A Modification of the Relative Weightings of Symptoms Utilizing a Logistic Function to Enhance the Linearity of the Brief Psychiatric Rating Scale: A Retrospective Analysis

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Received November 16, 2011; revised January 22, 2012; accepted February 22, 2012

ABSTRACT

Introduction: Although the Brief Psychiatric Rating Scale (BPRS) is widely used for evaluating patients with schizophrenia, the meaning of the weights of the individual symptoms is ambiguous. The aims of the study were 1) to investigate whether the modification of relative weights of items of the BPRS is able to enhance its correlation with the Clinical Global Impression-Schizophrenia scale (CGI-SCH) and 2) to construct a potential modified BPRS. Methods: We evaluated 200 schizophrenia patients using the BPRS and the CGI-SCH and drew the scatter plot distributions of the two scales. Next, univariate regression for the CGI-SCH using individual symptoms of the BPRS was performed. Multivariate regression utilizing the “logistic function” was then conducted to allocate marks to each item and Pearson’s r correlation coefficient and r-squared between the two scales were assessed. After that, we constructed an example of a potential modified BPRS. Results: With the scatter plot for the two scales, a logarithmic curve was obtained; this was described by [CGI-SCH] = 3.2248 × ln[18-item BPRS] – 7.2044 (p < 0.001). Pearson’s r for the relationship between the scales was 0.8216 and r-squared was 0.7718 (both p < 0.001). The univariate regression indicated a positive association between all symptoms of the BPRS and the CGI-SCH, although some of them were significant (p < 0.05) and others were not (p ≥ 0.05). Multivariate regression utilizing a logistic function provided the values “Pi” that could express the relative weights of individual symptoms. Subsequently, modification of point allocations according to “Pi” yielded a Pearson’s r of 0.8491 and an r-squared of 0.7718 (not changed) (both p < 0.001). An example of a potential modified BPRS was constructed. Conclusions: Within the limits of our data, the weightings of items of the BPRS improved the correlation of the BPRS with the CGI-SCH for evaluating schizophrenia.

Keywords: Evaluation Scale; Linearity; Weightings; Modification; BPRS; Schizophrenia

1. Introduction

Schizophrenia is a serious mental disorder characterized by a number of symptoms. To evaluate the effects of treatment for schizophrenia, it is important to assign quantitative values to the symptoms. Many rating scales have been used to evaluate various symptomatic domains in schizophrenia [1]. This has led to confusion regarding the suitability of the different scales available, not only for evaluation and treatment of the disease but also in research and clinical studies of the effects of medication. Currently, consensus is lacking about which rating scales are most appropriate for evaluating schizophrenia. Evaluation scales that are relevant, quick, user-friendly, graduated at equal intervals and with high linearity are needed to facilitate measurement-based treatment of schizophrenia. Conventionally, we often utilize the evaluation scales for mental disease as if there were a perfect linear relationship between the scores and the global state of illness. However, it is uncertain that these scales have perfect linearity and that they reflect the true states of patients with schizophrenia. The Brief Psychiatric Rating Scale (BPRS) [2] is one of the standard instruments used most frequently in daily practice for evaluating the severity of schizophrenia. Other than the BPRS, also popular are the Clinical Global Impression-Schizophrenia scale (CGI-SCH) [3], the Positive and Negative Syndrome Scale (PANSS) [4], the Scale for Assessment of Positive Symptoms (SAPS) [5] and the Scale for Assessment of Negative Symptoms (SANS) [6]. Although the BPRS includes 18 items and the allocation of marks is defined clearly, as all items have the same range of marks (from 1 (not present) to 7 (extremely severe), with “0” meaning “not as-
2. Methods

2.1. Participants

This was a retrospective study of outpatients and inpatients treated at the Tokyo Women’s Medical University, Miyazaki Hospital and Depression Prevention Medical Center, Kyoto Jujo Rehabilitation Hospital, Japan, who met the DSM-IV-TR [8] criteria for schizophrenia. A total of 200 patients (99 males, 101 females) with a mean age of 45.13 years (range, 16 - 83) were included in this study. Fifty patients were suffering their first episode of schizophrenia or attending for initial treatment (Group A) and 150 were randomly selected during either the acute or chronic phase of schizophrenia (Group B). The study involved a retrospective chart review and was approved by the ethics committee of our institution.

2.2. Research Design

All patients were evaluated and rated from their medical records using the BPRS and the CGI-SCH during the same session, but at the initial consultation for Group A and at a random treatment session for Group B. In this study, we utilized the CGI-SCH as a scale that substituted for the evaluation made by the patients’ psychiatrists, under the assumption that the CGI-SCH had perfect linearity and that it represented the precise clinical global impression of the treating psychiatrists, in order to simplify the analysis.

Two experienced psychiatrists shared their evaluations, and the scores for the BPRS and the CGI-SCH were presented graphically. At this stage, we examined the distribution on a scatter plot of the two scales and, if the linearity of the BPRS to the CGI-SCH was not initially apparent, we aimed to express the relationship in a more precise mathematical equation. Next, univariate linear regression analysis was performed with the CGI-SCH as the dependent variable and with individual symptoms of the BPRS as the independent variables. We examined whether the relationship between an individual symptom of the BPRS and the CGI-SCH had a positive or negative correlation with or without significance. After the univariate regressions, the variables that were positively associated with the CGI-SCH were entered into a multivariate model, while those that were negatively correlated with the CGI-SCH were excluded from this trial regardless of whether they were significant (p < 0.05) or not (p ≥ 0.05). After that, multivariate non-linear regression analysis utilizing the logistic function as the regression equation was conducted, with the CGI-SCH as the dependent variable and with all 18 items of the BPRS as independent variables. In multivariate regression, we ordinarily do not utilize a logistic function as a regression function in the “least-squares method” but in the “maximum-likelihood method” at which the dependent variable takes only the binominal number “0” or “1”, because logistic regression was devised for outcomes with only two states, e.g., “remission” or “non-remission” [9-14], “coronary heart disease” or not [15-17].
However, we decided to adopt a way of utilizing the logistic function as the regression function in a “non-linear least-squares method” because the dependent variable of the CGI-SCH could take polychotomous points, ordinarily one to seven, and putting a cut-off value on the CGI-SCH score might cause a loss of data in terms of the raw distribution of the scatter plot between the BPRS and the CGI-SCH. Another crucial reason for this choice is that, with multivariate regression analyses, we often obtain regression coefficients of independent variables that are inversely associated with the dependent variable. In our previous study, by performing multivariate regression, some symptoms of the BPRS were inversely correlated with the CGI-SCH, although the phenomenon of the higher score on some symptoms implying a less ill state was a departure from clinicians’ experiences [7]. To be sure, there might be a case where independent variables are inversely correlated with a dependent variable in multivariate regression, even though the independent variables have positive correlations in their respective univariate regression analyses (utilizing each variable as the only independent variable). However, to our knowledge, it seems likely that symptoms that are significantly and positively correlated with the CGI-SCH tend to have more meaning for evaluating the true state of schizophrenic patients, and that symptoms that are insignificantly and/or inversely associated with the CGI-SCH tend to have less meaning for that. If so, by increasing the point allocations of the symptoms significantly and positively correlated with the CGI-SCH and decreasing the point allocations of those inversely associated with the CGI-SCH, we might be able to obtain a modified almost 18-item BPRS that would have a higher correlation with the CGI-SCH, in other words, that might be closer to clinicians’ impressions than that of the original 18-item BPRS. If some form of modification of point allocation could enhance the correlation between the two scales, that might indicate a possibility that point allocation itself is associated with the linearity of the BPRS to the CGI-SCH. Considering these aspects, we conducted a series of manipulations as below.

Historically, the logistic function was explored in the Framingham study to identify risk and protective factors for coronary heart disease [15,16] (e.g., LDL cholesterol, triglycerides, blood glucose, systolic blood pressure, dia-stolic blood pressure, cigarettes/day, age, relative weight, etc.), and the methodology was based on that of Walker and Duncan [17], who proposed the logistic function that provided the advantage of the probability of occurrence of an event such as the presence/absence of heart failure in a dichotomous model. They used the logistic function in line with the least-squares method for estimating the relative weights of risk and protective factors for coronary heart disease through the rough comparison of the standardized coefficients obtained by multiplying partial regression coefficients by the individual standard deviation of the characteristic. Here, a larger standardized coefficient represented a stronger risk factor, and vice versa. We presumed that this method might be applicable for enhancing the linearity of an evaluating scale such as the BPRS, especially to improve the relative weights of symptoms.

As it is usually known, a logistic function has a value between 0 and 1 and the function transforms both positive and negative numbers that exceed “1” or are less than “0” into a positive number within the interval “0 - 1” according to its characteristic behavior on a graph (that is, an ascending sigmoid curve). By adjusting the size of the CGI-SCH score into “a ratio to 1” as “P” (0 ≤ P ≤ 1), (e.g., the CGI-SCH score of “2” is converted into “2/7 = 0.2857”), and inserting the variables of the BPRS into the logistic function described below, we were able to conduct non-linear multivariate regression analysis utilizing the logistic function as the regression function that provides values of “P” ranging between “0 - 1” continuously.

\[
P = \left\{ 1 + \exp\left( -\left( b_0 + b_1 \cdot x_1 + b_2 \cdot x_2 + b_3 \cdot x_3 \\
+ \cdots + b_{18} \cdot x_{18} \right) \right) \right\}^{-1}
\]

(0 ≤ P ≤ 1, strictly, 0 < P < 1), \( -\infty < x_i < +\infty, i = 1 - 18, x_i \) a score of symptom of number \( i \) of the BPRS, usually within 1 - 7; \( b_i \): a coefficient of the symptom of number \( i \) (which is able to take a positive or negative value). Strictly, “P” could not take “0” or “1” exactly; however, this problem also occurs in the ordinal logistic function as the ordinal logistic regression of the maximum-likelihood method.

The \( b_i \) terms are neither regression coefficients of linear multivariate regression analysis nor of logistic regression. These are coefficients that were optimized to meet the condition of the least-squares method, which minimizes the sum of squared differences between values adjusted from the CGI-SCH score into “0 - 1” and expected values according to the BPRS.

The logistic function provides the probability that the value of the predictor variable (symptom) of the BPRS will give the CGI-SCH outcome variable its full mark of “7”. In other words, it expresses the ratio or degree of share in the full score of the CGI-SCH = “7”. For example, \( P = 0.4 \) means a value that provides that ratio to the full score of the CGI-SCH “7”, indicating that the expected score of the CGI-SCH will be 2.8 (calculated as \( 0.4 \times 7 = 2.8 \)). Moreover, if the size of the partial regression coefficient of the number-“i”-symptom, \( b_i \), is significant (p < 0.05), inserting the parameter (as \( x_i = 7 \), where \( x_i = 0 \) (i ≠ i)) utilizing “b_i” (when the i-th symptom of the BPRS takes the full score “7” and other symptoms of the BPRS take nothing) provides an expected ratio P,
18 variables of the BPRS

Coef ≥ 0 → Univariate regressions → Coef < 0

Perform the non-linear multivariate regression utilizing the logistic function as a regression function

Insert the respective size of the $b_i$ into the below function individually for the $i$-th item of the BPRS, $P_i = \{1 + \exp(-(b_0 + b_1 \cdot x_1 + b_2 \cdot x_2 + b_3 \cdot x_3 + \ldots + b_i \cdot x_i + \ldots + b_18 \cdot x_{18}))\}^{-1}$ (i=1-18)

i) Coef ≥ 0 and $p < 0.05$
   insert $x_i=7$, $x_j=0$ (j ≠ i)
   $P_i = \{1 + \exp(-(b_0 + b_1 \cdot 7))\}^{-1}$
   both $b_0$ and $b_i$ are influential on $P_i$

ii) Coef ≥ 0 or <0, and $p \geq 0.05$
   insert $x_i=7$, $x_j=0$ (j ≠ i), $b_i=0$
   $P_i = \{1 + \exp(-(b_0))\}^{-1}$
   only $b_0$ is influential on $P_i$

iii) Coef <0 and $p < 0.05$
   insert $x_i=7$, $x_j=0$ (j ≠ i)
   $P_i = \{1 + \exp(-(b_0 + b_1 \cdot 7))\}^{-1}$
   both $b_0$ and $b_i$ are influential on $P_i$

To assign the magnitude proportional to the size of $P_i$s to the $i$-th item and compose a potential example of a prototype of the modified BPRS

Figure 1. A flow chart of the manipulation. The non-linear multivariate regression analysis utilizing the logistic function as a regression function after the selection of items of the BPRS with the univariate linear regressions is illustrated. For the $i$-th item where the p-value is significant ($p < 0.05$), the number $b_i$ is inserted into the logistic function under the condition $x_i = 7$ and $x_j = 0$ (j ≠ i), while, for the $i$-th item where the p-value is not significant ($p \geq 0.05$), the number $b_i$ is ignored because its size is considered less meaningful as a regression coefficient, and those coefficients are regarded as “0” except for $b_0$. After that, $P_i$ terms would be provided for each item according to the sizes and significance of regression coefficients. Multiplying $P_i$ equally by an appropriate constant would be expected to yield an example of a prototype of the modified BPRS. As a further improved algorithm, the selection of items conditioned on whether coefficients are positive and significant ($p < 0.05$) is permissible at the first step of the algorithm.

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BPRS”, which would express the relative weights of respective symptoms and be expected to have a higher correlation with the CGI-SCH within the limitations of the applicability for our data at this stage. We used Stata Release 10.0 [18] for the multivariate linear/non-linear regression analysis, used SPSS for Windows, version 14 [19] for calculating the p-values of r-squared at analysis of variance (ANOVA), and Microsoft Excel 2003 [20] for plotting the graph.

3. Results

The sequence of the series of manipulation is presented as a flow chart in Figure 1. Table 1 shows the results of univariate linear regression analysis performed with the CGI-SCH score as the dependent variable and with each symptom in the BPRS as the independent variable. Within the limits of our data, each symptom by itself was positively correlated with the CGI-SCH score, although some had significance (p < 0.05) and others did not (p ≥ 0.05). Accordingly, we did not exclude any symptom from the BPRS through all subsequent manipulations. Figure 2 shows the relationship between the 18-item BPRS score and the CGI-SCH score (p < 0.001). Pearson’s r coefficient for the relationship between the 18-item BPRS and the CGI-SCH was 0.8216 (p < 0.001) and r-squared (that of multivariate linear regression using all items of the BPRS) was 0.7718 (p-value of ANOVA was less than 0.001). On the scatter plot, there was a rough correlation where a curve with upper convexity was obtained and the straight-line relationship that had been thought to exist between the two scales was not apparent (this is also described in our previous report [7]). Because the shape of the curve was similar to a logarithmic curve, we performed a natural logarithmic transformation of the 18-item BPRS total score. The curve was then modified to an almost linear distribution, which was described by the equation [CGI-SCH] = 3.2248 × ln[18-item BPRS] – 7.2044 (p < 0.001; Figure 3).

Table 1. Results of univariate linear regression using each variable of the BPRS in sequence.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate Regression Coefficient</th>
<th>Standard Error</th>
<th>t</th>
<th>p-Value</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somatic concern</td>
<td>0.134296</td>
<td>0.102633</td>
<td>1.31</td>
<td>0.192</td>
<td>–0.068098 - 0.336689</td>
</tr>
<tr>
<td>Anxiety</td>
<td>0.525204†</td>
<td>0.061410</td>
<td>8.55</td>
<td>0.000</td>
<td>0.404103 - 0.646305</td>
</tr>
<tr>
<td>Emotional withdrawal</td>
<td>0.680804†</td>
<td>0.065076</td>
<td>10.46</td>
<td>0.000</td>
<td>0.552473 - 0.809136</td>
</tr>
<tr>
<td>Conceptual disorganization</td>
<td>0.755212†</td>
<td>0.047434</td>
<td>15.92</td>
<td>0.000</td>
<td>0.661671 - 0.848753</td>
</tr>
<tr>
<td>Guilt</td>
<td>0.437912*</td>
<td>0.168409</td>
<td>2.60</td>
<td>0.010</td>
<td>0.105806 - 0.770018</td>
</tr>
<tr>
<td>Tension</td>
<td>0.620179†</td>
<td>0.057144</td>
<td>10.85</td>
<td>0.000</td>
<td>0.507491 - 0.732868</td>
</tr>
<tr>
<td>Bizarre behavior</td>
<td>0.723666†</td>
<td>0.073220</td>
<td>9.88</td>
<td>0.000</td>
<td>0.579275 - 0.868057</td>
</tr>
<tr>
<td>Grandiosity</td>
<td>0.248480</td>
<td>0.144781</td>
<td>1.72</td>
<td>0.088</td>
<td>–0.037029 - 0.533990</td>
</tr>
<tr>
<td>Depressed mood</td>
<td>0.153266</td>
<td>0.151392</td>
<td>1.01</td>
<td>0.313</td>
<td>–0.145281 - 0.451814</td>
</tr>
<tr>
<td>Hostility</td>
<td>0.619312†</td>
<td>0.066578</td>
<td>9.30</td>
<td>0.000</td>
<td>0.488020 - 0.750605</td>
</tr>
<tr>
<td>Suspiciousness</td>
<td>0.588463†</td>
<td>0.051793</td>
<td>11.36</td>
<td>0.000</td>
<td>0.486326 - 0.690599</td>
</tr>
<tr>
<td>Hallucination</td>
<td>0.548691†</td>
<td>0.039642</td>
<td>13.84</td>
<td>0.000</td>
<td>0.470516 - 0.626867</td>
</tr>
<tr>
<td>Motor retardation</td>
<td>0.645614†</td>
<td>0.087394</td>
<td>7.39</td>
<td>0.000</td>
<td>0.473271 - 0.817956</td>
</tr>
<tr>
<td>Uncooperativeness</td>
<td>0.712508†</td>
<td>0.053575</td>
<td>13.30</td>
<td>0.000</td>
<td>0.606856 - 0.818159</td>
</tr>
<tr>
<td>Unusual thought content</td>
<td>0.616432†</td>
<td>0.041045</td>
<td>15.02</td>
<td>0.000</td>
<td>0.535491 - 0.697373</td>
</tr>
<tr>
<td>Blunted affect</td>
<td>0.202363*</td>
<td>0.100449</td>
<td>2.01</td>
<td>0.045</td>
<td>0.004275 - 0.400451</td>
</tr>
<tr>
<td>Excitement</td>
<td>0.569729†</td>
<td>0.047974</td>
<td>11.88</td>
<td>0.000</td>
<td>0.475124 - 0.664334</td>
</tr>
<tr>
<td>Disorientation</td>
<td>0.777530†</td>
<td>0.182897</td>
<td>4.25</td>
<td>0.000</td>
<td>0.416855 - 1.138205</td>
</tr>
</tbody>
</table>

*p < 0.05, **p < 0.01, †p < 0.001. Data for schizophrenic patients (n = 200); Within the limits of our data, the data indicate that each symptom by itself was positively correlated with the CGI-SCH score, although some had significance (p < 0.05) and others did not (p ≥ 0.05). Univariate regression coefficients and the p values are also shown.
Together with this, Pearson’s r between the ln[18-item BPRS] and the CGI-SCH was 0.8530 (p < 0.001). The results of non-linear multivariate regression analysis utilizing a logistic function are shown in Table 2. In Table 2, some symptoms were significantly and positively/negatively correlated with the CGI-SCH, and others were insignificantly and positively/negatively associated with the CGI-SCH. Intriguingly, there was a tendency for the symptoms that did not have significant correlation (p ≥ 0.05) with the CGI-SCH score in the univariate linear regression analysis (Table 1) to have insignificant positive associations with the CGI-SCH and/or significant negative associations with the CGI-SCH in the non-linear multivariate regression utilizing the logistic function as the regression function (Table 2).

Inserting $x_i = 7, x_j = 0 (j \neq i)$, with $b_i = -1.779568$ consistently, without change for significant $b_i$ terms and with change (inserting $b_j = 0$) for insignificant $b_i$ terms in the above logistic function provided the set of “$P_i$” terms (Table 3). Because the “$P_i$” terms were considered as the

![Figure 2. Scatter plot of the 18-item BPRS total score and the CGI-SCH score.](image)

Figure 2. Scatter plot of the 18-item BPRS total score and the CGI-SCH score. An upper convexity curve similar to a logarithmic curve was evident and a linear relationship was not apparent. The range of the 18-item BPRS is 18 - 126, and that of the CGI-SCH is 1 - 7.

![Figure 3. Scatter plot of the natural logarithm of the 18-item BPRS total score and the CGI-SCH score.](image)

Figure 3. Scatter plot of the natural logarithm of the 18-item BPRS total score and the CGI-SCH score. After performing a natural logarithmic transformation on the 18-item BPRS score, the approximately logarithmic curve was modified to an almost linear distribution and the increase in the natural logarithm of the 18-item BPRS total score was almost proportional to the increase in the CGI-SCH score.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Multivariate Regression Coefficient</th>
<th>Standard Error</th>
<th>t</th>
<th>p-Value</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>-1.779568†</td>
<td>0.185907</td>
<td>-9.57</td>
<td>0.000</td>
<td>-2.146392 - -1.412744</td>
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<tr>
<td>Somatic concern</td>
<td>-0.116784**</td>
<td>0.044366</td>
<td>-2.63</td>
<td>0.009</td>
<td>-0.204325 - -0.029243</td>
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<tr>
<td>Anxiety</td>
<td>0.160431†</td>
<td>0.042822</td>
<td>3.75</td>
<td>0.000</td>
<td>0.075937 - 0.244925</td>
</tr>
<tr>
<td>Emotion withdrawal</td>
<td>-0.145482**</td>
<td>0.053187</td>
<td>-2.74</td>
<td>0.007</td>
<td>-0.250428 - -0.040536</td>
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<tr>
<td>Conceptual disorganization</td>
<td>0.246513†</td>
<td>0.039939</td>
<td>6.17</td>
<td>0.000</td>
<td>0.167706 - 0.325320</td>
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<tr>
<td>Guilt</td>
<td>0.081812</td>
<td>0.068298</td>
<td>1.20</td>
<td>0.233</td>
<td>-0.052952 - 0.216575</td>
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<td>Tension</td>
<td>0.056184</td>
<td>0.050869</td>
<td>1.10</td>
<td>0.271</td>
<td>-0.044188 - 0.156556</td>
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<td>Bizarre behavior</td>
<td>0.027406</td>
<td>0.054475</td>
<td>0.50</td>
<td>0.616</td>
<td>-0.080081 - 0.134893</td>
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<td>Grandiosity</td>
<td>-0.134379*</td>
<td>0.054680</td>
<td>-2.46</td>
<td>0.015</td>
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<td>-0.032677</td>
<td>0.060379</td>
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<td>0.140460†</td>
<td>0.065680</td>
<td>2.14</td>
<td>0.034</td>
<td>0.010863 - 0.270056</td>
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<td>Suspiciousness</td>
<td>-0.111373†</td>
<td>0.054806</td>
<td>-2.03</td>
<td>0.044</td>
<td>-0.219514 - 0.003232</td>
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<tr>
<td>Hallucination</td>
<td>0.102879**</td>
<td>0.033222</td>
<td>3.10</td>
<td>0.002</td>
<td>0.037326 - 0.168432</td>
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<td>Motor retardation</td>
<td>0.098488</td>
<td>0.050466</td>
<td>1.82</td>
<td>0.070</td>
<td>-0.008192 - 0.205167</td>
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<td>Uncooperativeness</td>
<td>0.059815</td>
<td>0.059308</td>
<td>1.01</td>
<td>0.315</td>
<td>-0.057209 - 0.176839</td>
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<td>Unusual thought content</td>
<td>0.081910*</td>
<td>0.038581</td>
<td>2.12</td>
<td>0.035</td>
<td>0.005783 - 0.158036</td>
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<td>Blunted affect</td>
<td>0.120072*</td>
<td>0.046739</td>
<td>2.57</td>
<td>0.011</td>
<td>0.027849 - 0.212294</td>
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<td>Excitement</td>
<td>0.097073*</td>
<td>0.046417</td>
<td>2.09</td>
<td>0.038</td>
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<td>Disorientation</td>
<td>0.167273</td>
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<td>1.73</td>
<td>0.085</td>
<td>-0.023567 - 0.358112</td>
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</tbody>
</table>

*p < 0.05, **p < 0.01, †p < 0.001. Data for schizophrenic patients (n = 200); Multivariate regression coefficients and the p values that were derived from non-linear multivariate regression utilizing the logistic function as the regression function are shown.
Table 3. The values of “P_i” terms.

<table>
<thead>
<tr>
<th>Variable</th>
<th>P_i [inserting x_i = 7, x_j = 0 (j ≠ i), with b_0 = -1.779568, b_i without change]</th>
<th>P_i [inserting x_i = 7, x_j = 0 (j ≠ i), with b_0 = -1.779568, b_i with change]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somatic concern</td>
<td>0.069328*</td>
<td>0.069328</td>
</tr>
<tr>
<td>Anxiety</td>
<td>0.341515*</td>
<td>0.341515</td>
</tr>
<tr>
<td>Emotional withdrawal</td>
<td>0.057435*</td>
<td>0.057435</td>
</tr>
<tr>
<td>Conceptual disorganization</td>
<td>0.486509</td>
<td>0.486509</td>
</tr>
<tr>
<td>Guilt</td>
<td>0.230252</td>
<td>0.144356</td>
</tr>
<tr>
<td>Tension</td>
<td>0.200002</td>
<td>0.144356</td>
</tr>
<tr>
<td>Bizarre behavior</td>
<td>0.169704</td>
<td>0.144356</td>
</tr>
<tr>
<td>Grandiosity</td>
<td>0.061971</td>
<td>0.061791</td>
</tr>
<tr>
<td>Depressed mood</td>
<td>0.118334</td>
<td>0.144356</td>
</tr>
<tr>
<td>Hostility</td>
<td>0.310807</td>
<td>0.310807</td>
</tr>
<tr>
<td>Suspiciousness</td>
<td>0.071812</td>
<td>0.071812</td>
</tr>
<tr>
<td>Hallucination</td>
<td>0.257421</td>
<td>0.257421</td>
</tr>
<tr>
<td>Motor retardation</td>
<td>0.251589</td>
<td>0.144356</td>
</tr>
<tr>
<td>Uncooperativeness</td>
<td>0.204100</td>
<td>0.144356</td>
</tr>
<tr>
<td>Unusual thought content</td>
<td>0.230374</td>
<td>0.230374</td>
</tr>
<tr>
<td>Blunted affect</td>
<td>0.281089</td>
<td>0.281089</td>
</tr>
<tr>
<td>Excitement</td>
<td>0.249729</td>
<td>0.249729</td>
</tr>
<tr>
<td>Disorientation</td>
<td>0.352365</td>
<td>0.144356</td>
</tr>
</tbody>
</table>

*: significant (p < 0.05) b_i (coefficient) in Table 2. The “P_i” terms of the middle column are obtained by inserting x_i = 7, x_j = 0 (j ≠ i), with b_0 = -1.779568, b_i without change in the logistic function for all symptoms whether the b_i is significant or not. The “P_i” terms of the right column are obtained by inserting x_i = 7, x_j = 0 (j ≠ i), with b_0 = -1.779568, b_i with change (=0) for insignificant symptoms. The “P_i” terms of the right column are expected to reflect the relative weights of symptoms.

degrees of the expected ratio (0 - 1) of the CGI-SCH score to its full score “7”, we regarded these as clinical weights. Moreover, allocating marks to each of the 18 items of the BPRS in proportion to the “P_i” term (multiplying each i-th score by P_i) provided the scatter plot of the total score modified using “P_i” terms and the CGI-SCH score (p < 0.001, Figure 4), in which Pearson’s r was 0.8491 (p < 0.001) and r-squared was 0.7718 (p-value of ANOVA was less than 0.001). Through all manipulations, Pearson’s r was increased from 0.8216 to 0.8491, and r-squared did not change (0.7718). As a result, the distribution on the scatter plot of the two scales changed from that shown in Figure 2 to that shown in Figure 4, yielding a more linear relationship between “the modified 18-item BPRS” and the CGI-SCH than was the case between the original 18-item BPRS and the CGI-SCH. In addition, we confirmed that the Pearson’s r when the BPRS was modified only through decreasing the magnitude of those items that were significantly inversely correlated with the CGI-SCH was 0.8325 (p < 0.001).

Between Figures 2 and 4, r-squared for the linear multivariate regression utilizing the unmodified and modified score of each symptom was not changed (0.7718). However, r-squared for the multivariate non-linear regression analysis utilizing the logistic function as the regression function (with the CGI-SCH score adjusted from 1 - 7 into 0 - 1 (as “P” where 0 ≤ P ≤ 1) as the dependent variable and with all the individual items of the BPRS as independent variables) was 0.9750, considerably higher than that for the ordinal multivariate linear regression using the same full set of items (although a p-value was not able to be calculated with the SPSS & Stata programs).

By utilizing the set of the individual “P_i” ratios, we composed a prototype of a potential modified 18-item BPRS: “the modified 18-item BPRS” (of tentative meaning, given the limits of our data at this stage) (Figure 5).

4. Discussion
The BPRS is one of the most frequently used standards for
Modified 18-item BPRS

<table>
<thead>
<tr>
<th>Somatic concern</th>
<th>Anxiety</th>
<th>Emotional withdrawal</th>
<th>Conceptual disorganization</th>
<th>Guilt</th>
<th>Tension</th>
<th>Bizarre behavior</th>
<th>Grandiosity</th>
<th>Depressed mood</th>
<th>Hostility</th>
<th>Suspiciousness</th>
<th>Hallucinations</th>
<th>Motor retardation</th>
<th>Uncooperativeness</th>
<th>Unusual thought content</th>
<th>Blunted affect</th>
<th>Excitement</th>
<th>Disorientation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
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<td>8</td>
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<td>14</td>
<td>15</td>
<td>16</td>
<td>17</td>
<td>18</td>
</tr>
</tbody>
</table>

**Total score : 100 points**

Figure 5. An example of a potential modified 18-item BPRS. Marks for each item were calculated by multiplying the ratio \( P_i \) (relative weight of the i-th symptom of the BPRS), obtained as the right column of numbers in Table 3, for each of the 18 items by 30.

Table 3: Modified 18-item BPRS

<table>
<thead>
<tr>
<th>Modified 18-item BPRS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somatic concern</td>
</tr>
<tr>
<td>Anxiety</td>
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<td>Tension</td>
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<td>Unusual thought content</td>
</tr>
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<td>Blunted affect</td>
</tr>
<tr>
<td>Excitement</td>
</tr>
<tr>
<td>Disorientation</td>
</tr>
</tbody>
</table>

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ables) was 0.9750. This value was also two scales. To evaluate the clinical severity of schizophrenia, we substi-
tuted the CGI-SCH score for the clinical impression.

The values of Pearson’s r were slightly higher between “the modified 18-item BPRS” (constructed by modifica-
tion of specific point allocation) and the CGI-SCH than between the original 18-item BPRS and the CGI-SCH
without decreases of r-squared in terms of the results of
greater than that for ordinal multivariate linear regression
using the same full set of items (0.7718, although p-value
could not be calculated with the SPSS & Stata programs).
Therefore, a sigmoid function such as the logistic func-
tion might be more suitable as a regression function than
a simple linear function, as shown in Figure 2 (although
we recognize that the results have applicability to only
this trial at this stage).

We then investigated whether modifying the allocation
of marks could affect the linearity of the BPRS, at least
within this trial, looking at the correlation of the BPRS
with the CGI-SCH in terms of Pearson’s r and r-squared,
which express one of the degrees of the fit between the
linear multivariate regression before and after modifica-
tion of point allocation. We inferred that because the
shape of the scatter plot between the two scales became
more linear after the modification of the score than be-
fore, there was a possibility that the clinical weights
might be related to the heightened values of Pearson’s r
between “the modified 18-item BPRS” and the CGI-SCH.
We presumed that there was a possibility that the weight-
ings themselves were associated with the linearity of the
BPRS.

Furthermore, by assigning different weights to each
item proportional to the “Pi” that was calculated from the
regression coefficients, “bi”, we were able to construct an
eample of a potential modified 18-item BPRS: “the modified 18-item BPRS” (Figure 5). We assumed that
the magnitude of each “Pi” represented the respective
clinical weight of each item because the value of “Pi”
was defined as a probability by the logistic function. We
were also able to consider that the value of “Pi” provides
a probability or ratio to the full score of the CGI-SCH
(“7”) according to the set of item scores of the BPRS.
The scale is only a tentative example of a potential modi-
fied BPRS subscale that we were able to construct within
our data, and as a result, the number of items need not be
18 consistently.

Some problems have been reported with multivariate
regression analysis. To compare the relative magnitudes
of variables, the partial regression coefficients are often
normalized using their respective standard deviations.
However, the predictor variable is at least partially re-
dundant with other predictors and the partial regression
coefficient is influenced by the range of the predictor
variable [29,30]. In addition, the relative importance of
predictor variables is a tenuous concept and comparison
of the importance of predictors is not always the best
approach in multiple regression. As the individual items
of the BPRS had the same range of marks (ordinarily, 1 -
7), we considered that there would not be crucial dif-
fences in the sizes of standard deviations for predictor
variables in this study. With this assumption, we treated
the partial regression coefficients (“bi” terms) as if they
expressed the value of the weight with which each symp-
tom affected the score of the CGI-SCH through the
logistic function. With each manipulation, the range of
point allocations to each symptom before the manipula-
tion might have to be coordinated with the same size of
range. On the other hand, the use of standardized regres-
sion coefficients is difficult because the values are not
included in the logistic function and are not connected
with the “Pi” terms directly. Perhaps, if we would use the
standardized regression coefficients themselves, a more
complex and/or especially technical adjustment might be
needed for derivation of the “Pi” terms. This might then
differ considerably from the operations that we have de-
vised to this point. For instance, J. Lee reported a method
of covariates-adjusted rates for ordinal logistic regres-
sion, in which inserting xi of each variable individually
provided more adequate results (although the independ-
ent variables were binominal) [31]. Also with reference
to this, we utilized the magnitude of the “Pi” (calculated
by inserting bi and xi = 7, x j = 0 (j ≠ i) into the logistic
function) to modify the distribution of marks of the
BPRS and to design a potential modified BPRS. Our
method, however, does not utilize insignificant “bi” terms
and this might cause a bias in the results.

As for the method we used in the present study, there
is a problem in utilizing the logistic function because it is
a non-linear function described as $P = \frac{1}{1 + \exp(-(b_0 + b_1 x_1 + b_2 x_2 + \ldots + b_n x_n))}$
and this might cause a bias in the results.
The 18-item BPRS” multiplied by “Pi” for each i-th item proportional to the scatter plot connecting the score of the 18-item BPRS” and the CGI-SCH showed a distribution plot representing the relationship between the modified ordinal least-squares method. This might produce more generalized results than those of the ordinal least-squares method.

When supplemented with this adjustment, the scatter plot representing the relationship between “the modified 18-item BPRS” and the CGI-SCH showed a distribution proportional to the scatter plot connecting the score of the 18-item BPRS” and the score of the CGI-SCH. This is because both have almost the same significance on the graph. Additional improvements in fit may be possible.

The limitations of the present study should be noted. The first was the use of the CGI-SCH as a scale that substituted for the evaluation made by the patients’ psychiatrists. The CGI-SCH is not a gold standard and there is no evidence that the CGI-SCH has perfect linearity; this was merely an assumption to allow modification of the BPRS under a determinate condition. For the CGI-SCH, only a certain degree of reliability has been reported [3, 22, 23]. Nonetheless, we thought that this kind of simplification was unavoidable and the trade-off necessary, even if this assumption would sacrifice rigor to some extent in exchange for examining the degree of an abstract value such as “linearity”.

Second, there is no evidence supporting the assumption that the BPRS score and the CGI-SCH score obtained retrospectively by coding of the symptoms reported in the clinical chart would be comparable to the data obtained prospectively. Mullins, et al. reported the utility of the Brief Psychiatric Rating Scale for Children (BPRS-C) for transcribing narrative medical records into a standard quantitative form in which the medical records were the primary sources of information and the inter-rater reliabilities were adequate in most major domains of psychopathology, the one notable exception being symptoms in the anxiety domain [33]. The value of Pearson’s r, 0.8216, might be to some extent considered high. We presume that this was because the study was retrospective. Therefore, some items of the BPRS might not have been marked, thus minimizing the distribution of the BPRS score. The ideal weighting of individual symptoms of the BPRS should be determined prospectively. However, one of themes intended to be examined in this study is whether increasing the magnitudes of independent variables of significance (e.g., symptom scores of the BPRS) that are positively associated with the dependent variable (e.g., the CGI-SCH score) and decreasing the magnitudes of those are negatively correlated with the dependent variable could heighten the degree of the correlation (e.g., Pearson’s r) of the two data sets, such as the BPRS and the CGI-SCH, keeping the same number of variables (symptom scores of the BPRS). From this standpoint, our report might be regarded as an experimental case report demonstrating some degree of validity for this manipulation (modification of point allocations utilizing the logistic function). At any rate, prospectively randomized trials are needed in future studies.

Third, the reproducibility of the result that all of the symptoms of the BPRS were positively correlated with the CGI-SCH using univariate linear regression is doubtful. As for the exclusion of any item, in general, the more variables we exclude from the model, the more r-squared tends to decrease. The selection of the subset for which the decrease of r-squared is smallest is preferred so that the loss of model fit would be minimal. As a result, because the items were not excluded after univariate linear regression in Figure 1 and the r-squared for the results of multivariate regression utilizing all 18 items did not change (0.7718), we did not address the problem of item selection in the present study. However, the true aim of this study was, if possible, to examine the effect of modification of point allocation alone on the degree of linearity (in this study, correlation between the two scales; e.g., Pearson’s r). As a further improved algorithm of Figure 1, after univariate regression, only positive and significant (p < 0.05) coefficients would be selected. In the further revised algorithm, the exclusion of items from the 18 item selection might occur in a first step of manipulation and different results might be obtained. This issue should be examined in a prospective study.

Fourth, there may be some problems in our treatment of the size of coefficients. We did not regard positive values for insignificant coefficients (whether those were positive or negative) for multivariate non-linear regression. Therefore, the size of insignificant “bi” terms was ignored by inserting “bi = 0”. As a result, relative point allocations of those insignificant items did not change and point allocations of items positively and significantly associated with the CGI-SCH score increased while those of negatively and significantly correlated items decreased. If there are few significant items after the procedure in Table 2, we infer that the degree of modification in this model is very low and that there might be some need of a device for adjustments. This is one of the future tasks that should be addressed rigorously.

Fifth, despite the manipulations employed here, the degree of change in Pearson’s r was rather ambiguous. The increases appear slight; as a total, from 0.8216 to

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0.8491. Moreover, it is considerably uncertain whether this change has statistical significance. However, from another viewpoint, despite the fact that the number of items remained the same, the degree of correlation (Pearson’s $r$) increased just slightly and this fact might indicate the possibility that modification of point allocation itself might be able to heighten the correlation of the BPRS with the CGI-SCH. In the supplement, we confirmed that the Pearson’s $r$ (when the BPRS was modified only through decreasing the magnitude of those items that were significantly inversely correlated with the CGI-SCH) was 0.8325, a value higher than that between the original 18-item BPRS and the CGI-SCH, but smaller than that between the fully modified 18-item BPRS and the CGI-SCH. This fact might imply that only decreasing the point allocation of inversely correlated symptoms of the BPRS could also heighten the linearity of the BPRS. However, as was said before, the reproducibility of point allocation is quite uncertain in this model. Therefore, a randomized prospective study of this question in the future is desirable.

Sixth, the modification of point allocation may have contributed some artifacts of multi-collinearity. There are likely to be inter-correlations among the data. In this study, variables that were inversely correlated with the CGI-SCH score, indicating that the more severe the BPRS item, the lower the CGI-SCH score (a phenomenon that was a departure from the clinicians’ experiences), were decreased in an ad hoc procedure. Additional unknown and complicated factors are predicted to exist as well; for example, that both inpatients and outpatients were evaluated by the CGI-SCH and that the results might have been negatively influenced by differences in cognitive ability [34].

Seventh, we consider that our model is only applicable for a pair of scales where one is a single score scale (e.g., the CGI-SCH) and the other is a plural score scale (e.g., the BPRS). The condition that those two scales are intended for the same state of illness and are in a positive relationship intrinsically, at least roughly, is presumed necessary. Otherwise, if the two are in an inverse relationship, for instance, as is the case between the CGI-SCH and the Global Assessment of Functioning (GAF) [8], the method we discussed might be expected to produce nothing.

Eighth, the range of scores from 1 to 7 on the CGI-SCH may have been narrow and floor and ceiling effects should not have been ignored. This problem would be remedied by prospective research to obtain a normally-distributed data set. In relation to details of the form of the scales, we speculate that a more precise way approached from another viewpoint might be possible, for example, utilizing a visual analogue scale (VAS) [35-39] or a numerical rating scale (NRS) [40,41] for the ratings by psychiatrists, both of which range from 0 to 10, for the scores that we substituted for the clinical impression (although the true estimation of their validity is in flux at present [42-48]). We chose instead the ordinal CGI-SCH scores, which range ordinarily from 1 to 7 (taking “0” as “not assessed”), to express the clinicians’ global impression of illness with schizophrenic patients. S. Stevens proposed a “ratio scale” on which four arithmetic operations could be possible [49]. As the “0” of the BPRS and of the CGI-SCH means “not assessed”, these might produce differences from the ordinal meaning of “0” (none) of the “ratio scale”. If so, the difference between the definitions of “0” might cause a distortion for the BPRS and the CGI-SCH. As we commented previously, the possible absence of linearity and of equal increments between each point of the CGI-SCH are serious problems that could not be ignored. In addition, the individual scores of the BPRS should ideally correspond to a visual analogue scale whose respective score ranges of 0 - 7 or 0 - 10 would have a more adequate degree of linearity than the CGI-SCH. If this condition were met, the BPRS would become one of the more linear evaluating scales.

Ninth, the modified 18-item BPRS should be regarded as a result based on mixed data from acute phase and chronic phase schizophrenic subjects. This origin might yield various types of biases and inadequate impressions (e.g., peculiar items that are likely to be observed strongly only in an acute or a chronic phase might be included in the modified scale presented in Figure 5). To define the “acute” or “chronic” phase of schizophrenia clearly was too complex and difficult an issue, so, ideally, the prototype we proposed tentatively in Figure 5 should be re-determined as several scales, one each for the acute phase, the chronic phase and others phases, through more rigorous definitions for various phases of schizophrenia, by way of prospective ratings.

Tenth, and above all, these results are not likely to be reproducible and our model has a meaning only for comparison purposes within a given study. If we performed the same procedure on new data, it is very likely that different point allocations would be assigned to individual items. We infer that a possible way to remedy this problem, even if partially, might be to perform a number of prospective trials in line with our method, and then summarize and calculate an average on items and point allocation. If these scales are composed as a summary, they might be less problematic than that of our trials. However, even in such scales, there would still be no assurance that they would have a greater degree of reproducibility. Therefore, the extent to which the results of this paper could be applicable may be quite limited. For this reason, future studies are necessary.

Eleventh, the problem that we have addressed may be insoluble in principle. This approach to optimizing many
parameters (variables) so that a certain value would be maximized might not always provide the ideal magnitudes for the other values. The challenge of the setting of this study was to find the optimized value of individual symptoms whose severities were recognized independently when they were rated. If the solution of these kinds of problems, in which many values should be determined ideally at the same instant under the condition that a certain parameter (e.g., Pearson’s r) would take the maximum value, is impossible in principle, the applications might then be quite limited.

The true aim of the present study was not always to determine the best point allocation, but to consider a specific example of a potential modified BPRS through pursuing “the ideally modified BPRS” reflecting an abstract “true score”. Therefore, “the modified 18-item BPRS” is merely a tentative idea at this stage to propose a new viewpoint of the importance of point allocation in the BPRS. The present study has many limitations and is thus only a half-step from which further studies may learn. We believe that improving evaluation scales to make them more linear could minimize distortions in evaluations for severity of illness, including over- and under-diagnosis and estimations for efficiency and effect in clinical research. We anticipate that our present results will serve as a useful reference for clinicians attempting to devise an evaluation scale, and that further research will focus on the optimal number of items, the fittest items for selection, and the allocation of marks in a rigorous methodology to maximize the linearity of the BPRS.

5. Conclusion

Within the limits of our data, a roughly logarithmic relationship was discerned between the two scales and the item-weightings of the BPRS (apart from item-selection) were identified as important for the improvement of the BPRS for evaluating schizophrenia.

6. Authors’ Contributions

JS performed the evaluation of the patients and the statistical analysis, and wrote the manuscript. SM also performed the evaluation of the patients and revised the manuscript. JI was responsible for checking the methodology of the study and evaluating the results of the statistical analysis. In addition, all authors read and approved the final version of the manuscript.

7. Acknowledgements

The authors wish to acknowledge Katsuji Nishimura, Ken Inada and Kaoru Sakamoto for providing us with very useful advice in this study.

REFERENCES


