituitary-adrenal (HPA) axis reactivity, emotional regulation, and cognitive function. We tested the ability of N-acetyl-cysteine (NAC) - a powerful anti-oxidant and anti-inflammatory compound - to counteract mHFD effects.
Methods: Our mHFD model consists of female C57BL/6N mice fed either HFD (fat 58%, carbohydrate 25.5%, and protein 16.4%) or control diet (CD, fat 10.5%, carbohydrate 73.1% and protein 16.4%) before and during pregnancy (13 weeks). After 5 weeks on diets, half of them received NAC (1g/kg) for 8 weeks, until delivery.
Gene expression of *Il-1b*, *Cd68*, *Tmem119*, *iNOS*, and *Arg1* was measured in fetal brains. Cognitive function and emotional phenotype were assessed in adult male and female offspring through the Morris Water Maze (MWM) and the Emergence test, respectively. HPA axis functionality was assessed by measuring plasma corticosterone levels by ELISA following acute stress. Gene expression of vesicular glutamate transporter 1 (*Vglut1*) and vesicular GABA transporter (*Vgat*) were assessed as markers of E/I balance.
Results: Exposure to mHFD induced inflammation and OS in the fetal brain of both sexes, by increasing *Il-1b* and *iNOS/Arg1*. Additionally, *Cd68* and *Tmem119* were specifically increased in females. In adulthood, mHFD reduced latency to emerge from the shelter in the Emergence test in both sexes. In females, mHFD impaired cognitive function, reducing time spent in the MWM target zone, and increased HPA reactivity in response to acute stress. Furthermore, mHFD decreased *Vgat* expression in both sexes, resulting in an imbalanced *Vglut1/Vgat* ratio towards excessive excitatory input. Maternal NAC supplementation rescued this imbalance.
Conclusions: Overall, these data show that mHFD increases inflammation and OS in fetal brains, with greater effects in female offspring, inducing alterations in the E/I neuronal balance with concomitant disruptions of the neuroendocrine system and the emotional and cognitive profiles during adulthood. The supplementation with NAC was effective in rescuing the E/I imbalance as well as the behavioral phenotype.

Disclosure of Interest: None Declared

O0095

Depressive Symptoms and Urbanization - A Cross-Sectional Network Analysis

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Introduction: With increasing urbanization, more people are exposed to mental health risk factors stemming from the urban social or physical environment. However, research on urbanization and depression is not clear.
Objectives: This study aimed to explore environmental and social factors with depression symptoms in view of a network theory of mental health disorders.
Methods: The study was conducted among a representative sample of 3,296 habitants of Metropolis GZM (63% of women)– the most urbanized region in Poland. The measurements used were PHQ-9, UCLA, Neighbourhood Cohesion (Neighbourhood Belonging and Social Cohesion), REAT 2.0 (Quality of architecture in neighborhood area), distance and frequency use of green public areas, Self-Rated Health, Physical Activity, size of place of residence per person.
Results: The prevalence of depression risk in villages (*N*=713), towns under 20,000 (*N*=219), towns (under 99,000; *N*=823), and cities (under 300,000; *N*=1541) was 44.2%, 44.7%, 39.2%, and 34.9% respectively.
The depression nodes with the highest centrality degree and expected influence were PHQ9 (suicidal thoughts), PHQ2 (feeling depressed), and neighborhood belonging. Living in a more urbanized area (UA) had a smaller centrality degree in the network.

Edges between PHQ9 and environmental factors were mediated by loneliness (UCLA). Poor architectural conditions (REAT) were linked positively with neighborhood belonging and adversely with social cohesion. Living in UA was negatively related to PHQ9, PHQ5 (eating control), and PHQ2, social cohesion, and green area distance, while positively to PHQ7 (problems with being focused), poor physical health, REAT, and neighborhood belonging (Figure 1).

Conclusions: Living in a city is negatively related to the most central depression symptoms. Even though social cohesion is negatively linked to UA, neighborhood belonging is higher in more urbanized areas.

The balance between detrimental environmental factors and those that protect mental health requires a better understanding of the interaction between urban living and depression.

Disclosure of Interest: None Declared

O0096

Brain magnetic resonance imaging outperforms clinical severity ratings in the prediction of treatment outcomes in major depressive disorder

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Introduction: Major depressive disorder (MDD) is a prevalent and disabling condition. Approximately 30-50% of patients do not respond to first-line medication or psychotherapy. Therefore, several studies have investigated the predictive potential of pretreatment severity rating or neuroimaging features to guide clinical approaches that can speed optimal treatment selection.

Objectives: To evaluate the performance of 1) severity ratings (scores of Hamilton Depression/Anxiety Scale, illness duration, and sleep quality, etc.) and demographic characteristic and 2) brain magnetic resonance imaging (MRI) features in predicting treatment outcomes for MDD. Second, to assess performance variations among varied modalities and interventions in MRI studies.

Methods: We searched studies in PubMed, Embase, Web of Science, and Science Direct databases before March 22, 2023. We extracted a confusion matrix for prediction in each study. Separate meta-analyses were performed for clinical and MRI studies. The logarithm of diagnostic odds ratio [log(DOR)], sensitivity, and specificity were conducted using Reitsma's random effect model. The area under curve (AUC) of summary receiver operating characteristic (SROC) curve was calculated.

Subgroup analyses were conducted in MRI studies based on modalities: resting-state functional MRI (rsfMRI), task-based fMRI (tbfMRI), and structural MRI (sMRI), and interventions: antidepressant (including selective serotonin reuptake inhibitors [SSRI]) and electroconvulsive therapy (ECT). Meta-regression was conducted 1) between clinical and MRI studies and 2) among modality or intervention subgroups in MRI studies.

Results: We included ten studies used clinical features covering 6494 patients, yielded a log(DOR) of 1.42, AUC of 0.71, sensitivity of 0.61, and specificity of 0.74. In terms of MRI, 44 studies with 2623 patients were included, revealing an overall log(DOR) of 2.53. The AUC, sensitivity, and specificity were 0.89, 0.78, and 0.75.

Studies using MRI features had a higher sensitivity (0.89 vs. 0.61) in predicting treatment outcomes than clinical features ($P < 0.001$). RsfMRI had higher specificity (0.79 vs. 0.69) than tbfMRI subgroup ($P = 0.01$). No significant differences were found between sMRI and other modalities, nor between antidepressants (SSRIs and others) and ECT. Antidepressant studies primarily identified predictive imaging features in limbic and default mode networks, while ECT mainly focused on limbic network.

Conclusions: Our findings suggest a robust promise for pretreatment brain MRI features in predicting treatment outcomes in MDD, offering higher accuracy than clinical studies. While tasks in tbfMRI studies differed, those studies overall had less predictive utility than rsfMRI data. For MRI studies, overlapping but distinct network level measures predicted outcomes for antidepressants and ECT.

Disclosure of Interest: None Declared

O0097

Rapid reduction of depressive symptoms with minimal dissociation: results from the KET01-02 and KET01-03 trials with oral prolonged-release (PR) ketamine KET01

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Introduction: Current ketamine-based therapies for treatment-resistant depression (TRD) often induce dissociative effects. A novel oral PR ketamine formulation (KET01) results in a low and delayed peak concentration of ketamine, high hydroxynorketamine concentration, and is associated with limited dissociative properties.

Objectives: To investigate efficacy, safety, and pharmacokinetics of KET01 in TRD.

Methods: KET01-02 was a randomized, double-blind phase 2 trial in outpatients with TRD comparing adjunct 120 mg (n=42) or 240 mg (n=40) oral KET01 once-daily for 3 weeks to placebo (PBO, n=40). The primary endpoint was change from baseline in the MADRS mean score on Day 21. KET01-03 was a randomized, double-blind, cross-over phase I trial in 26 healthy volunteers comparing single doses of 240 mg oral KET01 and 84 mg an approved intranasal formulation of eketamine. The primary endpoint was maximum change of Clinician-Administered Dissociative States Scale (CADSS) score from baseline.

Results: KET01-03 trial; the mean (±SD) maximum change of CADSS score within 24 hours after dosing was 29.6±12.5 for intranasal eketamine and 0.7±1.7 for KET01 (p<0.00000000001). KET01-02 trial; no differences in CADSS score (range: 0.2 to 1.3), and heart rate and blood pressure were observed between the groups on Day 1 and beyond. 10%, 12%, and 15% of patients in

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