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Evaluating Depressive Symptoms in Schizophrenia: A Psychometric Comparison of the Calgary Depression Scale for Schizophrenia and the Hamilton Depression Rating Scale

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Key Words

Schizophrenia · Depressive symptoms · Calgary Depression Scale for Schizophrenia · Hamilton Depression Rating Scale

Abstract

Background: The aim of this study was to compare two measures of depression in patients with schizophrenia and schizophrenia spectrum disorder, including patients with delusional and schizoaffective disorder, to conclude implications for their application. ***Sampling and Methods:*** A total of 278 patients were assessed using the Calgary Depression Scale for Schizophrenia (CDSS) and the Hamilton Depression Rating Scale (HAMD-17). The Positive and Negative Syndrome Scale (PANSS) was also applied. At admission and discharge, a principal component analysis was performed with each depression scale. The two depression rating scales were furthermore compared using correlation and regression analyses. ***Results:*** Three factors were revealed for the CDSS and HAMD-17 factor component analysis. A very similar item loading was found for the CDSS at admission and discharge, whereas results of the loadings of the HAMD-17 items were less stable. The first two factors of the CDSS revealed correlations with positive, negative and general psychopathology. In contrast, multiple significant correlations were found for the HAMD-17 factors and the PANSS subscores. Multiple regression analyses demonstrated that the HAMD-17 accounted more for the positive and negative symptom domains than the CDSS. ***Conclusions:*** The present results suggest that compared to the HAMD-17, the CDSS is a more specific instrument to measure depressive symptoms in schizophrenia and schizophrenia spectrum disorder, especially in acutely ill patients.

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Introduction

Depressive symptoms are thought to represent an important symptom domain in schizophrenia patients [1], with prevalence estimates ranging to as high as 80% [2]. Depressive symptoms have been associated with impairments in social and vocational functioning, quality of life and an increased risk of relapse [3, 4]. They were found to increase mortality rates in patients with schizophrenia by contributing to the alarmingly high rates of suicide [5]. Therefore, measuring symptoms of depression has become of increasing interest and importance in the past years in schizophrenia research [6].

However, a difficulty in assessing depressive symptoms in schizophrenia has been noted, mainly due to a lack of specifically developed rating scales to examine depressive symptoms in this patient population [7]. The most commonly used rating scale has been the Hamilton Depression Rating Scale (HAMD), developed during the late 1950s as a standardized scale for the measurement of the severity of depressive symptoms in inpatients with depressive disorders [8]. However, the HAMD was found to be significantly influenced by negative and extrapyramidal symptoms in schizophrenia, placing its use in this patient population in doubt [9]. The concern of using scales in populations for which they were not designed was already critically discussed by Hamilton himself. Consequently, to overcome these limitations, the Calgary Depression Scale for Schizophrenia (CDSS) has been developed to specifically assess depression in patients with schizophrenia [10]. The superiority of the CDSS originates from its psychometric properties [11, 12], and furthermore, its discriminant and convergent validity have been reported in many studies [13].

Addington et al. [14] were among the first to examine depressive symptoms in acutely hospitalized schizophrenia patients; they showed that the HAMD accounted for more of the variance in positive and negative symptoms than the CDSS, suggesting that the CDSS is a more specific measure of depression than the HAMD. In a similar analysis by Müller et al. [15] in 119 inpatients with acute schizophrenia, again significant advantages were found to emerge with the CDSS when compared to the HAMD. Collins et al. [16] were able to confirm these results in schizophrenia outpatients with a mean duration of illness of 14.95 years and comparing the CDSS not only to the HAMD but also to the depression subscale of the Positive and Negative Syndrome Scale (PANSS). However, previous research comparing the CDSS and the HAMD bears several methodological pitfalls such as very small sample sizes with fewer than 100 patients [9, 14] and mainly performing correlation analyses providing only limited information on the scales' individual properties.

Therefore, the aim of this study was to reevaluate these results within a larger and 'real-world' patient sample in order to provide an up-to-date recommendation regarding which rating scale is best to apply.

Methods

Subjects

Data were collected in a multicenter follow-up programme (German Research Network on Schizophrenia) [17] at eleven psychiatric university hospitals and three psychiatric district hospitals in the region surrounding Munich. All patients admitted to one of the above-mentioned hospitals between January 2001 and December 2004 with the diagnosis of schizophrenia, schizophreniform disorder, delusional disorder or schizoaffective disorder according to DSM-IV criteria were selected for inclusion. Patient selection was performed using randomization software. Subjects were aged between 18 and 65 years. The exclusion criteria of this study were defined as a head injury, a history of major medical illness or alcohol or drug dependency. Informed written consent had to be provided to participate in the study. The study protocol was approved by the local ethics committees [18].

Assessments

DSM-IV diagnoses were established by clinical researchers on the basis of the German version of the Structured Clinical Interview for DSM-IV [19]. Sociodemographic and course-related variables such as age at onset, age at first hospitalization or episodes of illness were collected using a standardized documentation system [20] during interviews with patients, relatives and care providers.

Depressive symptoms were examined by applying the CDSS [21]. The CDSS is a 9-item questionnaire (depression, hopelessness, self-depreciation, guilty ideas of reference, pathological guilt, morning depression, early wakening, suicide, observed depression) with a global score range of 0–27 points. The 17-item version of the HAMD (HAMD-17) [8] was also applied. The patients' positive, negative and general psychopathology was assessed using the PANSS [22]. All raters had been trained to use the applied scales. A high inter-rater reliability was achieved (Intra-Class-Correlation >0.8).

Statistical Analysis

To identify patients suffering from depressive symptoms, widely accepted cut-off scores of the CDSS and the HAMD-17 were applied. A cut-off score of >6 points has been proposed for the CDSS [21] and a cut-off score of ≥ 16 points for the HAMD-17 [23] to separate depressed and non-depressed patients.

Factor analysis using the principal component method was calculated in order to identify latent structures underlying the data. This procedure transforms a number of possibly correlated variables into a smaller number of variables called principal components. The first principal component accounts for as much of the data's variability as possible, with every succeeding compo-

nent accounting for as much of the remaining variability as possible. Given the naturalistic and descriptive approach of this study, an explorative factor analysis was performed descriptively examining the two depression scales.

Parallel plots were used in order to determine a reasonable number of factors. This technique compares the eigenvalues of the original data with the eigenvalues of its random permutations. This method was shown to be superior to the simple eigenvalue-greater-than-one rule [24]. Principal component analysis was performed using a correlation matrix; the oblique rotation was based on the assumption that significant correlations exist between the instrument factors (promax rotation). Principal component analysis was applied to both the CDSS and the HAMD-17 at admission and at discharge. To attain a clear arrangement of the results, only loadings with an absolute value greater than 0.4 are presented; by this means, only loadings of items which contribute substantially to a factor are shown. The signs of the loadings in this context are of secondary interest and only due to the rotation technique; if all loadings of a factor show the same sign, the involved items contribute in the same direction to this factor.

Accordingly, Pearson's correlation coefficient was used to examine the correlation between the factors of the CDSS, the factors of the HAMD and the PANSS subscores. The value of significance was calculated based on a t test for Pearson's correlation coefficient. Additionally, multiple regression analyses were performed with CDSS and HAMD factors as predictor variables and the PANSS subscores as dependent variables.

All statistical analyses were performed using the statistical program R 2.10.1 [25].

Results

Patients

In the entire multicenter study, 474 patients were enrolled. Forty-six patients had to drop out for different reasons (e.g. retrospective violation of inclusion criteria, withdrawal of informed consent). Another 150 patients were excluded from this analysis, 28 patients because they were discharged from hospital within 7 days after admission and thus no follow-up rating was available and 122 patients due to missing or inconsistent CDSS values. Therefore, the sample available for analysis comprised 278 subjects (163 males, 115 females). The mean age was 34.77 years (±11.07), and the mean duration of illness 7.68 years (±9.14). The mean number of hospitalizations was 3.94 (±5.68). The mean duration of the current hospitalization was 68.78 days (±49.65), and the mean age at first treatment, mirroring the patient's age at onset, was 27.03 years (±8.82). Forty-six percent of patients were employed and 54% were jobless. At admission, 26% of the patients suffered from suicidality. None of the patients had the diagnosis of a comorbid major depressive episode.

Patients were treated under naturalistic conditions; 51% of the patients received a first-generation antipsychotic, 79% of patients were given second-generation antipsychotic treatment and 41% of the patients were treated with first- as well as second-generation antipsychotics. Tranquilizers were administered to 66% of patients and mood stabilizers to 12%. Thirty-three percent of the patients were also treated with antidepressants.

Psychopathological Ratings

At admission, the mean CDSS total score was 6.41 (±4.71) and the mean HAMD-17 total score was 13.56 (±6.72). The mean PANSS positive subscore was 18.99 (±6.49); the mean PANSS negative subscore was 18.41 (±7.45); the mean PANSS general psychopathology subscore was 36.62 (±10.08), and the mean PANSS total score was 74.01 (±19.46). Applying accepted cut-offs, a similar number of patients were found to be depressed using the CDSS and the HAMD-17 at admission (CDSS: 90 patients; HAMD-17: 86 patients; 54 patients concurrently scored >6 on the CDSS and ≥16 on the HAMD-17).

At discharge, the mean CDSS total score was 2.63 (±3.55) and the mean HAMD-17 total score was 7.86 (±6.2). The mean PANSS positive subscore was 10.81 (±3.96); the mean PANSS negative subscore was 14.84 (±6.28); the mean PANSS general psychopathology subscore was 26.35 (±7.82), and the mean PANSS total score was 52 points (±15.43). Again, a very similar number of patients suffered from depressive symptoms at discharge when applying the CDSS and the HAMD-17 (CDSS: 27 patients; HAMD-17: 26 patients; 11 patients concurrently scored >6 on the CDSS and ≥16 on the HAMD-17).

Scatter plots analysed at admission and discharge showed that the CDSS and HAMD total scores moved in the same direction, suggesting a linear correlation between the scales' total scores (fig. 1).

Factor Analysis of the CDSS

Based on parallel plots, 3 factors were revealed for the CDSS factor component analysis.

At Admission

The loadings of the principal component factor analysis of the CDSS at admission are shown in table 1. The items 'depressed mood', 'hopelessness' and 'self-depreciation' as well as 'suicide' and 'observed depression' were found to load on factor 1, which accounted for 30% of the variance. The item 'self-depreciation' loaded on factors 1 and 2. Factor 2 was based on items referring to guilt, accounting for 19% of the variance, and factor 3 referred to

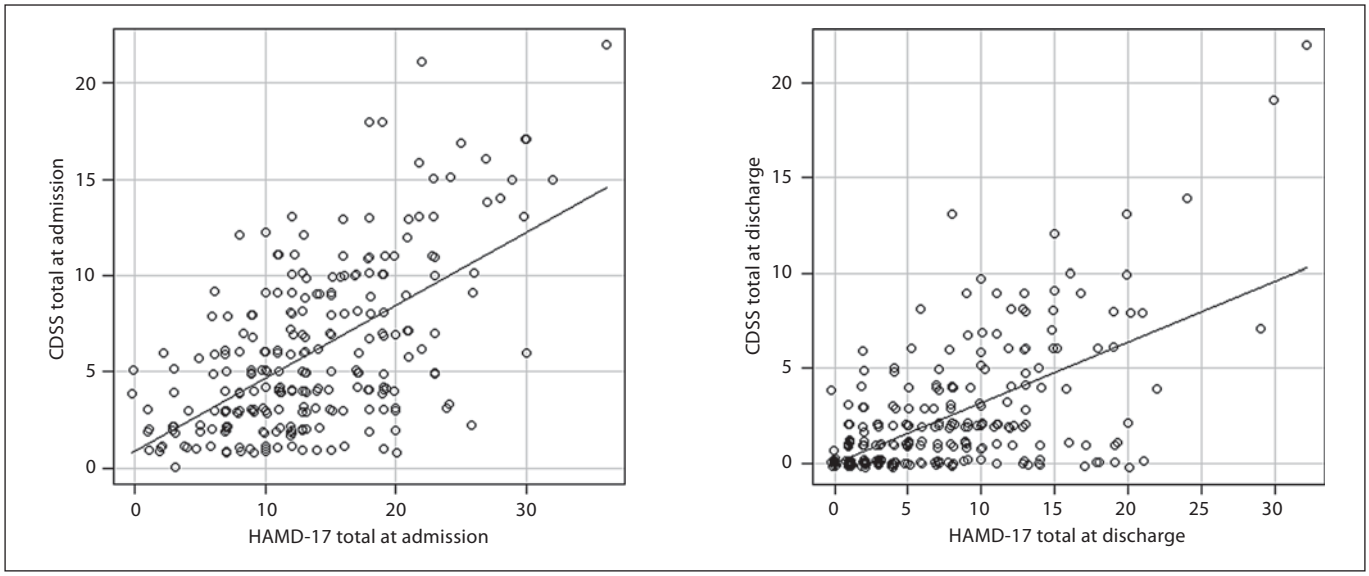

Fig. 1. Scatter plots of CDSS and HAMD-17 total scores at admission and discharge.

Table 1. Factor analysis of the CDSS at admission

	Factor 1	Factor 2	Factor 3
CDSS items			
1. Depressed mood	–0.83		
2. Hopelessness	–0.75		
3. Self-depreciation	–0.51	0.57	
4. Guilty ideas of reference		0.84	
5. Pathological guilt		0.76	
6. Morning depression			–0.71
7. Early wakening			–0.86
8. Suicide	–0.58		
9. Observed depression	–0.84		
Sum of square loadings	2.70	1.72	1.45
Proportional variance	0.30	0.19	0.16
Cronbach's α (overall variance: 0.78)	0.79	0.66	0.53

Table 2. Factor analysis of the CDSS at discharge

	Factor 1	Factor 2	Factor 3
CDSS items			
1. Depressed mood	–0.82		
2. Hopelessness	–0.69		
3. Self-depreciation		–0.64	
4. Guilty ideas of reference		–0.88	
5. Pathological guilt		–0.83	
6. Morning depression			0.76
7. Early wakening			0.86
8. Suicide	–0.68		
9. Observed depression	–0.83		
Sum of square loadings	2.54	2.18	1.57
Proportional variance	0.28	0.24	0.17
Cronbach's α (overall variance: 0.83)	0.82	0.74	0.60

the items 'morning depression' and 'early wakening', accounting for 16% of the variance. The overall Cronbach's α was 0.78, suggesting good internal consistency.

At Discharge

A very similar factor structure was found for the CDSS at discharge (table 2). The item 'self-depreciation' loaded solely on factor 2 at discharge; all other items were related to the same factors as at admission. The overall Cronbach's α was 0.83.

Factor Analysis of the HAMD-17

Based on parallel plots, 3 factors were revealed for the HAMD-17 factor component analysis.

At Admission

Results of the factor analysis of the HAMD-17 are shown in table 3. Items on somatic experiences, hypochondriasis, interest in work and retardation loaded on factor 1, accounting for 14% of the variance. Factor 2 referred to anxiety and insomnia, also accounting for 14% of the variance. The third factor loaded the depression

Table 3. Factor analysis of the HAMD-17 at admission

	Factor 1	Factor 2	Factor 3
HAMD items			
1. Depression			0.57
2. Guilt			0.50
3. Suicide			0.69
4. Insomnia – E		–0.68	
5. Insomnia – M		–0.78	
6. Insomnia – L		–0.68	
7. Work/interest	–0.70		
8. Retardation	–0.55		
9. Agitation		–0.45	
10. Anxiety – psychic		–0.42	
11. Anxiety – somatic	–0.45	–0.43	
12. Somatic – GI			0.48
13. Somatic – general	–0.66		
14. Libido			
15. Hypochondriasis	–0.43		
16. Loss of weight			0.42
17. Loss of insight			
Sum of square loadings	2.26	2.33	1.97
Proportional variance	0.14	0.14	0.12
Cronbach's α (overall variance: 0.72)	0.59	0.57	0.57

E = Early; M = middle; L = late; GI = gastrointestinal.

Table 4. Factor analysis of the HAMD-17 at discharge

	Factor 1	Factor 2	Factor 3
HAMD items			
1. Depression	–0.73		
2. Guilt		0.40	
3. Suicide		0.42	
4. Insomnia – E		0.66	
5. Insomnia – M		0.73	
6. Insomnia – L		0.69	
7. Work/interest	–0.61		
8. Retardation	–0.70		
9. Agitation			0.65
10. Anxiety – psychic			0.56
11. Anxiety – somatic			0.49
12. Somatic – GI	–0.51		
13. Somatic – general	–0.57		
14. Libido			
15. Hypochondriasis			0.60
16. Loss of weight			
17. Loss of insight			0.61
Sum of square loadings	2.68	2.20	2.21
Proportional variance	0.16	0.13	0.13
Cronbach's α (overall variance: 0.79)	0.69	0.62	0.60

E = Early; M = middle; L = late; GI = gastrointestinal.

item as well as items on guilt and suicide, accounting for only 12% of the variance. The overall Cronbach's α was 0.72.

At Discharge

The results of the factor analysis of the HAMD-17 at discharge differed considerably from the results at admission (table 4). Compared to admission, factor 1 included the item 'depression' at discharge, accounting for 16% of the variance. The items 'guilt' and 'suicide' loaded on factor 2 at discharge, whereas items on anxiety loaded on factor 3. The overall Cronbach's α was 0.79.

Pearson's Correlation Coefficients of the CDSS and HAMD-17 Total Scores and of the CDSS Factors, HAMD-17 Factors and PANSS Subscores

The CDSS total score and the HAMD-17 total score were significantly correlated at admission ($p < 0.001$; correlation coefficient 0.59) and at discharge ($p < 0.001$; correlation coefficient 0.59). The CDSS factors were found to be less often significantly correlated to the PANSS subscores than the HAMD-17 factors at admission and discharge (tables 5, 6). This applied especially to the third CDSS factor, which was not significantly correlated to any of the PANSS subscores at admission or discharge.

Multiple Regression Analysis of the CDSS Factors, HAMD-17 Factors and PANSS Subscores

At admission, the results of the multiple regression analysis indicated that the CDSS factors explained less of the PANSS subscores than did the HAMD-17 factors (table 7). However, at discharge, a similar level of explained variance was found between the CDSS and HAMD-17 factors and the PANSS subscores (table 8).

Association between CDSS, HAMD-17, CDSS Factors and HAMD-17 Factors and Gender and Patients' Outcome

At admission, female patients were found to score significantly higher ($p < 0.0001$) on the CDSS mean score as well as on CDSS factor 1. On discharge, men scored significantly higher on CDSS factor 3 ($p < 0.0001$) with the items 'morning depression' and 'early wakening'.

Comparing the mean CDSS and HAMD-17 values as well as the CDSS and HAMD-17 factors in terms of an association with the patients' outcome, no significant dif-

Table 5. Pearson correlation analysis of the CDSS factors, HAMD-17 factors and PANSS subscores at admission

	PANSS positive	PANSS negative	PANSS general
CDSS total score	–0.02 (–0.14 to 0.1)	0.32*** (0.22–0.43)	0.40*** (0.22–0.43)
CDSS factor 1	0.04 (–0.08 to 0.16)	–0.35*** (–0.45 to –0.24)	–0.39*** (–0.42 to –0.2)
CDSS factor 2	0.18** (0.06–0.29)	–0.06 (–0.17 to 0.06)	0.16** (0.08–0.31)
CDSS factor 3	0.04 (–0.08 to 0.16)	0.11 (–0.01 to 0.23)	–0.04 (–0.18 to 0.05)
HAMD-17 total score	0.21*** (0.09–0.32)	0.32*** (0.21–0.43)	0.46*** (0.32–0.52)
HAMD-17 factor 1	–0.17** (–0.28 to –0.05)	–0.31*** (–0.41 to –0.2)	–0.44*** (–0.49 to –0.29)
HAMD-17 factor 2	–0.07* (0.18–0.41)	0.37*** (0.27–0.47)	0.16** (0.01–0.24)
HAMD-17 factor 3	–0.27*** (0.37 to –0.15)	–0.14* (–0.25 to –0.02)	–0.18** (–0.33 to –0.11)

Figures in parentheses represent confidence intervals * p < 0.05; * p < 0.01; * p < 0.001.

Table 6. Pearson correlation analysis of the CDSS factors, HAMD-17 factors and PANSS subscores at discharge

	PANSS positive	PANSS negative	PANSS general
CDSS total score	0.34** (0.23–0.44)	0.34*** (0.23–0.44)	0.52*** (0.43–0.6)
CDSS factor 1	–0.33 (–0.43 to 0.22)	–0.35*** (–0.45 to –0.24)	–0.52*** (–0.6 to –0.43)
CDSS factor 2	0.01 (–0.21 to –0.12)	0.24 (–0.13 to 0.35)	0.06 (–0.06 to 0.17)
CDSS factor 3	–0.02 (–0.13 to 0.1)	0.09 (–0.03 to 0.2)	0.04 (–0.08 to 0.16)
HAMD-17 total score	0.32*** (0.21–0.42)	0.32*** (0.21–0.42)	0.41*** (0.31–0.5)
HAMD-17 factor 1	–0.29*** (–0.4 to –0.18)	–0.3*** (–0.4 to –0.19)	–0.39*** (–0.49 to –0.29)
HAMD-17 factor 2	–0.13* (–0.25 to –0.01)	–0.1 (–0.22 to 0.02)	–0.03 (–0.14 to 0.09)
HAMD-17 factor 3	0.17 (–0.06 to 0.28)	–0.25 (–0.36 to 0.14)	–0.02 (–0.13 to 0.1)

Figures in parentheses represent confidence intervals. * p < 0.05; * p < 0.01; * p < 0.001.

Table 7. Multiple regression analysis of the CDSS factors, HAMD-17 factors and PANSS subscores at admission

Predictor variable	Dependent variable	Multiple r	r^2	p value
CDSS factors	PANSS positive	0.04	0.19 (0.08–0.3)	0.02
	PANSS negative	0.13	0.37 (0.27–0.46)	0.00
	PANSS general	0.18	0.42 (0.27–0.48)	0.00
HAMD-17 factors	PANSS positive	0.10	0.32 (0.21–0.43)	0.00
	PANSS negative	0.23	0.48 (0.38–0.57)	0.00
	PANSS general	0.24	0.49 (0.36–0.56)	0.00

Figures in parentheses represent confidence intervals.

Table 8. Multiple regression analysis of the CDSS factors, HAMD-17 factors and PANSS subscores at discharge

Predictor variable	Dependent variable	Multiple r	r^2	p value
CDSS factors	PANSS positive	0.11	0.33 (0.19–0.48)	0.00
	PANSS negative	0.16	0.40 (0.3–0.5)	0.00
	PANSS general	0.35	0.52 (0.41–0.63)	0.00
HAMD-17 factors	PANSS positive	0.13	0.36 (0.25–0.47)	0.00
	PANSS negative	0.14	0.37 (0.27–0.48)	0.00
	PANSS general	0.20	0.40 (0.29–0.51)	0.00

Figures in parentheses represent confidence intervals.

ferences were found at admission. However, at discharge, a significant association was found comparing early responders/non-early responders in terms of the mean CDSS ($p = 0.0088$) and the mean HAMD-17 ($p = 0.0397$) and CDSS factor 1 ($p = 0.0101$). Comparing responders/non-responders and remitters/non-remitters, significantly lower scores were found for the mean CDSS ($p < 0.0001$), the mean HAMD-17 ($p < 0.0001$), CDSS factor 1 ($p < 0.0001$) and HAMD-17 factor 1 ($p < 0.0001$). Responders also scored significantly lower on HAMD-17 factor 2 ($p = 0.0357$).

Discussion

Analysing the CDSS

Factor Analysis

Our results of the factor analyses of the CDSS showed a stable underlying 3-factorial structure at both assessment time points with an almost identical loading of the CDSS items on factors 1–3. At admission, the cumulative variance of the factor analysis was 65%, and at discharge, it was 70%. This indicates that the revealed factors explain the distribution of the CDSS items for the most part. Our 3 identified factors ('general depression and hopelessness factor', 'guilt factor' and 'morning depression and early wakening factor') have already been described in the literature, which confirms the scale's satisfying psychometric properties [14, 26].

However, other authors have referred to the second factor as the 'cognitive factor', based more on the perception and cognition of guilt than on the domain of guilt itself [14]. The third factor, although only comprehending one item, or as in our own results two items, is thought to be of clinical relevance in representing melancholia. It was furthermore found to be an important specifier for a major depressive episode [14].

Interestingly, the loadings of the 3 factors were stable from admission to discharge, indicating that the factorial structure is stable independent of significant improvement in the clinical status of the examined patients throughout the course of the study. The same factorial stability was found by Addington et al. [14], who examined acutely relapsed schizophrenia patients with a 3-month follow-up assessment time point implying a time point of relative remission similar to the present study. These properties of the scale with high internal consistency are furthermore underlined by results of the psychometric properties of the scale in a healthy control group reporting reference values for clinical use [27].

Correlation and Regression Analyses of the Revealed CDSS Factors

In contrast to other trials examining the CDSS in schizophrenia patients, we found the CDSS total score as well as CDSS factor 1 to be significantly correlated to the PANSS negative subscore [16, 28, 29]. The negligible correlation between the CDSS and negative symptoms reported by other authors has always been thought to be a valuable and unique characteristic of the CDSS compared to other rating scales [14, 30]. However, our results finding a correlation between negative symptoms and the CDSS might be due to differences in the sample selection and methodological approaches (e.g. rater behaviour) compared to other studies. For example, in the present study the same raters performed the CDSS and PANSS ratings, which might at least partially contribute to the present findings. Also, suicidal patients and patients with severe depression, indicated by a greater standard deviation than reported in the comparative literature, were included. Still, this result somewhat challenges current research opinions stating that depressive symptoms are an integral part of schizophrenia psychopathology and independent of, for example, negative symptoms [2]. However, given the fact that both the depressive and negative psychopathological domains cover symptoms like social withdrawal or lack of spontaneity, an overlap and correlation between these domains is evident, thereby affecting the assessment of depressive symptoms [31]. However, if and to what extent depressive and negative symptoms in schizophrenia are divergent remains unclear and should be the focus of future research, resulting in a better understanding of schizophrenia psychopathology.

In line with current literature reports, we found a strong and significant correlation of CDSS factor 2 with positive symptoms [26]. It is believed that guilty ideas of reference are similar to the symptoms of delusions of guilt [14], contributing to the significant correlation between these domains.

Similar results were found at discharge, whereby factor 1 correlated significantly to all PANSS subscores and the CDSS factor on guilt was only found to significantly correlate to the PANSS positive subscore. Regarding the results of the multiple regression analysis, the CDSS was found to account for all three PANSS subscores, with the lowest association between the CDSS and positive symptoms, followed by negative symptoms and general psychopathology. Again, our findings of an association between the CDSS and negative symptoms are conflicting, as discussed above.

Analysing the HAMD-17

Factor Analysis

The factor analysis of the HAMD-17 at admission and discharge varied considerably, explaining 40% of the cumulative variance at admission and 42% of the cumulative variance at discharge. Comparative literature in schizophrenia patients is very limited, and to our knowledge there are only two other trials that have examined the HAMD factorial structure in schizophrenia [9, 14]. Both comparative studies applied a different statistical method to identify the number of factors for the principal component analysis, using 6 and 7 factors, respectively, and thus limiting comparability to the present results [9, 14]. However, both studies examined two different time points and also found the HAMD to be unstable. Goldman et al. [9] identified only 6 of 17 items loading on the same factors at both assessment time points. Also, Addington et al. [14] reported a massive change in factor loading occurring between the examined time points.

At admission in our study, the highest loading on the first factor was found for the item 'work interest', followed by 'general somatic', 'anxiety somatic', 'retardation' and 'hypochondriasis'. This loading of items on the first factor is at least partially different from data deriving from factor analyses of the HAMD performed in patients with depression [32]. Early on, Hamilton [33] found the first factor to measure general depression incorporating items like 'depressed mood' or 'suicide'. In our study, we did find a so-called 'general depression factor', namely the third factor, loading 'typical' depression items. The main explanation for these contradictory results probably lies in the different patient samples examined. It is not surprising that the dimension of depression in schizophrenia patients differs from what we observe in depressed patients [30]. Besides, in acutely ill schizophrenia patients, symptoms like anxiety or hypochondriac delusions might be more prominent than depressive symptoms, which might also explain the observed items' loading.

However, interestingly, even in factor analyses of the HAMD in depression, inconsistent results have been reported. In a review of 15 studies with 17 samples of depressed patients, Bagby et al. [34] found several differences regarding the item loading on specific factors and concluded that the HAMD is clearly not unidimensional.

At discharge, we were able to confirm the HAMD factors of anxiety and insomnia which have been described in patients with depression [35], whereas at admission, both symptom domains loaded on the same factor. Based on the better differentiated loading of items at discharge with greater similarity to the factors found in depression, our results suggest that measuring depression using the HAMD might be more appropriate in stable schizophrenia patients rather than acutely ill ones.

Correlation and Regression Analyses of the Revealed HAMD Factors

At admission, all HAMD factors as well as the HAMD total score were significantly correlated to the PANSS subscores, which has been consistently reported in patients suffering from schizophrenia [16, 28]. Comparison of our results between admission and discharge is limited due to different items loading on the 3 HAMD factors. However, considerably less significant correlations were observed between the HAMD factors and the PANSS subscores, with only HAMD factor 1 correlating to all PANSS subscores at discharge. This factor loaded items like 'work interest' and 'retardation', so that correlations with negative symptoms and general psychopathology are not surprising. The fact that we also found a significant correlation between this factor and positive symptoms, which was even higher than the correlation at admission, might be explained by the well-known phenomenon that due to the patients' psychopathological improvement, both symptom domains move to a minimum.

When examining the factorial structure of the HAMD in schizophrenia patients, Goldman et al. [9] correlated the HAMD total score only to negative symptoms, reporting no correlation at their initial assessment but finding a significant correlation at the time point of follow-up. Similar to our own results, Addington et al. [14] also identified a significant correlation between their first HAMD factor and negative symptoms, with factor 1 loading items like 'depression' or 'somatic gastrointestinal' as in the present analysis.

Performing multiple regression analyses, we found all PANSS subscores to be significantly explained by the HAMD factors; however, the lowest score was for positive symptoms, followed by negative symptoms and general psychopathology. This result is in line with the only other trial that performed multiple regression analyses using HAMD factors and found the poor discriminant validity of the HAMD depression factors to be confirmed [14].

Clinical Implications

The HAMD was found to be less stable and accounted for considerably less variance than the CDSS at both assessment time points. Considering the correlation analyses, more HAMD factors were significantly correlated to the PANSS subscores than CDSS factors. Moreover, the

correlation pattern of the CDSS factors and the PANSS subscores was very similar at admission and discharge compared to that of the HAMD factors and the patients' psychopathology. Also, the results of the multiple regression analyses revealed a stronger association between the results of the HAMD factors and the PANSS subscores compared to the CDSS factors. This indicates that the HAMD factors explain more of the PANSS subscores than do the CDSS factors or, in other words, that there is 'more' HAMD in the PANSS subscores compared to the CDSS. Both the CDSS and the HAMD mean scores as well as CDSS and HAMD factor 1 were significantly associated with the patients' outcome, suggesting that patients with less depressive symptoms were significantly more likely to achieve early response, response and remission. In terms of gender, we found female patients to suffer from more depressive symptoms when applying the CDSS.

Taking these results together, the HAMD seems to be more confounded by symptoms of the PANSS positive and negative subscales than the CDSS. Future trials should further examine the association between the CDSS and patients' psychopathology and should continue the discussion regarding the overlap between depressive and negative symptoms [36]. The stability and satisfying variance of the CDSS at both assessment time points suggest its advantage in the assessment of depressive symptoms in schizophrenia patients.

Strengths and Limitations

Advantages of the present analysis compared to previous research in this field are the large sample size and the fact that patients were treated under naturalistic conditions with liberal inclusion and exclusion criteria. Including patients suffering from suicidality as well as chronically ill and first-episode patients might increase the generalizability of our findings and exhibit higher external validity. Moreover, the study at hand is among the first to concurrently use a variety of different statistical methods (factor, correlation and regression analyses), thus providing broad information on the scales' properties and use. Also, compared to other available studies, patients in this analysis were predominantly treated with atypical antipsychotics, which mirrors current treatment guidelines. A potential limitation, however, might be that at discharge, most patients scored rather low on the CDSS and the HAMD, which has to be kept in mind when discussing the resolving factorial structure of the scales.

Conclusion

Performing principal component analysis, the CDSS was found to hold a stable 3-factorial structure at admission and discharge whereas the item loadings of the HAMD were less stable, suggesting that the CDSS might be a more appropriate instrument to measure depressive symptoms in schizophrenia. Factors of both scales were significantly correlated to positive and negative symptoms as well as to the patients' general psychopathology, with fewer and less significant correlations for the CDSS factors. The fact that both scales correlated with negative symptoms revives the discussion on whether or not the negative and depressive symptom domains in schizophrenia are really independent psychopathological phenomena.

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