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Background: Long-stay patients with severe schizophrenia are frequently treated with high doses of first-generation antipsychotics (FGA). Dose reduction or switching to ziprasidone may reduce the severity of negative symptoms or side effects.
Methods: In a randomized double-blind trial, we compared the effect of FGA dose reduction (to equivalent of 5 mg/day haloperidol) (n=24) or switching to ziprasidone 160 mg/day (n=24). Negative symptoms after 1 year of treatment were primary outcome measure. Treatment failure was defined as a prolonged (>4 weeks) or repeated relapse.
Results: Negative symptoms did not change significantly during dose reduction nor was there a significant difference between treatments. Neurological side effects diminished in both conditions. Positive symptoms, excited symptoms, and emotional distress worsened over time with ziprasidone, resulting in a significant difference in favour of FGA dose reduction. More patients in the ziprasidone condition (46%) than in the FGA condition (21%) relapsed. Although some recovered within 4 weeks, treatment failed in 25% of the patients in the ziprasidone condition and in 17% of the patients in the FGA condition (non-significant differences). In about 80% of patients, doses could be reduced without a prolonged increase in symptom severity.
Discussion: In long-stay patients with severe schizophrenia, reducing high doses of FGA to a dose equivalent of 5 mg/day haloperidol or switching to ziprasidone did not improve negative symptoms. Reducing antipsychotic doses was feasible in most patients, although the risk of relapse is substantial. Neither FGA dose reduction nor ziprasidone seems an adequate alternative to clozapine for treatment-resistant schizophrenia.

F54. PHARMACOLOGICAL ENHANCEMENT OF COGNITION AND SOCIAL COGNITION IN THE PSYCHOSIS SPECTRUM

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Background: Abnormalities in cognition and social cognition represent a core feature of the schizophrenia spectrum disorders. Schizotypal personality disorder (SPD) is a milder disorder within the schizophrenia spectrum, characterized by attenuated, schizophrenia-like traits without overt psychosis.
Study 1: Working memory impairments are a core cognitive deficit in schizophrenia and SPD. The dopamine D1 receptor is a promising target to enhance working memory. We aimed to test the effect of the D1 agonist dihydrexidine (DAR-0100A) to enhance working memory in patients with SPD.
Study 2: Oxytocin modulates social cognition. However, oxytocin's effect on social cognitive errors in the schizophrenia spectrum remains unexplored. We aimed to: 1) characterize social cognitive (mentalizing) errors in SPD patients and test their relationship with positive and negative symptoms of psychosis; 2) test the effect of intranasal oxytocin on mentalizing errors.
Methods: Study 1: We performed a randomized, double blind, placebo-controlled trial of DAR-0100A (15 mg/150 ml of normal saline i.v. over 30 min) in medication-free SPD patients (n=16). Study 2: Subjects: 15 SPD patients, 15 healthy controls [HC], and 15 psychiatric controls (PC). Intervention: intranasal oxytocin 24/40IU/placebo. Measures: Movie for the Assessment of Social Cognition (MASC), a naturalistic video task measuring mentalizing accuracy, "no mentalizing" errors, "hypomentalizing" errors and "hypermentalizing" errors. The "hyper-hypomentalizing ratio" can be computed to capture the predominant mentalizing tendency; PANSS; Schizotypal Personality Questionnaire, SPQ. Mentalizing measures were compared across groups (SPD, HC, PC), and treatments (oxytocin 24IU/40IU vs placebo) using ANOVA. Pearson correlations assessed the relationship between social cognition and symptoms.
Results: Study 1: Treatment with dihydrexidine (DAR-0100A) was associated with significantly improved working memory performance relative to placebo, with a very large effect size (Cohen's d=1.14). Study 2: SPD patients had lower mentalizing accuracy (F=10.11;df=1;p=0.003), made more "No mentalizing" or "hypomentalizing" errors (F=12.92;df=1;p=0.001), and had lower hyper-hypomentalizing ratios than HCs (F=2.84; df=1;p=0.099,trend level). In a subset of patients –including 8 SPD-, a single dose of intranasal oxytocin significantly increased the hyper-hypomentalizing ratio (F=6.84, df=1,p=0.019) and increased visual attention to social cues.
"No mentalizing" and "hypomentalizing" errors were significantly correlated with negative symptoms. "Hypermentalizing" errors were significantly correlated with positive symptoms and the "ideas of reference" and "suspiciousness" SPQ subscales.
Discussion: Study 1: These preliminary findings lend further clinical support to the potential of D1 receptor agonists to treat schizophrenia-spectrum working memory impairments.
Study 2: As hypothesized, SPD patients had impaired, less accurate social cognition, and made more "no mentalizing" and "hypomentalizing" errors, correlated with negative symptoms. Conversely, "hypermentalizing errors" were correlated with positive symptoms. Oxytocin increased the tendency to hypermentalize. This effect may normalize the abnormalities found at baseline in SPD patients. These results support the role of social cognitive impairments as an underlying factor of positive and negative symptoms of psychosis, with specific associations with paranoid and delusional traits. Our results also suggest that intranasal oxytocin modulates social cognitive errors in the psychosis spectrum.

F55. EFFICACY OF COMPUTER ASSISTED COGNITIVE REMEDIATION IN MID-AGED AND OLDER INPATIENTS WITH CHRONIC SCHIZOPHRENIA IN KOREA

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Background: Accumulating evidence indicates that cognitive remediation(CR) is effective for improving various cognitive deficits in adult patients with schizophrenia. Although reports of brain plasticity in older adults and the service needs of chronic mid-aged and older patients with schizophrenia are increasing, very few randomized controlled trials of CR have been conducted in mid-aged and older inpatients with schizophrenia. We investigated the efficacy of individualized CR on the cognitive impairments of mid-aged and older inpatients with schizophrenia within the context of comprehensive psychiatric rehabilitation(PR) by comparing the results obtained with PR only and treatment as usual(TAU).
Methods: Fifty-seven mid-aged and older individuals with schizophrenia (age mean: 50.07 sd: 6.01) and mild to moderate cognitive deficits were enrolled. All participants stayed in long-stay closed ward hospital. Thirty-eight who were undergoing PR were randomly assigned to CR + PR (N = 19) or PR-only (N = 19) groups. For PR groups (CR+PR group and PR only group) received comprehensive inpatient PR, including optimal