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

statistical package developed in R, to perform effect size calculations and conversions as well as statistical tests.
Results: In a large-scale analysis of 1,182 participants across 51 primary studies, repeated-dose administration of intravenous ketamine demonstrated statistically significant effects ($p<0.05$) compared to placebo-controlled as well as other experimental conditions in patients with TRD, as measured by standardized clinician-administered and self-report depression symptom severity scales.
Conclusions: This study provides large-scale, quantitative support for the effectiveness of intravenous, repeated-dose ketamine as a therapy for TRD and a report of the relative effectiveness of several treatment parameters across a large and rapidly growing literature. Future investigations should use similar analytic tools to examine evidence-stratified conditions and the comparative effectiveness of other routes of administration and treatment schedules as well as the moderating influence of other clinical and demographic variables on the effectiveness of ketamine on TRD and suicidal ideation and behavior.

Disclosure of Interest: None Declared

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

O0100

Electroconvulsive Therapy (ECT): A Scotland Wide Naturalistic Study of 4,826 treatment episodes

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Introduction: Despite its apparent efficacy in the treatment of a range of psychiatric disorders, electroconvulsive therapy (ECT) is viewed by some as a contentious treatment. Although most clinicians and researchers consider ECT a safe and effective treatment, there are ongoing and significantly publicised concerns about potential side effects.
Objectives: To explore use of ECT across Scotland in a large naturalistic clinical sample across an 11-year period from 2009 to 2019. To consider the efficacy and side effects of ECT for a range of common psychiatric disorders including, depression, bipolar depression, schizophrenia, and mania.
Methods: Using data from the Scottish Electroconvulsive Therapy (ECT) Accreditation Network (SEAN), information was collected for all adults who had received ECT. Variables included age, sex, Scottish Index of Multiple Deprivation (SIMD) quintile, International Classification of Diseases, Tenth Edition (ICD-10) diagnosis, indication for ECT, Mental Health Act status, consent status, entry and exit Montgomery-Asberg Depression Rating Scores (MADRS), entry and exit Clinical Global Index Severity CGI-S) scores and reported side effects. Side effects were recorded as present if the side effect was reported at any point during the episode of treatment.
Results: 4826 ECT episodes were recorded. The majority of episodes were in women (68.4%, n=3,301). Average age at treatment onset was 58.52 years. Males were slightly younger (m=58.24 years vs f= 58.65 years, p= 0.20). Mean number of treatments/episode was 9.59 (95% CI 9.32 – 9.85). Mean treatment dose delivered was 277.75mC (95%CI 272.88 – 282.63mC).
2920 episodes of treatment had CGI-S entry and exit recorded. At entry, mean CGI-S indicated marked illness (5.03 95% CI 4.99-5.07). Recipients with schizophrenia had the highest CGI-S score (5.45 95% CI 5.21-5.60), followed by those with post-partum disorders (5.38, 95% CI 4.61-6.14). At exit, mean CGI scores indicated borderline illness (2.07, 95% CI 2.03-2.11), recipients diagnosed with mixed affective state had the lowest CGI-S score (1.72, 95% CI 0.99-2.47) followed by those with schizoaffective disorder (2.01, 95% CI 1.76-2.42).
Anaesthetic complications (n=34) and prolonged seizures (n=38) were rare, occurring in <1% of treatment episodes. Cardiovascular complications were reported in 2.2% (n= 102). Nausea was reported in 7.2% (n= 334) and muscle aches in 12% (n=560). Confusion was reported in 19% (n=879) and cognitive side effects were reported in 26.2% (n=1212). One third of treatment episodes reported confusion or cognitive side effects (33.1%, n=1545).
Conclusions: From this large naturalistic clinical sample, ECT appears to be effective in improving illness severity as measured by CGI-S score. While some side effects (such as prolonged seizures and cardiovascular complications) were rare, others (such as confusion or cognitive side effects) were relatively common.

Disclosure of Interest: None Declared

Schizophrenia and other psychotic disorders

O0101

The Phase III CONNEX programme assessing the efficacy and safety of iclepertin in patients with schizophrenia: Trial design and recruitment update

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Introduction: In a 12-week, Phase II (NCT02832037) trial, iclepertin (BI 425809), an inhibitor of glycine transporter-1, was generally well tolerated and significantly improved cognition in 509 patients with schizophrenia.
Objectives: The Phase III CONNEX programme aims to confirm the efficacy, safety and tolerability of iclepertin in improving cognition and functioning across a larger cohort of patients with schizophrenia.
Methods: The CONNEX programme includes 3 randomised, double-blind, placebo-controlled parallel group trials in patients with schizophrenia (NCT04846868, NCT04846881, NCT04860830) receiving stable antipsychotic treatment. Each trial aims to recruit ˜586 patients, 18–50 years old, treated with 1–2 antipsychotic