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A brief version of the Subjects' Response to Antipsychotics questionnaire to evaluate treatment effects

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ABSTRACT

Background: Monitoring patients' experiences with antipsychotics may help to improve medication adherence and outcome. We aimed to develop a shorter version of a comprehensive 74-item self-report questionnaire suitable for routine monitoring of desired and undesired effects of antipsychotics.
Methods: Included were patients with psychotic disorders from seven mental health care organizations in The Netherlands, using antipsychotic medication, who completed the Subjects' Response to Antipsychotics (SRA-74). Exploratory factor analysis (EFA) and similarity analysis based on mutual information were used to identify the latent factor structure of the SRA. Items were reduced according to their metric properties and clinical relevance upon consensus by an expert panel, using a Delphi procedure of three rounds. We determined the internal consistency of the shorter version using Cronbach's alpha.
Results: SRA data of N = 1478 patients (mean age of 40 years, 31% females) were eligible for analysis. EFA extracted thirteen factors from the SRA-74, including four factors for desired effects (e.g. recovery of psychosis, cognition and social functioning) and nine factors for undesired effects (e.g. weight gain, flattened affect and increased sleep). Based on this solution 12 items were eliminated for statistical reasons. The expert panel eliminated another 28 items with redundant content, resulting in a 34-item version. The SRA-34 includes 10 desired and 24 clinically relevant undesired effects. Both the subscales for desired and undesired effects have a Cronbach's alpha coefficient of 0.82.
Conclusions: The SRA-34 can be used to evaluate desired and undesired effects of antipsychotics in routine clinical practice and research.

1. Introduction

Schizophrenia is a chronic psychiatric disease, commonly necessitating lifelong treatment with antipsychotics. Antipsychotics increase the burden of disease, when they affect patients' physical, psychological, sexual and social functioning (Voruganti et al., 2002). The patients' experience of desired and undesired effects in response to antipsychotic medication has been identified as a strong predictor of adherence and outcome (Naber et al., 1994; Awad et al., 1996). Systematic monitoring of the balance between desired and undesired effects with antipsychotics is important for disease management (Budd et al., 1996; Perkins, 2002). This requires a reliable and valid instrument.

Self-report is most optimal for the detection of often neglected, yet disturbing experiences, such as sexual side effects (Peuskens et al., 1998; Knegtering et al., 2003). Furthermore, self-report may save time and costs in routine clinical practice. Existing self-rating scales assessing experiences with antipsychotics either focus on quality of life, like the Subjective Well-being on Neuroleptics (SWN) (Naber, 1995; Naber et al., 2001) and the Personal Evaluation of Transitions in Treatment (PETiT) (Voruganti and Awad, 2002), or focus on undesired effects, like the Liverpool University Neuroleptic Side Effect Rating Scale (LUNSERS) (Day et al., 1995), and the Glasgow Antipsychotic Side-effect Scale (GASS) (Waddell and Taylor, 2008), see Wolters et al. (2009). In contrast, the Subjects' Response to Antipsychotics (SRA) is a comprehensive assessment of 74 desired and undesired effects attributed to antipsychotic medication, divided over

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8 subscales (Wolters et al., 2006). It is constructed of lay term expressions, based on original patient statements which may be easier understood than some of the clinical terms in the LUNSERS (Waddell and Taylor, 2008). However, our own experience with the SRA-74 suggests that patients especially those with concentration difficulties find it a long questionnaire with many questions addressing the same clinical effect. Reducing the total number of items within the range of other scales (about 30 items) (Day et al., 1995; Naber et al., 2001; Voruganti and Awad, 2002; Waddell and Taylor, 2008) would increase its feasibility for screening purposes. The subscale structure of the SRA-74 has been established by a priori assumptions (Wolters et al., 2006) and so far, the latent structure has not been evaluated using more advanced statistical methods. The current study therefore explored the latent structure of the SRA by exploratory factor analysis (EFA) in a large cohort of patients with psychotic disorders. The main aim was to develop a shorter version of the SRA, while maintaining the latent structure.

2. Methods

2.1. Questionnaires

The SRA-74 consists of one subscale of 24 desired effects, seven subscales of 30 undesired effects of antipsychotics and 20 miscellaneous undesired effects not belonging to a subscale; Appendix A1 (Wolters et al., 2006). The subscales have good internal consistency (Cronbach's alpha 0.69–0.93) and test–retest reliability (Pearson's r correlation 0.39–0.60). The SRA is rated on a 3-point scale (not present/yes, mild/yes, severe). Patients received the SRA by mail to complete it at home. In case of difficulties in completing the questionnaire they received help from a trained nurse.

Trained nurses rated the level of psychotic symptoms using the Positive and Negative Symptom Scale for Remission (PANSS-R) (Opler et al., 2007). The patient's psychiatrist or case manager rated psychosocial functioning using the Global Assessment of Functioning scale (GAF; DSM-IV) (APA, 1994). A psychiatrist diagnosed each patient according to the Diagnostic and Statistical Manual of Mental Disorders—4th edition (DSM-IV) classification system (APA, 1994). Medication use over the past year was retrieved from medical records and confirmed with the patient.

2.2. Subjects

Patients with psychotic disorders receiving mental health care in the north of The Netherlands, Amsterdam and Dordrecht were invited to participate in the annual screening of their mental and physical health by the Pharmacotherapy Monitoring and Outcome Survey (PHAMOUS). Investigations were carried out between 2006 and 2010, in accordance with the latest version of the Declaration of Helsinki. Included were patients with psychotic disorders (DSM-IV codes 295.4–295.9, 297.1, 298.8 and 298.9), who used antipsychotics for at least one month and completed the SRA (maximally 2 items missing). In case a patient had participated in successive annual assessments, the first available measurement was selected for evaluation.

2.3. Latent structure

Exploratory factor analysis (EFA) was used to identify the latent factor structure of the SRA-74. Since one item of the SRA (about menstruation) was completed only by female participants, factor analysis was conducted on 73 items. In addition to EFA, we performed similarity analysis to visualize the latent structure of the SRA-74 (for a detailed description of the procedures, see Appendix A2).

2.4. Item reduction

Within each factor, items with loadings of $r < 0.30$ on all factors, cross-loading of $r > 0.30$ on two or more factors, or loading on a factor with a low main factor loading of $r < 0.50$ were considered non-factorable (Comrey and Lee, 1992). Non-factorable items were eliminated if there was no consensus about their clinical relevance by the expert panel (see below). Factorable items with high factor loadings ($r > 0.80$) and/or a highly similar content within the same factor were considered redundant. Of each pair of redundant statements, the item with least specific, most ambiguous or multi-interpretable (e.g. feelings that can be interpreted both literally and metaphorically) content was eliminated upon consensus by the expert panel.

2.5. Delphi procedure

A Delphi procedure consisting of three consecutive rounds was used to reach consensus about the clinical relevance of the items in the questionnaire (Hsu and Sandford, 2007). The expert panel, all native Dutch speaking, consisted of six psychiatrists, two neurobiologists and two psychologists. In the first round, the panelists received the full questionnaire including the results of the statistical analysis by e-mail. The experts were asked 1) to rank order the clinical relevance of the non-factorable items dropped for statistical reasons and 2) to mark redundant items until maximally three items within each factor were retained. Clinical relevance was defined as being relevant for a patient to (dis)continue antipsychotic therapy. In the second round, the panelists received a new proposal for the shortened questionnaire, including a summary of the arguments for item elimination or preservation. The experts were asked whether they agreed with the proposed item reduction. If not, they were asked to replace redundant items and to re-rank the clinical relevance of each item. In the third and final round, consensus was reached about the final version of the questionnaire. Items with consensus rates of more than 75% agreement within the panel were retained.

2.6. Statistics

Descriptive analyses and factor analysis were performed using Statistical Package for Social Sciences (PASW-18). Missing SRA-responses were imputed for patients with maximally 2 items missing, using the default settings of the multiple imputation method and random number generator (Mersenne Twister) of PASW-18. This cut-off was chosen as maximally 2.7% of responses were missing per patient which can be considered sporadically missing responses. Patients who completed all items of the SRA were compared to patients with maximally 2 items missing and to excluded patients (missing 3 or more items), with respect to: gender, age, duration of illness and inpatient/outpatient status using chi-square tests for categorical variables and Mann–Whitney *U* tests for continuous variables.

Prevalence rates of SRA items were based on dichotomized scores (no/yes). Factor analysis was conducted on the original 3-point scale of the SRA. The responses on the desired effects were reversed prior to factor analysis to obtain uniform scaling. The extraction method for EFA was Generalized Least Squares. The rotation method was Direct Oblimin with Kaiser Normalization, assuming a certain degree of correlation between factors (e.g. *increased sleep* with *sedation*). The number of factors to be retained was predefined by the Kaiser's criterion (eigenvalues ≥ 1). Kaiser-Meyer-Olkin (KMO) and Bartlett's tests for sphericity were calculated to test whether the relationships among variables in the sample are adequate for factor analysis.

The internal consistency of the final version of the SRA was calculated for the factorable items within the desired effects subscale and undesired effects subscale. A Cronbach's alpha ≥ 0.80 indicates good internal consistency (Streiner, 2003).