levels of PIM. Patients leaving the study (either at Week 6 of treatment or as a result of early termination) showed a 96.8% adherence rate.

Discussion: By employing rigorous screening procedures, including testing for AP treatment adherence, the ENHANCE study enrolled a representative sample of patients with a confirmed inadequate response to their current AP and achieved a high level of treatment adherence (both to patient’s AP treatment and study drug).

T43. PREDNISOLONE VERSUS PLACEBO AS AUGMENTATION THERAPY IN PSYCHOTIC DISORDERS

Nasib Lyliana†, Inge Winter*,1, René Kahn†, Iris Sommer2
1University Medical Center Utrecht; 2UMC Groningen

Background: An increasing body of evidence suggests that immune dysregulation is involved in the pathophysiology of psychotic disorders. Some, but not all, anti-inflammatory drugs have shown positive effects on symptom severity. Given the need for new treatment options in psychosis, anti-inflammatory medication should be explored as a potential treatment to improve outcome. Being a potent glucocorticosteroid that adequately passes through the blood-brain barrier, prednisolone qualifies as a potential candidate. This proof-of-concept study aims to explore the effect of prednisolone, compared to placebo, on symptom severity in patients with a psychotic disorder who are on a stable dose of antipsychotic medication.

Methods: The study was conducted from July 2015 until April 2019 in four centers in the Netherlands and Belgium. Patients with a psychotic disorder were randomized, double blind, 1:1 to prednisolone or placebo in addition to their antipsychotic treatment. Patients randomized to prednisolone started with 40 mg/day, tapered down to zero in six weeks. Several procedures were implemented to ensure patient safety during prednisolone exposure (e.g., regular safety labs). The primary objective was to compare change in symptom severity, measured through the Positive and Negative Syndrome Scale (PANSS), in patients treated with prednisolone versus placebo, in additional to a stable antipsychotic regimen. To this end, a mixed model repeated measures ANOVA was applied.

Results: 42 participants were randomized, equally divided across the treatment arms. The six week treatment period was completed by 20 patients randomized to placebo and 19 patients randomized to prednisolone. There were no baseline differences in demographics, symptom severity, depression or global functioning between the treatment groups. There was no difference in symptom improvement between patients treated with prednisolone compared to placebo at the end of the six week treatment period (p=0.4). Global functioning and depression were not significantly different between treatment arms at end of treatment. No Serious Adverse Events (SAEs) occurred during the treatment phase.

Discussion: The results of this proof-of-concept study do not support the immune hypothesis of psychosis: there was no difference in symptom improvement after a six week treatment with prednisolone compared to placebo, in addition to a stable regimen of antipsychotics. The small sample size is the main limitation of this trial. Even though prednisolone did not show to be a potential candidate for augmentation therapy in psychosis, it is of interest to note that patients did not deteriorate when using prednisolone nor were there more SAEs in the active treatment arm. This argues against the general safety concerns for prescribing prednisolone in patients with psychosis for the treatment of immune disorder, although additional research is needed.

T44. 12-MONTH FOLLOW UP OF METABOLIC MEASURES FOLLOWING A RANDOMISED CONTROLLED TRIAL OF TREATMENT OF CLOZAPINE ASSOCIATED OBESITY AND DIABETES WITH EXENATIDE (CODEX)

Dan Siskind*,1, Anthony Russell†, Steve Kisely1

1Metro South Addiction and Mental Health Service; 2University of Queensland; 3University of Queensland and MSAMHIS

Background: Clozapine is associated with high rates of obesity and type 2 diabetes (T2DM). Exenatide, a glucagon-like peptide-1 (GLP-1) receptor agonist, can counter clozapine-associated GLP-1 dysregulation. Our randomized, controlled (RCT), open-label, pilot trial of once-weekly extended-release subcutaneous exenatide or treatment as usual (TAU) for 24 weeks (n=28), found 6/14 people on exenatide achieved >5% weight loss vs 1/14 receiving usual care (P = .029). Compared with TAU, participants on exenatide had greater mean weight loss body mass index (BMI) reduction, and reduced fasting glucose and glycated haemoglobin (HbA1c) levels.

Methods: We followed up CODEX trial participants at 12 months following the end of the trial. We collected information on weight, BMI, waist circumference, blood pressure, fasting glucose, HbA1c, and use of metformin. The primary outcome of interest was change in weight. Change in these parameters from trial baseline to 12 months post endpoint and trial endpoint to 12 months post endpoint was compared between those formerly in the exenatide and TAU arms.

Results: There were no significant differences between baseline and 12-months post endpoint for any of the variables. Data from endpoint to 12-month follow up point showed significantly greater increases among the former exenatide group compared to the former TAU group for weight, BMI, and proportion with >5% weight gain. Stratifying the dataset by whether participants were on metformin six months after the end of the trial did not alter the overall results.

Discussion: There were significant increases in weight and BMI in the 12 months post endpoint for the former exenatide group, however there were no significant differences in weight and BMI between baseline and 12-month post endpoint. This is in keeping with other GLP-1RA studies. This information suggests the need for continued use of exenatide among people on clozapine who have achieved weight loss.

T45. THE EFFICACY AND HETEROGENEITY OF ANTIPSYCHOTIC RESPONSE IN SCHIZOPHRENIA: A META-ANALYSIS

Rob McCutcheon*,1, Toby Pilling*,1, Yuya Mizuno,1 Adam Montgomery2, Haridha Pandian2, Luke Vano1, Tiago Reis Marques1, Oliver Howes1
1King’s College London, Institute of Psychiatry; 2South London and Maudsley NHS Foundation Trust

Background: Antipsychotics are more effective than placebo in reducing symptoms in schizophrenia. However, response to treatment appears to vary, and as such it has been proposed that different subtypes of schizophrenia exist, defined by treatment-response. This has not been formally examined using meta-analysis.

Methods: Randomised controlled trials comparing placebo and antipsychotics for the acute treatment of schizophrenia published between January 1 1950 and November 30, 2018 were examined. Mean change and variance of change in symptoms were extracted from each study, alongside publication year, participant age and gender, baseline symptom severity, antipsychotic dose, and use of placebo lead-in. Relative variability of symptomatic improvement in antipsychotic-treated individuals compared to placebo-treated individuals was quantified using coefficient of variation ratio (CVR). Mean difference in symptom change was quantified using Hedges’ g. The significance of potential moderating factors was assessed using meta-regression and sensitivity analyses. In addition, individual patient data from two clinical trials (N=522) was examined in terms of both the distribution of total symptom change, and the variability of individual symptoms and symptom factors.

Results: 11,006 articles were identified. 66 met inclusion criteria, reporting on 17,202 participants. Compared with placebo, antipsychotic-treated...
patients demonstrated both greater symptomatic improvement (g=0.47, p<0.001) and reduced variability in symptomatic improvement (CVR=0.86, p<0.001). Lower variability in antipsychotic-response was associated with studies including younger patients (z=3.07, p=0.002), those published earlier (z=3.98, p<0.001), with higher dose treatments (z=2.62, p=0.009), and greater mean-difference in symptom-change (z=-5.70, p<0.001). In the individual patient data antipsychotic treated patients did not show significantly increased variability for any individual symptom, and there was no evidence of a bimodal distribution of response.

Discussion: Compared to placebo, in addition to a greater mean change, antipsychotic treatment shows lower variability of change in total, positive, and negative symptoms. This is contrary to the hypothesis that there exists a subtype of antipsychotic non-responsive schizophrenia, instead providing evidence for a relatively homogeneous effect of antipsychotic treatment in improving symptoms of schizophrenia.

T46. THE EFFECT OF COMPREHENSIVE COGNITIVE REMEDIATION IN INDIVIDUALS AT ULTRA-HIGH RISK FOR PSYCHOSIS: A SINGLE-BLIND, RANDOMISED, CLINICAL TRIAL (FOCUS)

Louise Birkdal Glenthøj1, Mariegaard Lise1, Birgitte Fagerlund2, Jens Richard Jeppsen3, Tina Dam Kristensen4, Christina Wenneberg4, Kristine Krakauer4, Alice Medalia1, David Roberts6, Carsten Hjorthøj7, Merete Noredentoft1

1Mental Health Centre Copenhagen, University of Copenhagen; 2Center for Clinical Intervention and Neuropsychiatric Schizophrenia Research (CINS) & Center for Neuropsychiatric Schizophrenia Research (CNSR), Mental Health Centre Glostrup, University of Copenhagen; 3CNSR; Child and Adolescent Mental Health Center, Mental Health Services, Capital Region of Denmark; 4Mental Health Centre Copenhagen; 5Columbia University; 6University of Texas Health Science Center, San Antonio; 7Copenhagen University Hospital, Mental Health Center Copenhagen

Background: Individuals at ultra-high risk (UHR) for psychosis display significant cognitive deficits that constitute a barrier to functional recovery. Applying cognitive remediation (CR) before the onset of manifest psychosis may improve cognition and the clinical and functional prognosis of UHR individuals.

Methods: This randomised, clinical trial randomly assigned 146 UHR individuals aged 18–40 years to treatment as usual (TAU) or TAU plus cognitive remediation. The cognitive remediation consisted of 20-weeks of neurocognitive and social cognitive remediation. Assessments were carried out at 6- and 12-months post baseline. Primary outcome was composite score on the Brief Assessment of Cognition in Schizophrenia (BACS) battery at 6-months.

Results: Between April 2014 and January 2017, 73 UHR individuals were assigned to TAU and 73 were assigned to TAU + cognitive remediation. Compared to the control group, cognitive remediation did not result in significant improvement on the BACS composite score at 6-month follow-up (β=-0.125, 95%CI: -0.23 to 0.172, p=0.41). Nor did the intervention improve secondary outcomes in clinical symptoms or functioning. Exploratory analyses found emotion recognition latencies to be significantly more reduced in the intervention group than the TAU group at 6-months follow-up. At 12-month follow-up the intervention group exhibited significantly better performance on two exploratory outcomes of executive function and visual memory. The participants in the intervention group attended an average of 12 sessions out of 20. No adverse events were reported relating to the intervention.

Discussion: While the brief course of treatment did not impact global cognition, symptoms and functioning measures, treatment related benefit was found in exploratory component neuro- and social cognitive measures. Future studies should evaluate whether more personalized interventions such as the separate application of neurocognitive and social cognitive remediation may produce beneficial effect on cognition and functioning compared to treatment as usual, along with establishing the optimal number of training hours to produce cognitive and functional gains.

T47. GUANIFACINE AUGMENTATION OF ATTENTIONAL FUNCTIONING IN THE SCHIZOPHRENIA SPECTRUM

Abstract not included.

T48. DEVIATIONS IN MICRO AND MACRO WHITE MATTER STRUCTURES IN PSYCHOSIS PRONENESS

Seda Arslan1*, Tuba Şahin1, Didemur Şahin1, Timothea Toulopoulou1

1Bilkent University

Background: Psychotic disorders are characterized by neurobiological deviations, including in the macro and microstructure of white matter. White matter alterations are also seen in psychosis-proneness and in individuals who have a high risk of psychosis. For example, studies have indicated decreases in white matter integrity in the genu/forceps minor of corpus callosum (CC) in the latter populations. Anterior corona radiata (ACR) is one crucial white-matter tract connecting the anterior cingulate cortex to the striatum. Indeed, reductions in the white matter structure of anterior genu of CC significantly predict the transition from ultra-high risk to psychosis. However, there is a gap in the literature related to observing the psychosis-proneness by applying both micro and macrostructural brain analyses, and most of the microstructural white matter studies in psychosis focus on fractional anisotropy (FA) and not include mean diffusivity (MD). Thus, the current study aims to assess whether white matter deviations in CC, ACR, and CC, are associated with psychosis proneness by combining both tract-based statistical (TBSS) and voxel-based morphometry (VBM) analyses in a sample of participants with psychosis proneness (PP) and without psychosis proneness (NPP).

Methods: The study included 53 participants (29 PP vs. 24 NPP) whose ages were between 17 and 24 years. Participants were split into two groups based on their scores on Structured Interview for Schizotypy assessment, a well-validated instrument of psychosis proneness. White matter integrity was analyzed via diffusion tensor imaging (DTI) and white matter volume (WMV) via VBM. Two sample t-test was used in GLM for both DTI and VBM analyses. FA, MD, and WMV were compared between two groups to observe micro and macro white matter structure alterations in the region of interest.

Results: DTI analysis revealed decreased FA values in the right ACR and right genu of the CC in the psychosis-proneness group (F(1,52)= 7.37, p= 0.009). Moreover, VBM showed a significant WMV decreases in the right CG, Brodmann areas 8, 9, and 32 in the PP group (F(1,52)= 50.85, uncorrected p<0.01). However, MD did not differ between the two groups (F(1,51)= 3.65, p=0.06).

Discussion: These findings suggest that PP associated with decreased white matter integrity in ACR, genu of CC, and also reduced white matter volumes in the right CG, Brodmann areas 8, 9, and 32. Significant FA decreases might result from alterations in radial or axial diffusivity since we did not observe significant MD differences between two groups. The current findings suggested that participants with PP had both macro and micro white matter structure disruptions, mostly in frontal parts of the right cerebrum, compared to no PP group.

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