in Schizophrenia Working Group criteria (RSWGcr). For assessments of symptom severity, cognitive function and functional outcome, scale such as Positive and Negative Syndrome Scale (PANSS), K-WAIS-IV, and Global Assessment of Functioning (GAF) were measured. MMN of the patients were evaluated at the frontocentral site. A regression analysis was used to identify the factors that significantly predicted symptom improvement and remission including MMN at frontal site assessed at baseline, and anticipated clinical variables as predictive factors.
Results: MMN amplitudes in frontal sites were further decreased in the groups without remission compared to the groups with remission. MMN amplitude was significantly correlated with measures of symptom change and functional outcome measurements in patients with schizophrenia. Regression analysis revealed that symptom severity and MMN significantly predicted remission in patients with schizophrenia. Symptom improvement significantly predicted PANSS at baseline, illness duration, and antipsychotic dose, as did MMN amplitude at frontal site.
Discussion: This study explored the relationship of MMN with remission in patients with schizophrenia. The remitted patients with schizophrenia showed larger MMN amplitude in frontal electrode site than those of non-remitted patients. MMN in frontal sites was correlated with symptom improvement and functional outcomes through PANSS and GAF scales. The present study found that MMN was significantly correlated with variables related to remission such as PANSS and GAF evaluated at 6 months later. MMN indexes appears to be a promising candidate for predicted factor of remission of schizophrenia.

T16. SCHIZOPHRENIA SPECTRUM DISORDER: DEPRESSION TRAJECTORIES AND IMMUNE MARKERS

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Background: Genetic findings imply a role of the immune system in the complex psychopathology of schizophrenia, and elevated serum levels of pro-inflammatory cytokines have been found in patients. Altered levels of cytokines are linked to severe depression and cognitive dysfunction, both of which are common among patients suffering from schizophrenia. Depression is important to diagnose in this patient population as consequences of untreated depression can be severe. In this study we will investigate if the level and change of immune markers in blood are related to depression in patients with schizophrenia spectrum disorders.
Methods: The study is part of the Bergen-Stavanger-Innsbruck-Trondheim study (BestIntro) which is a multicenter randomized controlled trial comparing treatment with amisulpride, aripirazole and olanzapine. The study included patients with schizophrenia spectrum disorders (ICD-10 F20-F29) above 18 years with a score of 4 or more one of the following items on the Positive and Negative Syndrome scale (PANSS): Delusions, hallucinations, grandiosity, suspiciousness/persecution and unusual thought content. Participants were followed throughout one year, and for this sub-study participants from all treatment arms were analyzed together. Blood samples were drawn at week 0, 1, 3, 6, 12, 26, 39 and 52. Depression was measured with the Calgary Depression Scale (CDSS) which distinguishes depression from negative symptoms. A panel of 9 immune markers were analyzed: interferon gamma (IFN-γ), interleukin 1-β (IL-1β), interleukin 10 (IL-10), interleukin 12p70 (IL-12p70), interleukin 17A (IL-17A), interleukin 2 (IL-2), interleukin 4 (IL-4), interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF-α). We examined whether the level and change in inflammation parameters could be predicted by latent classes describing CDSS trajectories.
Results: The preliminary results suggest three different CDSS trajectories: high, moderate and low level of depression. In the three class model, the different groups were found to be related to some differences in level and change in the inflammation parameters. Baseline differences were found with higher IL-10 in the high depression group. In the 0–1 week interval, the low depression trajectory group reduced their IL1-beta, while the other two groups did not.
Discussion: Different courses of change in depression were identified suggesting that trajectories exist. With regard to temporal patterns of inflammatory parameters, findings point in the opposite direction of the established links between pro-inflammatory cytokines and depression. Further studies should explore if cytokine alterations in schizophrenia per se can explain this difference, or if depression in schizophrenia differs in its underlying biology from regular depressive states.

T17. GLUTAMATE IN DORSOLATERAL PREFRONTAL CORTEX IN PATIENTS WITH SCHIZOPHRENIA: A META-ANALYSIS OF 1-HMRS STUDIES

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Background: Glutamate especially in frontal cortical areas was proposed to be altered in patients with schizophrenia. In the dorsolateral prefrontal cortex (DLPFC), glutamate levels might serve as functional markers of schizophrenia since this region is involved in working memory function which is impaired in schizophrenia patients. To date, there is no systematic overview on glutamate in dorsolateral prefrontal cortex at high-field intensities. We here meta-analyze magnetic resonance spectroscopy (1-HMRS) studies comprising measurement in dorsolateral prefrontal cortex (DLPFC).
Methods: Preregistration of the study was performed on September 20th 2019 (osf.io/5uyr6). Predefined literature search on pubmed comprised articles with search terms: (Magnetic Resonance Spectroscopy OR MRS) AND (Glutamate OR Glut* OR GLX) AND (schizophrenia OR psychosis OR schizophren*). We screened for case-control studies comprising glutamate levels as measured by 1-HMRS in DLPFC. Meta-analysis with a fixed and random effects model with inverse variance method, DerSimonian-Laird estimator for tau2 and Cohen's d were estimated.
Results: 329 studies were initially screened. 13 Studies were included into quantitative analysis comprising n=436 patients and n=365 controls. The random effects model revealed no difference between patients and controls (d=0.033 [-0.19; 0.26], z=0.29, p=0.77). The test for heterogeneity shows a moderate amount of heterogeneity (tau2=0.096, I2=57.4%). Subsequent sensitivity analysis reveals significant between group effect for medication status (Q=7.94, p=0.0473) i.e. an increased glutamate level in antipsychotic naïve patients (d=0.46 [0.08; 0.84], z=2.37, p=0.018).
Discussion: We conclude that care has to be taken when evaluating metabolite levels in such a heterogeneous group and interpret that increase cortical glutamate in antipsychotic naïve patients with schizophrenia might be due to possible allostatic mechanisms.

T18. EFFECTS OF COGNITIVE REMEDIATION ON WHITE MATTER IN INDIVIDUALS AT ULTRA-HIGH RISK FOR PSYCHOSIS – A RANDOMIZED, CONTROLLED CLINICAL TRIAL

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Background: Individuals at ultra-high risk for psychosis (UHR) present with subtle white matter alterations, which have been associated with clinical and functional outcome. The effect of cognitive remediation on white matter (WM) in UHR-individuals has not been investigated.
Methods: In a randomized, clinical intervention-trial (FOCUS), UHR-individuals aged 18–40 years were assigned to treatment as usual (TAU) or TAU plus cognitive remediation (CR) for 20 weeks. CR comprised 20 x 2-hour sessions of neurocognitive and social-cognitive training (SCIT). Primary outcome was whole brain fractional anisotropy (FA) derived from diffusion weighted imaging. Secondary outcomes pertained to regions of interest analyses. Planned post-hoc analyses explored dose-response effects of CR on WM. Main analyses of treatment effect of CR on primary and secondary outcomes were conducted using linear mixed models, assessing the interaction of timepoint by group (CR and TAU). Analyses were conducted according to the intention-to-treat principle.
Results: 111 UHR-individuals and 59 healthy controls were included. Attrition-rate was 30% at 6 months post-treatment follow-up. The CR group completed a mean of 12 hours of neurocognitive training.
We found no effect of CR on whole-brain or regional FA. Planned post-hoc analyses revealed significant time*group (high- and low-attendance to CR) interactions in left superior corona radiata ($p<0.01$), left cingulum cingulate gyrus ($P=0.03$), and right superior longitudinal fasciculus ($P<0,01$), corrected. Specifically, when compared to UHR-individuals with high attendance (UHR-high >12 hours), those with low attendance (UHR-low <12 hours) had more co-morbid diagnoses, larger recreational smoking (nicotine and cannabis), more depressive and negative symptoms, and had significantly lower global FA at baseline, and showed a significant increase in FA after treatment. Furthermore, UHR-low displayed large effect-size (ES) improvements on depressive and negative symptoms, and moderate to large ES improvements in several cognitive functions (verbal fluency, verbal working memory, and processing speed). In contrast, UHR-high displayed large ES improvements in UHR-symptoms, and moderate ES improvement on social and occupational functioning.
Discussion: Contradicting our main hypothesis, we found no effect of CR on whole-brain or regional FA after six months. This may be explained by both the low number of neurocognitive training sessions and the attrition rate. The average of 12 hours of neurocognitive training is considerably lower than the recommended dosage of 25–30 hours necessary for cognitive improvements. The continuous need to develop feasible interventions and enhance adherence is stressed.
Nevertheless, non-specific treatment may improve WM-integrity in UHR-individuals with lower global baseline FA in those with more severe psychopathology. The UHR-low subgroup exhibited improvements with large ES in levels of depressive and negative symptoms, as well as cognitive functions. We speculate, whether our results reflect that UHR-individuals with higher baseline FA (approaching the healthy controls), present with a preserved structural capacity for increased demands and new learning, while UHR-individuals characterized by lower FA at baseline may be more amendable to neuroplastic treatment-effects. The results support the value of subgrouping in a clinically heterogenous UHR-population, which also applies to examining WM integrity.

T19. GLUTAMATE AND RESPONSE TO CLOZAPINE IN TREATMENT RESISTANT SCHIZOPHRENIA

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Background: The mechanisms that underlie and may mediate the therapeutic response to clozapine in treatment resistant schizophrenia (TRS) are unclear. Basic science studies have indicated that clozapine may modulate brain glutamate, but this has not yet been investigated in man. The aim of this study was to determine whether clozapine alters brain glutamate levels in patients with TRS, and the associations with clinical outcome.
Methods: The study included patients with TRS who were about to start clozapine as part of their normal clinical care. Glutamate levels were measured in the anterior cingulate cortex (ACC) and right caudate nucleus using proton magnetic resonance spectroscopy (1H-MRS) before clozapine initiation (n=37) and again after 12-weeks of clozapine treatment (n=27). Symptoms were principally assessed using the PANSS. 1H-MRS scans were also acquired in a comparator group of healthy volunteers (n = 16).
Results: Over the 12 weeks of clozapine treatment there was a significant reduction in glutamate in the caudate ($n = 22$, $F = 7.61$ $P < 0.05$) but not in the ACC. The percentage reduction in caudate glutamate was positively associated with the percentage reduction in total PANSS score ($n = 23$, $r = 0.42$, $P = 0.04$). ACC Glx (glutamate plus glutamine) prior to clozapine initiation was higher in patients with TRS than in healthy volunteers ($P=0.03$).
Discussion: Improvements in symptoms following clozapine initiation in TRS may be related to reductions in glutamate in the caudate nucleus. In contrast, ACC glutamate levels appear to remain high during the first three months of clozapine treatment.

T20. ADVANCED GLYCATION END PRODUCTS IN RECENT ONSET PSYCHOSIS INDICATE INCREASING CARDIOVASCULAR RISK

Abstract not included.

T21. DEVELOPMENT OF PROTEOMIC PREDICTION MODELS FOR OUTCOMES IN THE CLINICAL HIGH RISK STATE AND PSYCHOTIC EXPERIENCES IN ADOLESCENCE: MACHINE LEARNING ANALYSES IN TWO NESTED CASE-CONTROL STUDIES

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