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The influence of self-esteem and therapeutic alliance on psychotic symptom severity

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Introduction: The therapeutic alliance (TA) is increasingly acknowledged as a fundamental quality of care indicator. Numerous guidelines advocate TA awareness in practice, but lack specifics on building a strong TA. Yet, previous studies have found independent associations between levels of self-esteem, the quality of TA and severity of clinical symptoms in people with schizophrenia and other psychotic disorders. It suggests that the TA possibly mediates the relationship between self-esteem and psychotic symptoms. The present study therefore examined the relationships between these three factors in people with psychotic disorders.

Objectives: Investigating the mediating effect of TA on the relationship between self-esteem and psychotic symptom severity.

Methods: The short forms of the *Self-Esteem Rating Scale* and the *Working Alliance Inventory*, respectively, were used to assess self-esteem and TA. Psychotic symptoms were evaluated using the *Positive and Negative Syndrome Scale*. Linear regression models were applied, followed by a mediation-model when appropriate.

Results: A higher self-esteem significantly predicted less severe psychotic symptoms ($B = -.312$; $\beta = -.46$, $p < .001$) and better TA ($B = .123$, $\beta = .255$, $p = .009$). There was no significant relation between TA and psychotic symptom severity ($B = -.161$; $\beta = -.109$, $p = .289$), therefore no mediation-analysis was performed.

Conclusions: We found no association between TA and psychotic symptoms, which may be explained by the mild psychotic symptoms and overall high satisfaction scores on TA in our chronic sample. Another factor might be that current measurements assume a one-on-one relationship between a client and a professional, while nowadays multiple professionals are involved. We recommend re-evaluating the definition and assessment of the TA within chronic psychiatric populations. Our study results also offer practical guidelines for clinicians to improve their quality of care, such as the recommendation to focus on enhancing self-esteem in people with psychosis.

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EPV1844

Augmenting clozapine with other antipsychotics: results from two nationwide cohorts

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Introduction: A large proportion of patients with schizophrenia do not have a sufficient response even to clozapine. Very little is known if any pharmacological augmentation treatment can improve the long-term outcome of these patients.

Objectives: We studied the comparative effectiveness of oral risperidone, olanzapine, quetiapine, and aripiprazole augmentation of clozapine treatment on the risk of hospitalization due to psychotic episode as a marker for severe relapse among patients with schizophrenia.

Methods: In this population-based study, patients with schizophrenia or schizoaffective disorder using clozapine were included from Finnish (years 1996-2017) and Swedish (years 2006-2021) nationwide registers of inpatients care, specialized outpatient care, sickness absence, and disability pension. The risk of hospitalization associated with periods of antipsychotic augmentation vs. clozapine monotherapy (expressed as adjusted hazard ratio, aHR) was assessed by a within-individual design, using each individual as his/her own control, and analyzed with stratified Cox models. The two national cohorts were first analyzed separately, and then results were combined using a random-effect meta-analysis. Secondary outcomes were somatic hospitalization and composite outcome of psychosis/ somatic hospitalization.

Results: In the meta-analysis of 23,206 clozapine users, medium dose (9-16.5 mg/day) aripiprazole augmentation was associated with the lowest risk of relapse among patients with low-dose (< 180 mg/day) (meta-analysis aHR 0.67, 95% CI 0.46-0.97, $p=0.03$), medium-dose (180-330 mg) (0.79, 0.70-0.91, $p=0.0006$), and high-dose (>330 mg) clozapine (0.68, 0.62-0.75, $p<0.0001$), compared with the same clozapine dose as monotherapy. Augmentation with higher dose of aripiprazole or with other antipsychotics was associated with less favorable outcome. Only aripiprazole augmentations were associated with decreased risk of psychosis/somatic hospitalization, and the lowest risk was observed for medium-dose aripiprazole plus high-dose clozapine (0.70, 0.58-0.84, $p=0.0001$). Medium-dose aripiprazole plus high-dose clozapine was not associated with the risk of somatic hospitalization (0.66, 0.30-1.44, $p=0.29$), when compared with clozapine monotherapy in the same dose category.

Conclusions: This meta-analysis of two nation-wide cohorts totaling over 23,000 clozapine using patients indicates that 10-15 mg/day aripiprazole augmentation of clozapine treatment is associated with about 20-30% decreased risk of relapse compared with clozapine monotherapy periods within the same individuals.

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EPV1846

Attitudes of patients with psychotic disorders towards psychoactive substances

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