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ABSTRACT

Objective: Using data from the Research on Asian Psychotropic Prescription Patterns for Antipsychotics (REAP-AP), our study aimed to establish the remission and severity ranges (mild, moderate, and severe) of schizophrenia on the Brief Psychiatric Rating Scale-6 (BPRS-6).
Methods: A total of 1,438 patients with schizophrenia from India, Indonesia, Japan, Malaysia, and Taiwan were enrolled in the study. Using the receiver operating characteristic (ROC) curve analyses, the optimal cut-off scores for the remission and severity ranges on the BPRS-6 were established.
Results: The scalability of the BPRS-6 was considered to have an acceptable "unidimensionality" (coefficient of scalability = 0.43). The cut-off scores for the remission of schizophrenia and mild, moderate, and severe schizophrenia can be optimally defined as the BPRS-6 total score of <5, 5–9, 10–19 and >20, respectively.
Conclusion: The BPRS-6 can be a promising, brief, and unidimensional rating scale to supplement the measurement-based care of schizophrenia.

Introduction

Based on the findings of Lin et al. [1], the 30-item Positive and Negative Syndrome Scale (PANSS-30) has not been scalable according to the Rasch analyses, whereas the PANSS-6 which consists of items on delusions (P1), conceptual disorganization (P2), hallucinations (P3), blunted affect (N1), social withdrawal (N4), and lack of spontaneity and flow of conversation (N6) has been scalable [2,3]. The item response theory (IRT), which has been developed by Rasch, is used to identify the items covering the low end of the dimension, the severe end of the dimension, and part of the dimension [4]. Therefore, the PANSS-6 is proposed as a brief rating scale to evaluate the core positive and negative symptom-related severity, remission, and efficacy in clinical trials on schizophrenia [2,3]. Likewise, based on the findings of Bech et al. [5], the 18-item Brief Psychiatric Rating Scale (BPRS-18) has not been scalable according to the Mokken scale analyses, whereas the

BPRS-6 which consists of items on expressed delusions (unusual thought content), conceptual disorganization, hallucinations (hallucinatory behaviour), blunted affect, emotional withdrawal, and poverty of speech (retardation) has been scalable. The Mokken scale analysis, which is also based on the IRT, is used to confirm the optimal number of items for establishing a coherent scale [6]. The "unidimensionality" of the BPRS-6 has been regarded as an acceptable level, since a study has found that its Mokken homogeneity coefficient is 0.45. Thus, the construct validity of the BPRS-6 has been confirmed with the Mokken scale analysis. Moreover, since the intra-class coefficient is 0.81, its inter-rater reliability is considered to be at acceptable levels. Therefore, BPRS-6 has been proposed as a promising psychometric method to evaluate the severity of schizophrenia [5–7].

However, to our knowledge, the BPRS-6 cut-off scores for remission and severity ranges have not

been established in patients with schizophrenia. Remission is considered an important measure in the clinical practice and research studies regarding any psychiatric aspects [8]. Furthermore, remission can be defined as the total score lower than a certain cut-off point from a psychometric assessment [9]. Hence, using data from the Research on Asian Psychotropic Prescription Patterns for Antipsychotics (REAP-AP) which has been the largest international collaborative survey in the realm of psychiatry in Asia [10,11], we aimed to evaluate the scalability of the BPRS-6 items using the Mokken scale analysis [6,7] and establish the cut-off scores for remission and severity ranges (mild, moderate, and severe) on the BPRS-6 in patients with schizophrenia.

Methods

Study subjects

As described elsewhere [10,11], a total of 3,744 patients with schizophrenia were consecutively recruited from 71 centres in 15 Asian countries (Bangladesh, China, Hong Kong, India, Indonesia, Japan, Korea, Malaysia, Myanmar, Pakistan, Singapore, Sri Lanka, Taiwan, Thailand, and Vietnam) from March to June 2016 in the REAP-AP. The study protocol and informed consent form of the REAP-AP were approved by the institutional review boards of Taipei City Hospital, Taipei, Taiwan (receipt number, TCHIRB-10412128-E) and other survey centres. Because the study subjects were recruited from different countries with diverse languages, the English versions of the case report forms and several assessment scales were used. Before the initiation of the survey, a conference was held to improve the consistency of data collection and diagnosis of schizophrenia between the survey centres. In our study, only data from subjects who met the following inclusion criteria were used: (i) diagnosis of schizophrenia, based on the International Classification of Diseases, 10th revision [12], by psychiatrists at the survey centres; (ii) use of any antipsychotic and/or other psychotropic medications; and (iii) availability of the complete BPRS-18 [13]. Finally, 1,438 patients with schizophrenia, who were recruited from 5 countries, including India, Indonesia, Japan, Malaysia, and Taiwan, were included in our study.

Rating scales

Based on the definition of Bech et al. [5], the BPRS-6 and BPRS-18 were rated on a 7-point scoring scale from 0 (absent) to 6 (very severe) with the Likert scale. The clinimetric properties of the BPRS-6 and BPRS-18 were confirmed [5,13,14]. The individual scores on the BPRS-6 items were derived from those on the BPRS-18 items.

Based on the definition of Leucht et al. [15], the BPRS-18 total score was converted into the Clinical Global Impression–Severity (CGI-S) score. In terms of the association between the BPRS-18 and CGI-S, the BPRS-18 was converted into a 7-point scoring scale from 1 (absent) to 7 (very severe) with the Likert scale [14,16], and the CGI-S was rated on a 7-point scoring scale from 1 (normal) to 7 (extremely ill) [17]. The remission and severity ranges of the CGI-S were defined as follows: remission and mild, moderate, and severe schizophrenia were defined as having CGI-S scores of 1 (normal) and 2 (borderline ill), 3 (mildly ill), 4 (moderately ill) and 5 (markedly ill), and 6 (severely ill) and 7 (extremely ill), respectively [18].

Statistical analyses

The Mokken scale analysis [6,7] was used to evaluate the scalability. The coefficient of scalability denotes the contribution degree of each scale item to the measurement of the severity of schizophrenia from its lowest to its highest extremes. The scalability coefficient between 0.30 and 0.39 indicates that the scale is considered to be at a marginally acceptable level to measure the severity, and the coefficient of 0.40 or higher indicates that the scale can be considered acceptable as having unidimensionality to measure the severity [6,7]. The association between the BPRS-6 and BPRS-18 total scores was determined using the Pearson correlation. Statistical significance was set at a P-value < 0.05 (two-tailed) in all tests.

The exploratory receiver operating characteristic (ROC) curve analyses were conducted to establish the optimal cut-off scores for the remission and severity ranges (mild, moderate, and severe) in patients with schizophrenia. As described elsewhere [18], this statistical method was developed from the signal-detection theory and was frequently used in biological and behavioural studies. In terms of calculating overall predictor performance, the sensitivity and specificity of all possible threshold levels were considered to determine the cut-off score generating the lowest number of false positives and false negatives. The Mokken scale analysis was conducted using R version 3.4.3 (https://www.r-project.org/) and the Pearson correlation and ROC curve analyses were conducted using IBM SPSS 24 (IBM Co., Armonk, NY, USA).

Results

Baseline characteristics of the study subjects

The study subjects consisted of 400 Indian, 261 Indonesian, 98 Japanese, 299 Malaysian, and 380 Taiwanese individuals. The mean (standard deviation [SD]) age was 39.9 (12.5) years and age ranged from 10 to 81 years. More than half of the subjects were male ($n =$

830, 57.7%), had more than 10 years of disease duration ($n = 788$, 54.8%), were enrolled as outpatients ($n = 774$, 53.8%), and had normal weight ($n = 749$, 52.1%). Of the subjects, 36.4% had untreated psychosis of less than 3 months in duration ($n = 524$). The mean (SD) chlorpromazine equivalent dose of the used antipsychotics was 501.5 (396.5) mg/day.

Scalability of items in the BPRS-6

The Mokken coefficient of scalability for the total score on the BPRS-6 was 0.43. Moreover, the scalability coefficients for the expressed delusions, conceptual disorganization, hallucinations, blunted affect, emotional withdrawal, and poverty of speech items were 0.45, 0.50, 0.37, 0.42, 0.45, and 0.40, respectively. Thus, while the scalability for the hallucinations item was considered to have marginally acceptable unidimensionality, the scalabilities for the total score on the BPRS-6 and other items were considered to have acceptable unidimensionality.

Correlation between the BPRS-6 and BPRS-18 total scores

As shown in Figure 1, the BPRS-6 total score was significantly correlated with the BPRS-18 total score ($r = 0.895$, $P < 0.0001$).

Cut-off scores for the remission and severity ranges of schizophrenia on the BPRS-6

As shown in Table 1, using the ROC curve analyses, the optimal cut-off score for the remission of schizophrenia on the BPRS-6 was <5, whereas those for the

Figure 1. Correlation between the Brief Psychiatric Rating Scale-6 (BPRS-6) and BPRS-18 total scores in the Research on Asian Psychotropic Prescription Patterns for Antipsychotics (REAP-AP) ($n = 1,438$). The commonly used antipsychotics, including risperidone, clozapine, olanzapine, haloperidol, and chlorpromazine, are presented on the right side of the figure.

Table 1. Cut-off points for the remission and the severity ratings of schizophrenia in the Brief Psychiatric Rating Scale-6 (BPRS-6) ($n = 1,438$).

CGI-S	N	Mean BPRS-6 (SD)	Cut-off score	Sensitivity	Specificity
1–2 (remission)	388	1.4 (0.2)	4	0.75	0.88
3 (mild)	303	5.3 (0.2)	9	0.79	0.89
4–5 (moderate)	732	12.3 (0.1)	19	0.87	0.89
6–7 (severe)	15	22.5 (1.0)			

CGI-S, Clinical Global Impression-Severity.

severity ranges of mild, moderate, and severe were 5–9, 10–19, and >20, respectively. The BPRS-6 total score was found to accurately distinguish between remission and mild schizophrenia (area under the curve [AUC] = 0.898, $P < 0.0001$), between mild and moderate schizophrenia (AUC = 0.913, $P < 0.0001$), and between moderate and severe schizophrenia (AUC = 0.937, $P < 0.0001$) in 1,438 patients.

Discussion

The scalabilities for the total score and most of the BPRS-6 items were considered to have a acceptable unidimensionality (coefficient of scalability = 0.43), which was consistent with the findings of Bech et al. [5]. These findings suggest that the BPRS-6 should be considered a coherent scale with an optimal number of items. The BPRS-6 total score was significantly correlated with the BPRS-18 total score in the study subjects. Remission of schizophrenia can be optimally defined as having a BPRS-6 total score <5. Moreover, the severity ranges of schizophrenia can be defined as follows: mild, moderate, and severe schizophrenia can be optimally defined as having a BPRS-6 total score of 5–9, 10–19, and >20, respectively. The BPRS-6 items including expressed delusions, conceptual disorganization, hallucinations, blunted affect, emotional withdrawal, and poverty of speech are consistent with the DSM-5 diagnostic criteria of schizophrenia [12] and the Clinician-Rated Dimensions of Psychosis Symptom Severity (CRDPSS) [19,20]. Hence, based on our findings, the BPRS-6 can be used as a rating scale to evaluate the severity ranges of schizophrenia in order to supplement the CRDPSS. Herein, our findings support the idea that the BPRS-6 could be a promising, simple, and useful scale to evaluate the severity of schizophrenia.

However, there are several limitations in our study. First, the REAP-AP has been designed not in a longitudinal manner but in a cross-sectional manner. Thus, cut-off scores for the remission and severity ranges have been defined from the cross-sectional perspective. To more precisely establish the cut-off scores for the remission and severity ranges, further studies with longitudinal design may be needed. Second, the score on the CGI-S has been evaluated not with the direct method but with the indirect method of converting the BPRS-
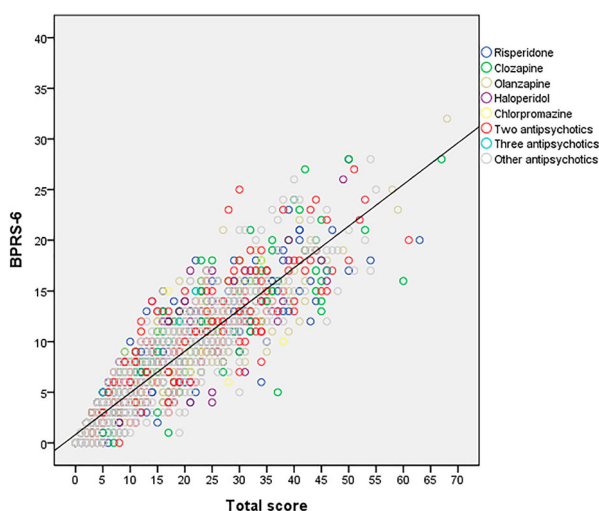
18 total score into the CGI-S score. Thus, the possibility that this approach can affect the degree of correlation between the BPRS-6 and CGI-S scores and the findings of ROC curve analyses cannot be excluded. However, a logarithmic relationship between the BPRS-18 and the Clinical Global Impression-Schizophrenia Scale (CGI-SCH) has been confirmed by Sawamura et al. [21]. Thus, it is thought that the influence of the conversion of the BPRS-18 total score into the CGI-S score on the relationship between the BPRS-6 and CGI-S scores is modest. Lastly, the inter-rater reliabilities for the BPRS-6 and BPRS-18 have not been evaluated. Despite these limitations, our study is significant in establishing the cut-off scores for the remission and severity ranges of schizophrenia on the BPRS-6. Our findings support the report of Bech et al. [5] that the BPRS-6 can be considered a promising, brief, and unidimensional rating scale to evaluate the remission and severity of schizophrenia. In addition, it is expected that defining the severity ranges of the BPRS-6 scale will enhance the sophistication of the BPRS-6. Therefore, it is proposed that the clinimetric property of the BPRS-6 can supplement measurement-based care in the treatment of schizophrenia.

Disclosure statement

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