



Medication adherence in schizophrenia: The role of insight, therapeutic alliance and perceived trauma associated with psychiatric care



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ABSTRACT

Medication non adherence in schizophrenia is a major cause of relapse and hospitalization and remains for clinicians an important challenge. This study investigates the associations between insight, therapeutic alliance, perceived trauma related to psychiatric treatment and medication adherence in patients with schizophrenia. In this multicenter study, 72 patients were assessed regarding symptomatology, self-reported adherence with medication, insight, medication side-effects, therapeutic alliance and perceived trauma related to psychiatric treatment. Structural Equation Modeling (SEM) was used to test predicted paths among these variables. The data fit a model in which medication adherence was directly predicted by insight, therapeutic alliance and perceived trauma related to psychiatric treatment. Perceived trauma moderates the role of insight on medication adherence. The final model showed good fit, based on four reliable indices. Greater adherence was correlated with higher insight, higher therapeutic alliance and lower perceived trauma. These three variables appear to be important determinants of patient's medication adherence. Medication adherence could be enhanced by reducing perceived trauma and by increasing insight. The need for mental health providers to acknowledge patients' potentially traumatic experience with psychiatric treatment and the need to encourage greater involvement in care are discussed.

1. Introduction

Rates of medication non-adherence among patients with schizophrenia have been estimated at approximately 50% (Gilmer et al., 2004; Lacro et al., 2002; Velligan et al., 2009), leading to higher rates of relapse and hospitalization as well as to decreasing clinical, cognitive and functional prognosis (Ascher-Svanum et al., 2006; Llorca, 2008; Robinson et al., 1999; Weiden et al., 2004). While the identification of determinants of poor adherence has yielded valuable results, additional research is needed as the identification and characterization of cluster of patients with poor medication adherence remains an important challenge (Misdrahi et al., 2016).

Insight into illness is commonly observed as a determinant of poor adherence (Mohamed et al., 2009; Novick et al., 2015; Rocca et al., 2008) but its effect may be indirect and mediated by other potential

factors including attitudes toward medication (Baloush-Kleinman et al., 2011; Beck et al., 2011; Drake et al., 2015; Samalin et al., 2016), therapeutic alliance (Day et al., 2005; Roche et al., 2014) or perceived coercion (Day et al., 2005; Jaeger and Rossler, 2010). Engaging patients in treatment requires an efficient therapeutic alliance (Frank and Gunderson, 1990) which is a key factor in the care of patients with severe psychiatric disorders as it is associated with better adherence (Lecomte et al., 2008; McCabe et al., 2012; Misdrahi et al., 2012). Despite the hypothesized association between the therapeutic relationship and the experience of coercion (Gilbert et al., 2008), literature is scarce to test quantitatively this link. Few studies have investigated whether traumatic and coercive experiences related to psychiatric care are associated with medication adherence.

That being said, most studies have examined the impact of each determinant in isolation. However, from a methodological perspective,

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these studies did not use analytical techniques that allow for an examination of the direction and the structure of the relations between the determinants and medication adherence. More specifically, these studies did not differentiate direct and indirect determinants of adherence. Some of the determinants that have no direct effect may have an indirect effect through mediating factors.

The aim of the present study was to investigate the complex relationship among insight, therapeutic alliance, perceptions of trauma experiences related to psychiatric treatment and medication adherence in patients with schizophrenia. We used structural equation modeling (SEM), which is a useful statistical procedure, to test a theory involving non-straightforward relationships and is therefore well suited to the management of cross-sectional data for inferential purposes.

2. Methods

2.1. Participants

In this multicenter study, 72 patients were recruited consecutively in three comparable psychiatric hospitals located in Bordeaux ($n = 47$), Clermont-Ferrand ($n = 8$) and Paris ($n = 17$). Recruited patients did not differ on socio-demographic data between the three centers. Patients were recruited during hospitalization, less than one week prior to scheduled discharge, after the remission of acute symptomatology, when patients were considered to be clinically stable (judged compatible with answering questionnaires) and ambulatory routine care was organized. Once discharged, patients received post-discharge care as usual with a monthly appointment with their psychiatrist. Inclusion criteria were (1) a diagnosis of schizophrenia or schizoaffective disorder according to DSM-IV-TR criteria (American Psychiatric Association, 2000), (2) at least 18 years old, (3) able to understand the protocol, and (4) fluent French speaker. Exclusion criteria included traumatic head injury, any past or present major medical or neurological illness and mental retardation. The study conformed to France's laws on bioethics and clinical research, and on data protection (CPP-Ile de France III, N° ID RCB: 2008-A00504-51). All subjects gave their written informed consent to participate in this study.

2.2. Measures

Socio-demographic data were collected using a standardized semi-structured questionnaire. Variables included the following: age, gender, marital status, parental status, educational level and employment status.

The severity of psychopathology was assessed by the PANSS (Kay et al., 1987), which comprises three different subscales (positive, negative and general psychopathology). Current and lifetime comorbid substance use disorders were determined using the MINI International Neuropsychiatric Interview (Lecrubier et al., 1997). Overall functioning was estimated with the Global Assessment of Functioning scale (GAF) (American Psychiatric Association, 2000). Depressive symptoms were assessed using the Beck Depression Inventory (BDI) (Beck et al., 1988).

Perceived traumatic experiences associated with prior psychiatric treatment and hospitalization was indicated by a positive response to the following question: "Have you ever been the witness or the subject of events perceived as traumatic during your care or hospitalization (s)?" To specify the context of subjective traumatic experiences the following items were explored: "receiving forced medication like injection drugs, physical restraint by belt or restraint by security ties or being put in seclusion". The responses to the latter items were not included in the analyses.

Insight into illness was assessed using the Birchwood Insight Scale (BIS) (Birchwood et al., 1994). This is an 8-item scale that has been shown to have good reliability and validity in people who experience acute and chronic psychotic symptoms. The BIS scored on a three-point Likert-type scale (from 0 to 2). The total score for the BIS ranges from 0

to 12. Higher scores indicate greater insight.

Medication Adherence was evaluated using the French translation of the MARS (Fond et al., 2016; Misdrahi et al., 2016). The sum of items yields a total score ranging from 0 (poor adherence to treatment) to 10 (good adherence to treatment). Patients were asked to report on their medication adherence over the 7 days preceding hospitalization.

Therapeutic alliance with the prescriber was obtained on a self-reported 4-Point ordinal Alliance Scale (4PAS) (Misdrahi et al., 2009). A higher 4PAS score indicates greater therapeutic alliance.

Side-effects using the UKU (Udvalg for Kliniske Undersogelser) side-effect rating scale (Lingjaerde et al., 1987).

2.3. Statistical analysis

Descriptive data are first presented: quantitative parameters are described with means and standard deviations, qualitative parameters in frequencies and percentages. Normality of quantitative data was checked using the Kolmogorov–Smirnov 1-sample test. The pairwise covariance and Pearson correlation matrices for measured variables and medication adherence were presented. All tests were two-sided, and statistical significance was defined as $P < 0.01$ to correct for multiple hypothesis testing.

Then, Structural Equation Model (SEM) (Davies et al., 2016; Gunzler et al., 2013; Thomas et al., 2017) was used to examine the hypothetical relationships between variables. The final model was obtained by a step-by-step procedure (Muthén and Muthén, 1998), with strong indices evaluating the model (chi-square, RMSEA, CFI and SRMR indices) and did not include GAF, BDI, comorbidity and demographic. In the end, the 5 latent variables include were insight (BIS), symptomatology (PANSS total), therapeutic alliance (4PAS), adherence (MARS) and perceived trauma related to psychiatric treatment. PANSS total score was used to prevent collinearity abnormality.

The level of significance was set at $p < 0.05$. Model fit was evaluated using four indices:

- Chi-square: a value less than 3 indicates that the observed correlations are not significantly different than the expected correlations;
- RMSEA (Root Mean Square Error of Approximation): indicates how well the model would fit the hypothetical population covariance matrix. A value lower than 0.05 is indicative of a close-fitting model, between 0.05 and 0.08 a reasonable fit, and 0.10 or greater a poor model;
- CFI (Comparative Fit Index): indicates the extent to which the model provides a better fit than the null model, range from 0 to 1. A value Greater than 0.90 suggests a good fit;
- SRMR (Standardized Root Mean square Residuals): the average difference between the correlations predicted by the model and the observed correlations. A value less than 0.10 indicate a good fit.

On the SEM model, links are modeled by paths with a coefficient, which can range from -1 to $+1$, indicating the strength and direction of the paths. The significance of the path coefficient is assessed using the standard errors and t-values for each coefficient. In addition to the statistical significance of the paths coefficients, the strength of the relationship plays a role in determining whether the relationships are weak (< 0.2), moderate (0.2–0.5) or strong (> 0.5).

Analyses were performed with the Statistical Procedures for Social Sciences (SPSS v.20) (SPSS Inc, an IBM Company, Chicago, IL) and Structural Equation Modeling was carried out using MPlus Version 7.1 software for Windows (Muthén and Muthén, 1998).

3. Results

3.1. Sample characteristics (Table 1)

Of the 72 participants, the majority met criteria for schizophrenia

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