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