Introduction: Novel, evidence-based treatments are required for treatment-resistant post-traumatic stress disorder (PTSD). 3,4-Methylenedioxymethamphetamine (MDMA) has beneficially augmented psychotherapy in several small clinical trials.
Objectives: To review the use of MDMA-assisted psychotherapy in treatment-resistant PTSD.
Methods: Systematic searches of four databases were conducted from inception to February 2020. A meta-analysis was performed on trials which were double-blinded, randomised, and compared MDMA-assisted psychotherapy to psychotherapy and placebo. The primary outcomes were the differences in Clinician Administered PTSD Scale (CAPS-IV) score and Beck's Depression Inventory (BDI). Secondary outcome measures included neurocognitive and physical adverse effects, at the time, and within seven days of intervention.
Results: Four randomised controlled trials (RCTs) met inclusion criteria. When compared to active placebo, intervention groups taking 75mg (MD -46.90; 95% CI -58.78, -35.02), 125mg (MD -20.98; 95% CI -34.35, -7.61) but not 100mg (MD -12.90; 95% CI -36.09, 10.29) of MDMA with psychotherapy, had significant decreases in CAPS-IV scores, as did the inactive placebo arm (MD -33.20; 95% CI -40.53, -25.87). A significant decrease in BDI when compared to active placebo (MD -10.80; 95% CI -20.39, -1.21) was only observed at 75mg. Compared to placebo, participants reported significantly more episodes of low mood, nausea and jaw-clenching during sessions and lack of appetite after seven days.
Conclusions: These results demonstrate potential therapeutic benefit with minimal physical and neurocognitive risk for the use of MDMA-assisted psychotherapy in TR-PTSD, despite little effect on Beck's Depression Inventory. Better powered RCTs are required to investigate further.

Disclosure: James Rucker has attended trial related meetings paid for by Compass Pathways Ltd.
Keywords: MDMA; ptsd; Treatment-resistance; psychotherapy

O208

Suicidality in post-traumatic stress disorder (PTSD) and complex PTSD (CPTSD)

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Introduction: International Classification of Diseases 11th Revision (ICD-11) has inserted complex post-traumatic stress disorder (cPTSD) as a clinically distinct disorder, different from PTSD. The diagnosis of cPTSD has the same requirements for the one of PTSD, in addition to disturbances of self-organization (DSO – e.g., disturbances in relationships, affect dysregulation, and negative self-concept).
Objectives: This study aimed to explore suicidality in PTSD and cPTSD. We examined also the association between clinical dimensions of hopelessness (feelings, loss of motivation, future expectations) and other symptomatologic variables.
Methods: The sample, recruited at the Fondazione Policlinico Tor Vergata, Rome, Italy, consisted of 189 subjects, 132 diagnosed with PTSD, and 57 with cPTSD, according to the ICD-11 criteria. Participants underwent the following clinical assessments: Clinician-Administered PTSD Scale (CAPS), Impact of Event Scale-Revised (IES), Beck Depression Inventory (BDI), Symptom Checklist-90-Revised (SCL-90), Dissociative Experience Scale (DES), Beck Hopelessness Scale (BHS).
Results: cPTSD showed significantly higher BHS-total ($p = 0.01$) and BHS-loss of motivation subscale ($p < 0.001$) scores than PTSD. Besides, cPTSD showed significantly higher scores in all clinical variables except for the IES-intrusive subscale. By controlling for the confounding factor "depression", suicidality in cPTSD (and in particular the BHS-total) appears to be correlated with IES-total score ($p = 0.042$) and with DES-Absorption ($p = 0.02$). Differently, no such correlations are found in PTSD.
Conclusions: Our study shows significant symptomatologic differences between PTSD and cPTSD, including suicidality. Indeed, suicidality in cPTSD appears to be correlated with the "loss of motivation" dimension, which fits well within the ICD-11 criteria of DSO.

Disclosure: No significant relationships.
Keywords: cPTSD; ptsd; Suicidality; Hopelessness

O209

Efficacy and safety results from the first pivotal phase 3 randomized controlled trial of mdma-assisted psychotherapy for treatment of severe chronic PTSD

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Introduction: Posttraumatic stress disorder is a prevalent mental health condition with substantial impact on daily functioning that lacks sufficient treatment options. Previous research has led to the designation of 3,4-methylenedioxymethamphetamine (MDMA) as a Breakthrough Therapy for treatment of post-traumatic stress disorder (PTSD) when administered as an adjunct to psychotherapy.
Objectives: Here we report the findings of the first randomized, double-blind, Phase 3 trial assessing the efficacy and safety of 3 sessions with a flexible dose of MDMA or placebo administered under direct observation to participants with severe PTSD ($n = 100$) as an adjunct to inner-directed psychotherapy.
Methods: Change in PTSD symptoms (CAPS-5) and functional impairment (SDS) were assessed by a central, blinded Independent Rater Pool at baseline and following each treatment session. Adverse events (AEs), concomitant medications, suicidal ideation and behavior were tracked throughout the study. Vital signs were measured during experimental sessions. The primary endpoint was 18 weeks post-randomization.
Results: Change in CAPS-5 and SDS, placebo-subtracted Cohen's d effect size, and a responder analysis will be presented. There were three serious AEs of suicidal ideation or behavior reported. MDMA was well tolerated, with some treatment emergent AEs occurring at greater frequency for the MDMA group during and after experimental sessions.

Conclusions: If MDMA-assisted psychotherapy significantly attenuates PTSD symptomatology and associated functional impairment, these results will form the basis for marketing authorization applications worldwide, including among participants with dissociative subtype of PTSD, depression, history of alcohol and substance use disorders, and adverse childhood experiences.

Disclosure: No significant relationships.
Keywords: neuroplasticity; MDMA; psychotherapy; ptsd

Precision psychiatry

O210

Depression patient-derived cortical neurons reveal potential biomarkers for antidepressant response

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Introduction: Major depressive disorder is highly prevalent worldwide and has been affecting an increasing number of people each year. Current first line antidepressants show merely 37% remission, and physicians are forced to use a trial-and-error approach when choosing a single antidepressant out of dozens of available medications.
Objectives: We sought to identify a method of testing that would provide patient-specific information on whether a patient will respond to a medication using in vitro modeling.
Methods: Patient-derived lymphoblastoid cell lines from the STAR*D study were used to rapidly generate cortical neurons and screen them for bupropion effects, for which the donor patients showed remission or non-remission.
Results: We provide evidence for biomarkers specific for bupropion response, including synaptic connectivity and morphology changes as well as specific gene expression alterations.
Conclusions: These biomarkers support the concept of personalized antidepressant treatment based on in vitro platforms and could be utilized as predictors to patient response in the clinic.

Disclosure: This work was funded by Genetika+ Ltd, Jerusalem, Israel. YA, DK, EN, DL and TCS are employees of Genetika+ Ltd and received salary and/or stock options for the submitted work.
Keywords: Depression; personalized medicine; biomarkers; disease models

O211

Individual-specific and subgroup level associations between stress and psychopathology in daily life: A temporal network investigation

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Introduction: Stress is a risk factor for developing psychopathology. Emerging evidence suggests that daily experiences of stress may also predict symptoms during the day. It is unclear to what extent the influence of stress on psychopathology during the day is the same across individuals (including across diagnostic boundaries), and which effects are individual-specific
Objectives: This study aims to reveal how stress and symptoms are interrelated in a cross-diagnostic context by modeling individual level temporal networks, and examining subgroups with similar dynamics.
Methods: Hundred twenty two young adults (43.4% women) with a wide range of psychopathology in terms of severity and type of problems completed a six-month daily diary study. We used a temporal network approach (i.e., group iterative multiple model estimation) to model how stress and ten specific symptoms (e.g., feeling down, paranoia, restlessness) were related across time at the individual-specific, subgroup, and group level.
Results: After controlling for the lagged influence of stress on itself, stress level predicted the level of restlessness, worrying, nervousness, and feeling down during the same day for >70% of individuals. We observed three larger subgroups with each over 20 individuals, whose temporal networks showed different dynamic patterns involving specific symptoms. Effects of stress on other specific symptoms differed across individuals, and these were not subgroup-specific.
Conclusions: This study showed important overlap between individuals in terms of impact of stress on psychopathology in daily life. Subtle differences between individuals were also observed. Possibly, such differences are relevant for examining individual-specific vulnerability for future psychopathology. This requires further investigation.

Disclosure: No significant relationships.
Keywords: cross-diagnostic; Stress reactivity; person-specific analysis; temporal network analysis

O212

Pharmacogenetic drug use in young danish individuals with severe mental disorders

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Introduction: Pharmacogenetics (PGx) studies genetic variance and related differences in drug outcomes. PGx guidelines for