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Original Article

To use the brief psychiatric rating scale to detect disorganized speech in schizophrenia: Findings from the REAP-AP study



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KEYWORDS

Brief Psychiatric
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Conceptual
disorganization;
Disorganized speech;
Excitement;
Uncooperativeness

Abstract Our study aimed to assess the psychometric validity of the conceptual disorganization item and other items of the Brief Psychiatric Rating Scale (BPRS) for detecting disorganized speech in patients with schizophrenia. We included 357 schizophrenia patients with disorganized speech and 1082 without disorganized speech from the survey centers in India. Indonesia, Japan, Malaysia, and Taiwan, using the data from the Research on Asian Psychotropic Patterns for Antipsychotics (REAP-AP) study. After adjusting the effects of confounding variables, a binary logistic regression model was fitted to identify BPRS items independently associated with disorganized speech. Receiver operating characteristic (ROC) curves were used to identify optimum cut-off scores and their sensitivities and specificities for detecting disorganized speech. After adjusting the effects of confounding variables, the fitted binary logistic regression model indicated that conceptual disorganization (P < 0.0001), uncooperativeness (P = 0.010) and excitement (P = 0.001) were independently associated with disorganized speech. The ROC curve revealed that the conceptual disorganization item could accurately detect disorganized speech in patients with schizophrenia both separately and in combination with uncooperativeness and excitement. The subscale for conceptual disorganization, uncooperativeness and excitement items in the BPRS is a promising psychometric tool for detecting disorganized speech.

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Introduction

Disorganized speech has been regarded as a core symptom in schizophrenia. Its conceptual frame derives from the classical ideas about formal thought disorder in German psychopathology from the late 19th to early 20th century [1-3]. 'Inkorhärenz' (corresponding to incoherence) proposed by Wilhelm Griesinger [4], 'Zerfahrenheit' (corresponding to derailment) by Emil Kraepelin [5] and 'loosening of association' by Eugen Bleuler [6] have provided the classical ideas in terms of defining disorganized speech in the Diagnostic and Statistical Manual of Mental Disorders, 3rd, 4th, and 5th editions (DSM-III, DSM-IV, and DSM-5) [7-9]. Also, disorganized speech has been defined as one domain of the Clinician-Rated Dimensions of Psychosis Symptom Severity in appendices of the DSM-5 [10]. Furthermore, formal thought disorder is inversely associated with global outcomes in patients with schizophrenia [11,12]. Also, a study of subjects with new-onset psychosis has suggested that negative formal thought disorder is a predictor of clinical outcomes such as rehospitalization, whereas positive formal thought disorder has "little prognostic value [13]."

There have been difficulties in precisely conceptualizing disorganized speech and formal thought disorder due to its diverse etiologies [9]. The Scale for the Assessment of Thought, Language and Communication (TLC scale), clinical language rating scale (CLANG) and other measuring tools have been proposed as reliable identification methods, using optimum cut-off levels for disorganized speech and formal thought disorder [1,2]. Moreover, since the Brief Psychiatric Rating Scale (BPRS) was proposed as an assessment tool for disorganized speech, the conceptual disorganization item of the BPRS has been used to evaluate formal thought disorder in patients with schizophrenia [14—16]. The use of conceptual disorganization to detect disorganized speech has been highly controversial. In the

context of the BPRS the ratio of the score on suspiciousness to the sum of the scores on conceptual disorganization and suspiciousness has been defined as the paranoid quotient and this quotient has been proposed as an exploratory tool for differentiating subtypes of schizophrenia. In terms of the paranoid quotient, conceptual disorganization can be considered to correspond to disorganized speech [17]. Conversely, the clinical implications of that item as applied to detecting disorganized speech in patients with psychotic depression have been questioned by Keller et al. [18]. Despite the substantial controversy, to the best of our knowledge, the ability of the BPRS to detect disorganized speech has been rarely studied. Hence, in relation to detecting disorganized speech in patients with schizophrenia, we aimed to (i) assess the psychometric validity of the BPRS and/or its conceptual disorganization item and (ii) establish optimum cut-off points with appropriate sensitivities and specificities, using data from the Research on Asian Psychotropic Patterns for Antipsychotics (REAP-AP) study, which is the largest international collaborative survey in the realm of psychiatry in Asia [19,20].

Materials and methods

Study subjects and procedures

As stated elsewhere [19,20], the aims of the REAP-AP study were (i) to survey psychotropic prescription patterns and their clinical correlates and (ii) to explore ways to improve prescription patterns in patients with schizophrenia in Asian countries/areas. A total of 3744 consecutive patients with schizophrenia were recruited by the 4th REAP-AP study from 71 survey centers in 15 Asian countries/areas, namely Bangladesh, China, Hong Kong, India, Indonesia, Japan, Korea, Malaysia, Myanmar, Pakistan, Singapore, Sri Lanka, Taiwan, Thailand and Viet Nam, during the study

period of March 2016—June 2016. All the study subjects signed informed consent forms prior to participation of the study, and the institutional review boards of Tapei City Hospital, Tapei, Taiwan (receipt number: TCHIRB-10412128-E) and the other hospitals participating in the survey approved the study protocol and informed consent forms. Prior to the start of the study a conference meeting was held to improve the consistency of data collection and diagnosis of schizophrenia between the survey centers. Demographic data, clinical and treatment-related details as per protocol were collected by trained study coordinators supervised by clinical psychiatrists at the survey centers. The predefined questionnaires as per protocol were used to collect the data on the study subjects.

Since both short and long forms of questionnaires were used depending on the available resources of the participating countries/areas, the BRPS was included in the long questionnaire but not in the short one. Hence, in our study, we only used data from subjects who met the following inclusion criteria: (i) diagnosis of schizophrenia, based on DSM-5 [9], by clinical psychiatrists at the survey centers, (ii) medication with antipsychotics and/or other psychotropic drugs, and (iii) availability of the complete 18-item BPRS [21]. The exclusion criteria were: (i) presence of severe physical disease and (ii) inability to read or write. Finally, we included 1494 patients with schizophrenia recruited from the 5 countries/areas: India, Indonesia, Japan, Malaysia and Taiwan.

Defining disorganized speech

In DSM-5 [9], disorganized speech is defined as "switching from one topic to another in terms of an individual's speech," "answers obliquely related or completely unrelated to questions," or "nearly incomprehensible speech, or speech resembling receptive aphasia in its linguistic disorganization" with the need to be "severe enough to impair substantially effective communication." According to its definition of DSM-5 [9], the presence/absence of disorganized speech was evaluated by clinical psychiatrists or research coordinators under the supervision of clinical psychiatrists at each of the survey centers.

Brief Psychiatric Rating Scale (BPRS)

The 18-item BPRS [21] was used to evaluate disorganized speech and other psychiatric symptoms in the subjects. All the BPRS items were scored on a 7-point scale from "not present" to "very severe." Many studies have confirmed its psychometric properties including reliability, validity and sensitivity [22,23]. As mentioned earlier, the conceptual items of the BPRS have been previously used to evaluate disorganized speech or formal thought disorder in patients with schizophrenia [14–17]. Since our subjects were recruited from 5 countries/areas with different common languages, the English version of the BPRS was used by the clinical psychiatrists and study coordinators at the survey centers.

Classification of psychotropic medications

Using the Anatomical Therapeutic Chemical (ATC) classification system [24], we classified psychotropic drugs as:

antipsychotics (N05A), mood stabilizers (anti-epileptics and lithium; N03A and N05AN), antidepressants (N06A), anxiolytics and hypnotics (N05B and N05C) and antiparkinson drugs (N04). High-dose antipsychotic medication was defined as a cumulative dose of \geq 1000 mg/day chlor-promazine equivalent [25] or a ratio of prescribed daily dose (PDD) to defined daily dose (DDD) \geq 1.5 [26].

Statistical analyses

The baseline characteristics of patients with schizophrenia with and without disorganized speech were compared using independent t-tests for continuous variables and χ^2 tests for discrete variables. After adjusting the potential effects of confounding variables, the BPRS items of the two groups were compared using analysis of covariance (ANCOVAs). A binary logistic regression model was fitted to identify the BPRS items independently associated with disorganized speech after adjusting the potential effects of confounding variables. In the model, the group with disorganized speech was the dependent variable, the group without disorganized speech being the reference category. The BPRS items whose scores were significantly different in the 2 groups were defined as covariates. The final model was selected and validated by a goodness-of-fit test.

Exploratory receiver operating characteristic (ROC) curve analyses were conducted to identify the optimal cutoff scores for each of the conceptual disorganization and other potential items of the BPRS that distinguished accurately between schizophrenia patients with and without disorganized speech. As described elsewhere [27,28], this method was developed from signal-detection theory and is frequently used in biological and behavioral studies. To calculate overall predictor performance, we considered the sensitivity and specificity pairs for all possible threshold levels, to determine the optimum cut-off scores associated with the lowest number of false positives and false negatives. To reduce the familywise error rate due to multiple comparisons, statistical significance was set at P < 0.01(two-tailed) for all tests. All statistical calculations were carried out with the statistics software IBM SPSS for Windows, Version 21.0 (Armonk, New York: IBM Corp.).

Results

Baseline characteristics of schizophrenia patients with and without disorganized speech

As shown in Table 1, 357 patients with schizophrenia (24.8%) displayed disorganized speech. Subjects with disorganized speech differed from those without disorganized speech with respect to their distribution between the 5 countries/areas ($\chi^2=37.643$, P<0.0001), and had higher rates of hospitalization ($\chi^2=171.657$, P<0.0001), antipsychotic polypharmacy ($\chi^2=28.147$, P<0.0001), mood stabilizers ($\chi^2=11.781$, P=0.001) and electroconvulsive therapy ($\chi^2=20.808$, P<0.0001), and received higher daily chlorpromazine equivalent dose (t = 6.249, P<0.0001) and imipramine equivalent dose (t = -3.208, P=0.001). Although the differences were not significant, the patients with disorganized speech showed tendencies

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	Total sample	Disorganized speech	Statistical	P-value		
	(n = 1439)	Present (n = 357)	Absent (n = 1082)	coefficient		
Age, mean (SD) years	49.9 (12.5)	39.8 (13.0)	40.0 (12.4)	t = -0.180	0.857	
Male, n (%)	831 (57.7)	206 (57.7)	625 (57.8)	$\chi^2 < 0.0001$	0.984	
Country/area				$\chi^2 = 37.643$	< 0.000	
India, n (%)	400 (27.8)	90 (252)	310 (28.7)			
Indonesia, n (%)	261 (18.1)	100 (28.0)	161 (14.9)			
Japan, n (%)	98 (6.8)	31 (8.7)	67 (6.2)			
Malaysia, n (%)	299 (20.8)	58 (16.2)	241 (22.3)			
Taiwan, n (%)	381 (26.5)	78 (21.8)	303 (28.0)			
Regional classification ^a	. ,	,	, ,	$\chi^2 = 5.707$	0.058	
Eastern Asia, n (%)	479 (33.3)	109 (30.5)	370 (34.2)	,,		
Southeastern Asia, n (%)	560 (38.9)	158 (44.3)	402 (37.2)			
Southern Asia, n (%)	400 (27.8)	90 (25.2)	310 (28.7)			
Inpatient, n (%)	665 (46.2)	272 (76.2)	393 (36.3)	$\chi^2 = 171.657$	< 0.000	
Duration of illness	` ,	` '	,	$\chi^2 = 14.371$	0.026	
< 3 month, n (%)	52 (3.6)	18 (5.0)	34 (3.1)	, c		
3–6 months, n (%)	38 (2.6)	14 (3.9)	24 (2.2)			
6 months – 1 year, n (%)	46 (3.2)	10 (2.8)	24 (3.3)			
1-5 years, n (%)	274 (19.0)	70 (19.6)	204 (18.9)			
5-10 years, n (%)	240 (16.7)	64 (17.9)	176 (16.3)			
10-20 years, n (%)	429 (29.8)	83 (23.2)	346 (32.0)			
>20 years, n (%)	360 (25.0)	98 (27.5)	346 (32.0)			
Duration of untreated psychosis	` ,	,	,	$\chi^2 = 4.620$	0.202	
< 3 month, n (%)	525 (36.5)	121 (33.9)	404 (37.3)	, c		
3 months – 1 year, n (%)	492 (34.2)	121 (33.9)	371 (34.3)			
1-5 year, n (%)	270 (18.8)	67 (18.8)	203 (18.8)			
> 5 years, n (%)	152 (10.6)	48 (13.4)	104 (9.60)			
Antipsychotic polypharmacy, n (%)	536 (37.2)	175 (49.0)	361 (33.4)	$\chi^2 = 28.147$	< 0.000	
High-dose antipsychotic	259 (18.0)	79 (22.1)	180 (16.6)	$\chi^2 = 5.488$	0.019	
medication, n (%)	(),	,	,	χ		
Antiparkinson drugs, n (%)	560 (38.9)	154 (43.1)	406 (37.5)	$\chi^2 = 3.559$	0.059	
Mood stabilizers, n (%)	142 (9.9)	52 (14.6)	90 (8.3)	$\chi^2 = 11.781$	0.001	
Antidepressants, n (%)	129 (9.0)	21 (5.9)	108 (10.0)	$\chi^2 = 5.527$	0.019	
Anxiolytics and hypnotics, n (%)	521 (36.2)	142 (39.8)	379 (35.0)	$\chi^2 = 2.620$	0.106	
Electroconvulsive therapy, n (%)	42 (2.9)	23 (6.4)	19 (1.8)	$\chi^2 = 20.808$	< 0.000	

^a Defined by United Nations classification: Eastern Asia (Japan and Taiwan), Southern Asia (India) and Southeastern Asia (Indonesia and Malaysia).

to differ from those without disorganized speech in terms of duration of illness ($\chi^2=4.620,\,P=0.026$), prescription of high-dose antipsychotics ($\chi^2=5.488,\,P=0.019$) and prescription of antidepressants ($\chi^2=5.527,\,P=0.019$). However, there were no significant differences in age (t = $-0.180,\,P=0.857$), duration of untreated psychosis ($\chi^2=4.620,\,P=0.202$) and use of anxiolytics ($\chi^2=2.620,\,P=0.106$) between the two groups.

Scores on the BPRS items of schizophrenia patients with and without disorganized speech

As shown in Table 2, after adjusting potential effects of inpatient, duration of illness, antipsychotic polypharmacy, high-dose antipsychotic medications, mood stabilizer, antidepressant and electroconvulsive therapy, the subjects with disorganized speech had significantly higher scores than those without disorganized speech for: emotional

withdrawal (F = 22.598, P < 0.0001), conceptual disorganization (F = 230.035, P < 0.0001), tension (F = 30.180, P < 0.0001), mannerism and posturing (F = 93.100, P < 0.0001), grandiosity (F = 26.433, P < 0.0001), hostility (F = 67.093, P < 0.0001), suspiciousness (F = 29.801, P < 0.0001), hallucinatory behaviors (F = 30.329, P < 0.0001), uncooperativeness (F = 116.660, P < 0.0001), unusual thought content (F = 153.811, P < 0.0001), blunted affect (F = 21.390, P < 0.0001) and excitement (F = 120.110, P < 0.0001).

Although the differences were not significant, those with disorganized speech showed tendencies to differ from those without disorganized speech in terms of depressive mood (F = 5.569, P = 0.018), motor retardation (F = 5.596, P = 0.018), and disorientation (F = 6.554, P = 0.011). However, there were no significant differences in the scores for somatic concern (F = 3.037, P = 0.082), anxiety (F = 0.794, P = 0.373), and guilt feelings (F = 0.107, P = 0.743).

Table 2 Scores on the BPRS items of schizophrenia patients with and without disorganized speech.

	Total sample (n = 1439)	Disorganized speech		Statistical	Unadjusted	Adjusted
		Present (n = 357)	Absent (n = 1082)	coefficient	P-value	P-vale ^a
Somatic concern, mean (SD)	1.8 (1.2)	2.0 (1,2)	1.7 (1.1)	t = 3.341	0.001	0.082
Anxiety, mean (SD)	2.1 (1.2)	2.3 (1.3)	2.1 (1.2)	t = 2.252	0.025	0.373
Emotional withdrawal, mean (SD)	2.5 (1.5)	2.8 (1.6)	2.4 (1.4)	t = 5.004	< 0.0001	< 0.0001
Conceptual disorganization, mean (SD)	2.4 (1.5)	3.5 (1.6)	2.0 (1.2)	t = 15.709	< 0.0001	< 0.0001
Guilty feelings, mean (SD)	1.5 (0.9)	1.6 (1.0)	1.4 (0.8)	t = 2.067	0.039	0.743
Tension, mean (SD)	2.0 (1.1)	2.4 (1.3)	1.9 (1.0)	t = 6.575	< 0.0001	< 0.0001
Mannerism and posturing, mean (SD)	1.5 (1.0)	2.0 (1.3)	1.3 (0.7)	t = 9.146	< 0.0001	< 0.0001
Grandiosity, mean (SD)	1.5 (1.1)	1.8 (1.3)	1.4 (0.9)	t = 6.352	< 0.0001	< 0.0001
Depressive mood, mean (SD)	1.8 (1.1)	1.7 (1.1)	1.8 (0.10)	t = -0.645	0.519	0.018
Hostility, mean (SD)	1.9 (1.3)	2.5 (1.5)	1.7 (1.1)	t = 8.809	< 0.0001	< 0.0001
Suspiciousness, mean (SD)	2.4 (1%)	2.9 (1.6)	2.2 (1.4)	t = 6.990	< 0.0001	< 0.0001
Hallucinatory behaviors, mean (SD)	2.6 (1.6)	3.3 (1.7)	2.4 (1.6)	t = 8.086	< 0.0001	< 0.0001
Motor retardation, mean (SD)	1.7 (1.2)	2.0 (1.3)	1.7 (1.1)	t = 3.733	< 0.0001	0.018
Uncooperativeness, mean (SD)	1.9 (1.2)	2.6 (1.5)	1.6 (1.0)	t = 11.353	< 0.0001	< 0.0001
Unusual thought content, mean (SD)	2.5 (1.6)	3.5 (1.7)	2.1 (1.4)	t = 14.413	< 0.0001	< 0.0001
Blunted affect, mean (SD)	2.4 (1.4)	2.7 (1.6)	2.2 (1.4)	t = 5.096	< 0.0001	< 0.0001
Excitement, mean (SD)	1.6 (1.2)	2.3 (1.5)	1.4 (0.9)	t = 10.528	< 0.0001	< 0.0001
Disorientation, mean (SD)	1.4 (0.8)	1.6 (1.0)	1.3 (0.7)	t = 4.515	< 0.0001	0.011

^a Adjusted for the effects of inpatient status, duration of illness, antipsychotic polypharmacy, high-dose antipsychotic medications, mood stabilizer, antidepressant and electroconvulsive therapy.

A binary logistic regression model for identifying BPRS items independently associated with disorganized speech

As shown in Table 3, after adjusting potential effects of the confounding variables mentioned earlier, a binary logistic regression model was fitted to identify the BPRS items independently associated with disorganized speech. Scores for emotional withdrawal, conceptual disorganization. tension, mannerism and posturing, grandiosity, hostility, suspiciousness, hallucinatory behaviors, uncooperativeness, unusual thought content, blunted affect and excitement items were defined as the initial covariates. Forward selection was conducted to avoid multicollinearity, and the Hosmer-Lemeshow goodness-of-fit test ($\chi^2 = 18.898$, df = 8, P = 0.067) was used to validate the binary logistic model. The final model explained 37.0% (Nagelkerke R^2) of the variability of disorganized speech and showed that conceptual disorganization (adjusted odds ratio [aOR] = 1.641, P < 0.0001), uncooperativeness (aOR = 1.175, P = 0.010) and excitement (aOR = 1.247, P = 0.001) were independently associated with disorganized speech.

Receiver operating characteristic (ROC) curve analysis for detecting disorganized speech

In a ROC curve analysis (Fig. 1), the scores on the conceptual disorganization item were found to accurately distinguish between the subjects with and without disorganized speech (area under the curve [AUC] = 0.756, P < 0.0001). Using an optimal cut-off score of 2, the sensitivity and specificity of the conceptual disorganization item were 71.4% and 69.1%, respectively. Also, the summed scores on conceptual disorganization, uncooperativeness and excitement were found to accurately distinguish between the subjects with and without disorganized speech (AUC = 0.775, P < 0.0001), and, using the optimal cut-off score of 5, its sensitivity and specificity were 72.0% and 68.3%, respectively.

Discussion

In summary, after adjusting the effects of inpatient status, duration of illness, uses of antipsychotic polypharmacy, high-dose antipsychotic medications, adjunctive mood

Table 3 Binary logistic model for identifying the BPRS items independently associated with disorganized speech.						
	В	Standard	Wald	Adjusted <i>P</i> -value ^a	Adjusted odds ratio ^a	95% Confidence
		error		P-value	ratio	ıntervat
Conceptual disorganization	0.495	0.056	79.233	< 0.0001	1.641	1.471-1.830
Uncooperativeness	0.161	0.064	6.355	0.010	1.175	1.036-1.331
Excitement	0.221	0.065	11.507	0.001	1.247	1.098-1.417

^a Adjusted for the effects of inpatient status, duration of illness, antipsychotic polypharmacy, high-dose antipsychotic medications, mood stabilizer, antidepressant and electroconvulsive therapy.

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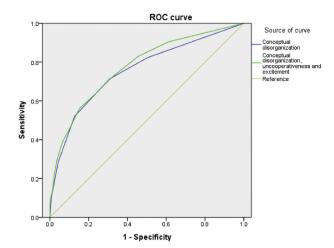


Figure 1. ROC curve analyses for detecting disorganized speech in schizophrenia subjects. ROC, receiver operating characteristics.

stabilizers, adjunctive antidepressants and electroconvulsive therapy, our binary logistic model showed that the conceptual disorganization, uncooperativeness, and excitement items (BPRS) were independently associated with disorganized speech in patients with schizophrenia. Moreover, ROC curve analyses showed that not only the scores on conceptual disorganization alone but also the summed scores on conceptual disorganization, uncooperativeness and excitement, with their defined optimum cutoff values, distinguished accurately between patients with schizophrenia with and without disorganized speech.

As mentioned earlier, the value of the conceptual disorganization item for defining disorganized speech has been questioned, since it involves only a single item [18]. However, conceptual disorganization has been used to identify disorganized speech or formal thought disorder in previous studies [14–17]. Hence, our findings have the virtue of identifying the cut-off value of 2, and its associated sensitivity of 71.4% and specificity of 69.1%, for the conceptual disorganization score as applied to identifying disorganized speech or formal thought disorder.

A previous study suggested that the excitement item corresponded to the mania factor based on a factor analysis of the expanded Brief Psychiatric Rating Scale in 100 inpatients with bipolar disorder [29]. In addition, the excitement item has been one component of the Brief Bipolar Disorder Symptom Scale, which was derived from the 24-item Brief Psychiatric Rating Scale [30]. Using a sample of 207 acute inpatients, the mean score on the excitement item was significantly greater in patients with bipolar disorder than in those with schizophrenia or major depressive disorder. Using the same study sample, the mean score on the uncooperativeness items was significantly greater in patients with bipolar disorder and schizophrenia than in those with major depressive disorder [31]. The uncooperativeness and grandiosity items were considered bipolarity factors based on a factor analysis of the 18-item BPRS in 258 patients with major depressive disorder [32]. Thus, we may speculate that the excitement item reflects the mania factor among the BPRS items, and that the uncooperativeness item is associated with the mania factor.

Moreover, despite inconsistent findings, there appears to be a close relationship between formal thought disorder and severe mood disorders, and formal thought disorder has been conceptualized as a distinct disease entity providing an operational diagnosis of bipolar disorder [33,34]. In addition, disorganized speech or formal thought disorder has been viewed as an associative array variable for symptomatological or neurobiological overlap between schizophrenia and severe mood disorders [18,35]. The subscale for the conceptual disorganization, uncooperativeness and excitement items (BPRS) that we have identified in the present work may partly reflect a relationship between formal thought disorder and bipolar disorder, and, as we have shown, accurately detects disorganized speech with a cut-off score of 5, sensitivity of 72.0% and specificity of 68.3%. A score of five or more on the subscale may reflect the presence of at least 2 of the 3 symptom items.

This study has several limitations. First, since the REAP-AP study was not designed in a strict epidemiological manner, our findings cannot be widely generalized and extrapolated. Second, inter-rater reliabilities in terms of the BPRS and disorganized speech were not evaluated, although a consensus meeting was held before initiation of the REAP-AP study. Third, disorganized speech was evaluated in terms of simple present or absent rather than positive or negative formal thought disorder. Despite these limitations, our study has the virtue of proposing that the conceptual disorganization item accurately detects disorganized speech in patients with schizophrenia both on its own and in combination with the uncooperativeness and excitement items, and of indicating the optimum cut-off scores and associated sensitivities and specificities. Moreover, our findings indicate that the subscale for conceptual disorganization, uncooperativeness and excitement can be interpreted in terms of a relationship between formal thought disorder and bipolar disorder, and deconstruction of the Kraepelinian dualism.

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