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

the PBO, 120 mg/day, and 240 mg/day KET01 groups, respectively had CADSS score >4 and increase from baseline. At 7 hours post first KET01 dose (240 mg), plasma concentration of ketamine (38.7 ±27.0 ng/ml) was lower than its metabolites norketamine (267.5 ±81.6 ng/ml) and hydroxynorketamine (190.2±85.5 ng/ml). 240 mg/day KET01 induced clinically relevant reduction from baseline in MADRS score already within the first 7 hours of treatment (-7.65; Δ vs PBO: -2.22, n.s.), with a statistically significant separation on Day 4 (-10.02; Δ vs PBO: -3.66, p=0.020) and Day 7 (-12.21; Δ vs PBO: -3.95, p=0.042). MADRS score decrease was sustained throughout Day 21 (-13.15; Δ vs PBO: -1.82, n.s.), and during 4-week follow-up (-12.51; Δ vs PBO: -3.35, n.s.). Treatment-emergent adverse events occurred in 47.5%, 50.0%, and 62.5% of patients in the PBO, 120 mg/day, and 240 mg/day KET01 group, respectively.

Conclusions: Oral 240 mg/day KET01 induces a rapid, and clinically relevant reduction of depressive symptoms with only minimal signs of dissociation, potentially due to lower ketamine levels and increased norketamine and hydroxynorketamine levels compared to intravenous administration. Our results suggest that KET01 may be an efficacious and safe take-at-home adjunct treatment for TRD.

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O0098

Working mechanisms of Cognitive Behavioral Therapy and Acceptance and Commitment Therapy: a dynamic network approach

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Introduction: Cognitive Behavioral Therapy (CBT) and Acceptance and Commitment Therapy (ACT) seem be similarly effective for the treatment of major depressive disorder (MDD). However, much remains unknown about the differences in underlying psychological mechanisms of change. Assessing dynamic change of depressive symptoms and treatment-specific psychological constructs over time may yield important insights.

Objectives: The current study will be the first to compare dynamic symptom networks in randomized groups of two psychotherapies by using dynamic time-warp (DTW) analyses.

Methods: We reanalyzed data from a randomized controlled trail of 82 patients suffering from MDD. Three depressive symptom subscales (mood, sleep, appetite/weight) and three treatment-related constructs (dysfunctional attitudes, decentering, and experiential avoidance) were collected at 7 time-points before, during, after treatment, and at up to 12 months follow-up. The DTW-analysis modeled the temporal dynamics of depressive symptoms and treatment-related constructs within each individual after which the findings were aggregated on the group-level. Undirected and directed networks were constructed, of which the latter yielded in- and out-strength for each node, that were compared between treatment arms.

Results: Networks based on symptom and construct dynamics markedly differed between treatment arms. Within the CBT-arm a decrease of experiential avoidance was related to a decrease in dysfunctional attitudes ($d = 0.059$, $p = 0.008$). Within the ACT-arm a decrease of mood symptoms was related to a decrease of experiential avoidance ($d = 0.051$, $p = 0.04$) and an increase of decentering was related to a decrease in sleep symptoms ($d = 0.038$, $p = 0.02$) and appetite/weight symptoms ($d = 0.049$, $p = 0.03$).

Conclusions: DTW offers a promising alternative approach to study and compare working mechanisms of different treatment interventions. Comparing CBT and ACT revealed a decrease in experiential avoidance within CBT and an increase in the ability to decenter within ACT. However, within both treatments a change in other constructs, suggesting that a first alleviation of mood symptoms is important to activate underlying psychological change.

Disclosure of Interest: None Declared

O0099

An Umbrella Review of Effectiveness of Intravenous Ketamine in Treatment-Resistant Depression

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Introduction: Major depressive disorder (MDD) is a tremendous global disease burden and the leading cause of disability worldwide. Unfortunately, individuals diagnosed with MDD typically experience a delayed response to traditional antidepressants and many do not adequately respond to pharmacotherapy, even after multiple trials. The critical need for novel antidepressant treatments has led to a recent resurgence in the clinical application of psychedelics, and intravenous ketamine, which has been investigated as a rapid-acting treatment for treatment resistant depression (TRD) as well acute suicidal ideation and behavior. However, variations in the type and quality of experimental design as well as a range of treatment outcomes in clinical trials of ketamine make interpretation of this large body of literature challenging.

Objectives: This umbrella review aims to advance our understanding of the effectiveness of intravenous ketamine as a pharmacotherapy for TRD by providing a systematic, quantitative, large-scale synthesis of the empirical literature.

Methods: We performed a comprehensive PubMed search for peer-reviewed meta-analyses of primary studies of intravenous ketamine used in the treatment of TRD. Meta-analysis and primary studies were then screened by two independent coding teams according to pre-established inclusion criteria as well as PRISMA and METRICS guidelines. We then employed metaumbrella, a