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ORIGINAL ARTICLE

Schneider's first-rank symptoms as predictors of remission in antipsychotic-naive first-episode psychosis

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Objective: German psychiatrist Kurt Schneider proposed the concept of first-rank symptoms (FRS) of schizophrenia in 1959. However, their relevance for diagnosis and prediction of treatment response are still unclear. Most studies have investigated FRS in chronic or medicated patients. The present study sought to evaluate whether FRS predict remission, response, or improvement in functionality in antipsychotic-naive first-episode psychosis.
Methods: Follow-up study of 100 patients at first episode of psychosis (FEP), with no previous treatment, assessed at baseline and after 2 months of treatment. The participants were evaluated with the standardized Positive and Negative Syndrome Scale (PANSS) and Global Assessment of Functioning (GAF) and for presence of FRS.
Results: Logistic regression analysis showed that, in this sample, up to three individual FRS predicted remission: voices arguing, voices commenting on one's actions, and thought broadcasting.
Conclusion: Specific FRS may predict remission after treatment in FEP patients. This finding could give new importance to Kurt Schneider's classic work by contributing to future updates of diagnostic protocols and improving estimation of prognosis.

Keywords: Schizophrenia; psychosis; antipsychotics; remission induction; treatment outcome

Introduction

The diagnosis and treatment of schizophrenia still challenge most psychiatrists.[1] Clinical presentation and outcome are widely heterogeneous among patients; insidious onset, early occurrence of negative symptoms, and loss of functionality are associated with poor prognosis.[2]

A clinical tool capable of predicting prognosis in schizophrenia would allow early, personalized treatment. Through the years, there have been several attempts to create such an instrument. One of the most important authors who endeavored to establish clear criteria for the diagnosis of schizophrenia was Kurt Schneider,[3] who, in 1959, described the concept of first-rank symptoms (FRS). According to Schneider, these paranoid symptoms (both hallucinatory and delusional) are particularly prevalent in severe psychotic disorders and hold great importance for the diagnosis of schizophrenia.[3] Although other preeminent authors, such as de Clerambault,[4] described these symptoms independently, only Schneider proposed that they might hold prognostic value. Many studies[5-14] have sought to assess the real utility of FRS as markers for schizophrenia, all of them with inconclusive results. Both the latest version of Schneider's seminal *Clinical Psychopathology*,[3] and Mellor in 1970[4] described FRS as in Box 1 below; these are the definitions employed in the present study.

The primary objective of this study is to assess the actual capacity of FRS (both the sum of all FRS as a scale and the occurrence of at least one such symptom) to predict remission from first-episode psychosis (FEP) at 2-month follow-up. As secondary objective, we aim to assess the power of FRS to predict treatment response and improvement in function.

Methods

Participants

This cohort study enrolled 100 drug-naive patients in FEP to undergo reevaluation after 2 months of risperidone therapy. The exclusion criteria were drug-induced

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Box 1 Kurt Schneider's first-rank symptoms

Delusional perception	Normal perception has a private, illogical meaning.
Thought broadcasting	The patient's thoughts escape into the outside world and are experienced by others.
Thought withdrawal	The patient's thoughts are being removed by an external force.
Somatic passivity	Experience of bodily sensations (including actions, thoughts, or emotions) imposed by external agency.
Voices commenting on one's actions	Voices describe the patient's activities as they occur.
Audible thoughts	Voices speaking the patient's thoughts aloud.
Voices arguing	The patient hears two or more voices, talking to each other, in his or her head.

psychosis, drug dependence syndrome, severe clinical disease, and/or inability to understand the informed consent form (including inability to name a legally responsible individual capable of understanding the form).

All patients were administered a multidisciplinary protocol for assessment of clinical, neuropsychological, genetic, and neuroimaging data, as part of a broader study approved by the ethics committee of Universidade Federal de São Paulo (UNIFESP) (protocol 0603/10). Participants were recruited from multiple centers in the state of São Paulo, Brazil.

Clinical assessment

Demographic information was collected from interviews with participants or caregivers. Diagnosis was assessed using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I).[15] Patients were administered the Positive and Negative Syndrome Scale (PANSS),[16] a structured interview for assessment of preexisting and current use of drugs (adapted from the ASI[17] by the authors), and the Global Assessment of Functioning (GAF) Scale.[18] FRS were evaluated by an additional investigator-completed checklist consisting of seven items, scored dichotomously as present or absent: 1) audible thoughts, 2) voices arguing, 3) voices commenting on one's actions, 4) somatic passivity, 5) thought withdrawal, 6) thought broadcasting, and 7) delusional perception. Trained raters assessed all patients at regular meetings.

Antipsychotic treatment during follow-up

All patients were initially treated with risperidone, at doses deemed necessary by their attending physician. After 2 months of regular treatment, patients were reassessed by the same rater, using the same standardized scales. Response to treatment was defined by the percent reduction in PANSS from baseline at 2-month follow-up. Reductions in PANSS were adjusted for a baseline score of 30, according to Leucht.[19]

Remission, response, and functionality criteria

Remission was defined as a severity of mild or less for the following selected PANSS items (score of 3 on a scale of 1-7): delusions (P1), conceptual disorganization (P2), hallucinatory behavior (P3), unusual thought content (G9), mannerism and posturing (G5), blunted affect (N1), passive/apathetic social withdrawal (N4), and lack of spontaneity and flow of conversation (N6). These are the specific items of the remission criteria developed by the Remission in Schizophrenia Working Group (RSWG).[20] The 6-month criterion was not considered in this study, because patients were reassessed after 2 months of therapy.

Response to treatment was considered positive when the subject presented at least a 50% reduction in PANSS score from baseline at 2-month follow-up, while gains in functionality were evaluated by percent improvement in GAF score from baseline at 2-month follow-up.

Outcomes

For the primary outcome, a logistic regression was performed with the seven FRS items, first as independent variables and then as a group, always with remission as the dependent variable. For secondary outcomes, we ran linear regressions: for response analysis, FRS baseline items were the independent variables and percent reduction in PANSS scores after treatment was the dependent variable; when analyzing change in functionality, percent improvement in GAF from baseline was the dependent variable, while FRS baseline items were the independent ones.

Age and gender were the initial control variables; when significant results were found, patient history of any substance abuse (yes or no) and duration of untreated psychosis (DUP) in days were added as control variables as well.

Statistical analysis was conducted in SPSS version 25.[21] P-value of 0.05 was considered statistically significant.

Results

The demographic profile of the sample and main results are shown in Table 1.

Respecting the exclusion criteria, 20% of the sample had some history of substance abuse. To make evaluation of diagnosis more objective, we used a categorical approach: 49% of the sample received a diagnosis of schizophrenia, 31% had schizophrenia spectrum disorders, and 20% had mood disorders. The mean (SD) dose of risperidone was 3.39 (1.34) mg per day; dose did not influence response or remission. The mean (SD) PANSS score was 77.29 (25.86) at baseline and 50.52 (28.28) after 2 months of therapy, which represents a 34.6% reduction. The prevalence of FRS in the overall sample is shown in Table 2.

On average, each subject had 3.01 (SD ±2.23) FRS. Sixteen participants did not have any FRS.

Primary outcome

Logistic regression with all diagnosis revealed that three FRS, when absent and considered individually, were capable of predicting remission (Table 3): voices arguing, voices commenting on one's actions, and thought broadcasting. Logistic regression with FRS by diagnostic group showed statistically significant findings as well, but only for voices commenting on one's actions and thought broadcasting (Table 4). When DUP and substance abuse history were added as control variables, these associations did not remain significant.

Table 1 Demographic and clinical results (n=100)

	n (%)	Mean (SD)
Gender		
Female	41 (41)	-
Male	59 (59)	-
Age (years)	-	26.31 (7.17)
Diagnosis		
Schizophrenia	49 (49)	-
Schizophrenia spectrum	31 (31)	-
Mood disorder	20 (20)	-
DUP (days)	-	172.92 (314.07)
Risperidone (mg/day)	-	3.39 (1.33)
PANSS, baseline	-	77.29 (25.86)
PANSS, 2 months	-	50.52 (28.28)

DUP = duration of untreated psychosis; PANSS = Positive and Negative Syndrome Scale; SD = standard deviation.

Table 2 Frequency of first-rank symptoms in first-episode psychosis (n=100)

First-rank symptom	n (%)
Delusional perception	77 (77)
Voices commenting on one's actions	48 (48)
Voices arguing	37 (37)
Audible thoughts	36 (36)
Thought withdrawal	41 (41)
Thought broadcasting	29 (29)
Somatic passivity	33 (33)

Regression applied to specific diagnosis groups (schizophrenia alone vs. combined with its spectrum vs. mood disorders alone) failed to present any significant results. Neither complete absence of any FRS nor the number of FRS present (scale 0 to 7), both as independent variables, was able to predict remission.

Secondary outcomes

In the linear regression considering all diagnoses, no single FRS was able to predict response (Table 5). Regression with percent improvement in GAF as the dependent variable excluded single FRS in every scenario. Both regarding response and GAF, the analysis was conducted for FRS individually and within-group FRS. Additional evaluations with subjects segregated by diagnosis also failed to reveal any statistically significant findings. Again, neither the absence of FRS nor the number of FRS present, both as independent variable, was able to predict response nor improvement in functionality. Finally, factor analysis applied to the seven Schneiderian FRS failed to demonstrate any categorical characteristics.

Discussion

Kurt Schneider[3] described FRS as experiences where there is loss of the boundaries of the self. Those include passivity, pseudo-hallucinations, and primary interpretation delusion. This description was used in the DSM-III[22] under the vague designation of bizarre delusions, in criteria 1 to 6 for schizophrenia. The importance of FRS for this diagnosis remained in DSM-IV,[23] as long as criteria B and C were present. The current classification, however, does not consider bizarre delusions as capital criteria for the diagnosis of schizophrenia. The DSM-5 gives much less credit to FRS importance, following the same path.[24] Considering the results of the present study, forthcoming diagnosis guides might give renewed importance to FRS.

Since Schneider's original publication, a number of studies have tried to validate the diagnostic significance of the FRS; however, few clearly established the definition of each symptom. Furthermore, in clinical psychiatry, different practitioners consider and evaluate FRS using their personal impressions. As this lack of objective criteria may result in biased results,[15] studies exploring FRS should establish their definitions clearly.

Table 3 Logistic regression analysis of FRS and specific diagnosis (n=100)

Variable	B	SE	Wald	df	p-value
Audible thoughts	-0.182	0.437	0.174	1	0.677
Voices arguing	-0.973	0.478	4.143	1	0.042
Voices commenting	-0.931	0.437	4.445	1	0.035
Somatic passivity	-0.445	0.441	1.017	1	0.313
Thought withdrawal	-0.433	0.427	1.030	1	0.310
Thought broadcasting	-0.947	0.482	3.867	1	0.049
Delusional perception	0.450	0.492	0.008	1	0.927

df = degrees of freedom; SE = standard error.
First-rank symptoms = independent variables (individual analysis); remission = dependent variable; age and gender = control variables.

Table 4 Logistic regression analysis of FRS and group diagnosis (n = 100)

Variable	B	SE	Wald	df	p-value
Audible thoughts	1.038	0.636	2.662	1	0.103
Voices arguing	-0.627	0.629	0.993	1	0.319
Voices commenting	-1.278	0.641	3.972	1	0.046
Somatic passivity	-0.183	0.553	0.109	1	0.741
Thought withdrawal	0.100	0.563	0.031	1	0.859
Thought broadcasting	-1.301	0.651	3.990	1	0.046
Delusional perception	1.040	0.613	2.878	1	0.090

df = degrees of freedom; SE = standard error.
First-rank symptoms = independent variables (individual analysis); remission = dependent variable; age and gender = control variables.

Table 5 Logistic regression analysis of FRS and response to treatment (n = 100)

Variable	B	SE	Wald	df	p-value
Audible thoughts	-0.393	0.461	0.728	1	0.394
Voices arguing	-0.304	0.469	0.420	1	0.517
Voices commenting	-0.038	0.435	0.008	1	0.930
Somatic passivity	-0.537	0.470	1.309	1	0.243
Thought withdrawal	-0.008	0.439	0.000	1	0,986
Thought broadcasting	-0.274	0.476	0.331	1	0.565
Delusional perception	0.675	0.550	1.506	1	0.220

df = degrees of freedom; SE = standard error.
First-rank symptoms = independent variables (individual analysis); remission = dependent variable; age and gender = control variables.

In our sample, three FRS showed significant discriminative power to predict remission: hearing voices arguing, hearing voices commenting on one's actions, and thought broadcasting. This finding suggests that, when detected, these symptoms may somehow be associated with worse outcomes. The most common FRS in our study, delusional perception, was not the most frequent in all relevant publications that explored the topic. Although Bland in 1980 found the same result,[13] Lewine et al. (1982) mentioned thought broadcast as the most common,[25] while Ndetei et al. (1983) found audible thoughts,[26] and Chandrasena (1987), voices arguing.[27] Interestingly, Gureje & Bamgboye (1987) found delusional perception to be the least common FRS, and passivity the most frequent.[28] These discrepancies are probably related to differences in sample; in fact, the study that also found delusional perception to be the most common FRS used a sample of patients with schizophrenia during first hospitalization, a somewhat similar profile to that of our FEP subjects. Moreover, as mentioned before, different studies apply different definitions of each FRS, which hinders comparisons.

As the importance of FRS for diagnosis and prognosis has been under discussion for decades, with consistent argumentation on both sides,[22,23,29] the results of this study provide additional evidence supporting FRS as an aspect to be considered. Clinical observation suggests that FRS can be found in a wide range of mental disorders where psychosis is present; this empirical view is supported by our heterogeneous sample, which included patients with schizophrenia, polymorphic psychosis, psychotic bipolar disorder, schizoaffective disorder, and even some mood disorders.[30,31] However, our secondary analysis failed to find any association of FRS with treatment response or functionality outcomes.

Schneider regarded the loss of the boundaries of the self as the core symptom of schizophrenia. However, in our sample, symptoms related to self-disorder were present in less than 50% of participants, which is in line with other studies reporting the low sensitivity of FRS.[29,31,32] In addition, we observed that only 11% of subjects presented all seven FRS, while 20% had two, 14.8% had three, 10% had four, 12% had five, 5% had six, and 16% did not have any FRS. This suggests that FRS can be widely distributed among patients and, as our factor analysis revealed, cannot be clearly divided into two or more dimensions.

It is important to note that DUP and positive history of substance abuse, when used as control variables, nullified the statistically significant results of initial logistic regression. This finding reinforces the clinical and research impressions that both variables influence remission prognosis in psychosis.

A number of limitations should be acknowledged. Our sample was relativity small and consisted only of first-episode patients, although this homogeneity could also be considered a strength of the study. Most patients originally studied by Kurt Schneider were chronically institutionalized individuals. In addition, the FRS were evaluated by their presence or absence, instead of measuring their intensity. The 6-months of symptom stability proposed by Andreasen et al. as a remission criterion[20] could not be assessed, because patients were evaluated only at 2-month follow-up. Finally, we included other psychotic disorders rather than selecting only patients with schizophrenia, although this could also be considered a strength.

In conclusion, our results suggests, even considering the aforementioned limitations and the lack of positive findings regarding treatment response and functionality,

specific FRS have some capacity to predict remission in a heterogeneous group of patients in first-episode psychosis. These findings may indicate a possible path for future research into basic psychopathology, regarding both diagnosis and prognosis. Finally, forthcoming studies which use the FRS should define each symptom clearly so as to minimize subjective bias and help other publications structure their own criteria.

Disclosure

The authors report no conflicts of interest.

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