ORIGINAL ARTICLE

Psychiatry and Clinical Psychopharmacology 2020;30(3):307-312
DOI: 10.5455/PCP.20200302022126

Reliability and Diagnostic Validity of A Novel Visual Disturbance Subjective Experience Scale in Chinese Patients with Schizophrenia

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Abstract

Background: Visual abnormalities are common among patients with schizophrenia and have been associated with retinal thickness impairment (RTI). A reliable tool for assessing altered visual experiences in this population is not yet available. The objective of this work was to establish a novel scale based on visual perception disturbance (VPD) items extracted from the Bonn Scale for the Assessment of Basic Symptoms (BSABS) and to examine the scale's reliability and validity in Chinese patients with schizophrenia.

Methods: A total of 100 first-diagnosed, non-medicated patients with schizophrenia (FUSCH) and 100 healthy controls (HCs) were enrolled. The reliability of our BSABS-based visual perception subjective experience scale (VPSES), called the BSABS-VPSES, was assessed by calculating the inter-rater correlational coefficient for five psychiatrists' patient evaluations. The discriminative validity of the BSABS-VPSES was determined by assessing the relationship between VPD symptom scores and RTI severity as determined by optical coherence tomography (OCT) performed by two ophthalmologists.

Results: The BSABS-VPSES provided reliable data (Cronbach's $\alpha = 0.90$), and BSABS-VPSES scores correlated with RTI magnitude ($r = 0.88$, 0.84, and 0.65, for mild-, moderate-, and severe-grade RTI groups, respectively; all $p < 0.05$), affirming the scale's validity. Using the BSABS-VPSES, we found that 67% of FUSCH patients had VPD symptoms and that 52% of FUSCH patients had both VPD symptoms and an RTI.

Conclusions: The BSABS-VPSES scale provides reliable and valid results in Chinese FUSCH patients. This scale can be used to assess VPD symptom severity in people with schizophrenia and may contribute to future personalized treatment plans.

ARTICLE HISTORY

Received: Mar 02, 2020
Accepted: May 22, 2020

KEYWORDS: schizophrenia, visual distortion, BSABS-visual perception scale, reliability, validity

INTRODUCTION

Visual perception disturbances (VPDs) are prevalent among patients with schizophrenia. VPDs occur in multiple stages of the disorder, including the prodromal stage, first psychotic episode, and later in disease progression. Individuals also experience vPDs at ultra-high risk of developing schizophrenia [1-5]. About one-third of patients with schizophrenia report experiencing visual hallucinations [6], and almost two-thirds experience VPD symptoms [2, 7, 8]. However, in general, VPD symptoms are not assessed by psychiatrists with the same vigilance as other symptoms, such as auditory hallucinations and cognitive impairments. Likewise, VPD symptoms are rarely the focus of schizophrenia clinical studies.

Interestingly, the onset of new visual symptoms and retinal abnormalities, indicating possible pathogenic processes in the eye, may reflect related changes in the brain. Therefore, assessments of the eye could provide useful clinical information about potential diseases of the brain [9-15]. Notably, retinal thickness impairment (RTI) severity, revealed by optical coherence tomography (OCT), has been

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To cite this article: Huang J, Song X , Xu Y, Wang L, Li Y, Tian H, Zhang Y, Li G, Zhou C, Zhuo C, Yu H. Reliability and Diagnostic Validity of A Novel Visual Disturbance Subjective Experience Scale in Chinese Patients with Schizophrenia. Psychiatry and Clinical Psychopharmacology 2020;30(3):307-312, DOI: 10.5455/PCP.20200302022126

reported to correlate with Positive and Negative Symptoms Scales (PANSS) scores in patients with schizophrenia [16]. However, few studies exploring the relationships between structural alterations of the retina and visual symptoms have been conducted.

For the last three decades, VPDs have been considered symptoms of schizophrenia [17-22]. The Bonn Scale for the Assessment of Basic Symptoms (BSABS) [23] includes items that assess 18 VPD categories: blurred vision; transitory blindness; partial seeing; visual hypersensitivity; photopsia; porropsia; micropsia; macropsia; metamorphopsia; prosometamorphopsia; mirror phenomena; metachromopsia; a pseudo movement of objects; double, oblique, slanting, or reverse vision; disturbed distance estimation; disintegration of spatial grounding of objects; dysmegalopsia; and visual persistence [23]. However, the BSABS is not applied as frequently as other schizophrenia symptom scales, such as the PANSS [24]. Because VPDs in patients with schizophrenia occur often and can have significant impacts on their lives, there remains an important unmet need for a tool that can assess subjective VPD symptoms in patients with schizophrenia-like the way the Psychotic Symptom Rating Scale [25] is used to assess auditory hallucination symptom severity.

The aims of the present study were first to establish a specific tool for assessing VPD symptoms in patients with schizophrenia, and secondly to examine the tool's utility in analyzing the relationship between VPDs and RTI. Additionally, we assessed the reliability and validity of a BSABS-based visual perception subjective experience scale (VPSES) and the relationship between VPSES scores and RTI severity in an adult Chinese population.

METHODS

Item Compilation

We extracted VPD-related items from the BSABS to establish an 18-item scale for assessing the subjective experience of VPD symptoms. Each item was scored as present (2 points), doubtful (1 point), or absent (0 points). We defined the resultant scale as the BSABS-VDSES. The total score of all BSABS-VDSES items was used as an index of VPD symptom severity [26].

Participants

Patients with schizophrenia were recruited from the Tianjin Mental Health Center, Tianjin Anning Hospital, Tianjin Ankang Hospital, and Tianjin Kantai Hospital in July 2019. Healthy controls (HCs) were recruited from among the Tianjin Mental Health Center staff. The inclusion criteria for patients were: 18–35 years of age; fulfillment of schizophrenia criteria according to the 4th Edition Diagnostic and Statistical Manual of Mental Disorders; first schizophrenic episode and diagnosis made by a professional at a participating facility; personal awareness of disease symptoms; ability to complete interview fluently; and no use of antipsychotic agents for at least 3 weeks prior to the study. The inclusion criteria for HCs included: 18–35 years of age, no diagnosed psychiatric disorder, and no first-degree relative with a psychotic disorder.

The common exclusion criteria for both groups included: substance abuse; diabetes or glycosylated hemoglobin level outside normal range; ophthalmic disease or concurrent OCT-related condition; concurrent systemic (e.g., respiratory, cardiovascular, endocrine, neurological, liver, or kidney disease) or chronic disease; a history of severe head trauma; current electroconvulsive therapy; high-grade myopia (≥600 diopters); and an intelligence quotient below 80. Participants included in the final analysis had stable psychotic symptoms, high-quality OCT images, and a completed BSABS-VPSES. This study was approved by the human research ethics committees of Wenzhou Seventh Peoples Hospital and the Tianjin Mental Health Center (IRB no. WT-0218). Written informed consent was obtained from all participants.

Reliability

Reliability was assessed by calculating a Spearman-Brown coefficient for five psychiatrists' BSABS-VPSES scores of first episode unmedicated patients with schizophrenia (FUSCHs). Cronbach's α coefficient was used to assess inter-rater internal consistency. We considered the minimum of Cronbach's α for satisfactory reliability to be 0.7 [27].

Validity

The validity of the BSABS-VPSES was assessed by calculating its discriminatory ability among RTI severities diagnosed by ophthalmologists. Each patient's impaired severity in the foveal region was graded on a 1–3 scale, with scores of 1, 2, and 3 representing mildly (≥30 mm), moderately (≥60 mm), and severely (≥90 mm) reduced thickness, respectively, compared to the mean total retinal thickness of HCs. Receiver operating characteristic (ROC) curves [28] were used to calculate BSABS-VPSES score cutoffs for RTI severity grading.

Oct Acquisition and Processing

For each participant, both retinas were scanned by an OCT 4000 system (Zeiss Company, Germany) with a mounted hand-held probe [24]. Each subject was positioned with his or her chin on a chin rest and instructed to focus on an external fixation target. A 5-second volumetric 10-mm × 5-mm scan of the foveal center, delimited by outer segment layer thickening, was captured. Each scan consisted of 500 A-scans for every 50 B-scans, with acceptable scans containing ≥5 consecutive B-scan frames of the foveal center with no movement artifacts. Retinal layers were segmented manually in ImageJ (version 1.49; National Institutes of Health, Bethesda, MD) [29], and this process was performed masked by allocating random numbers to B-scan images before the analysis. Average individual and combined layer thickness measurements were extracted from three macular regions relative to the foveal center (0 mm): 1) the foveal region (−750 to 750 mm); 2) the nasal

parafoveal region (−1500 to −750 mm); and 3) the temporal parafoveal region (750 to 1500 mm).

Statistics

All analyses were performed in SPSS version 23.0 software (SPSS Inc., Chicago, IL), and results were considered significant at $p < 0.05$. ROC curves were subjected to the area under the curve (AUC) analysis. Two-tailed t-tests were performed to detect differences between patients and HCs.

RESULTS

Sociodemographic Characteristics and Vpd and Retina Impairments

Of the 100 FUSCH patients included in the study, 67 reported experiencing VPD symptoms. Age, gender, education, schizophrenia duration, and schizophrenia severity in the 67 FUSCH patients with VPD symptoms and the remaining 33 FUSCH patients without VPD symptoms were similar (Table 2). The mean BSABS-VPSES score of the FUSCH patients with VPD symptoms was 14.2 ± 2.2 (range, 6–29). The five most frequently reported VPD symptoms on the BSABS-VPSES were visual persistence, photopsia, partial seeing, the disintegration of spatial grounding of objects, and micropsia. Thirty-two percent of patients (21 individuals) indicated they experienced all five phenomena, 18% (12 individuals) indicated they experienced four, 25% (17 individuals) indicated they experienced three, and 25% (17 individuals) indicated they experienced two of the five phenomena. The 67 patients with VPDs included 52 who also had an RTI. The mean retinal thickness reduction in the 52 FUSCH patients with RTIs was 72.7 ± 11.2 mm (range, 27–115; Fig. 1A-C), and the mean BSABS-VPSES score of the FUSCH patients with both VPD symptoms and RTI was 20.9 ± 2.5 (range 12–29).

Table 1. Abbreviations of the terms.

Abbreviation	Term
RTI	Retinal thickness impairment
VPD	Visual perception disturbance
BSABS	Bonn Scale for the Assessment of Basic Symptoms
VPSES	Visual perception subjective experience scale
BSABS-VPSES	BSABS-based visual perception subjective experience scale
FUSCH	First-diagnosed, non-medicated patients with schizophrenia
ROC	Receiver operating characteristic

Table 2. Sociodemographic, VPD, and RTI characteristics of FUSCH patients and HCs.

Characteristic	FUSCH N = 100	HC N = 100	*t*	*P*
Age, years	23.0 ± 2.5	23.5 ± 3.0	0.256	0.741
Gender, no. males/females	56/44	56/44	N/A	N/A
Education, years	14.2 ± 3.5	16.0 ± 2.5	3.245	0.018
Illness duration, months	2.5 ± 0.7	-	-	-
PANSS score	80.9 ± 12.5	35.4 ± 3.0	25.89	<0.001
BSABS-VPSES scores				
67 FUSCHs with VPDs vs. 67 matched HCs	14.2 ± 2.2	2.6 ± 1.0	17.18	<0.001
52 FUSCHs with VPDs and total RTI vs. 52 matched HCs	20.9 ± 2.5	1.8 ± 1.0	24.18	<0.001
Top 5 BSABS-VPSES item frequency, N (%)				
Visual persistence	59 (93.6%)	-	-	-
Photopsias	53 (84.1%)	-	-	-
Partial seeing	49 (77.8%)	-	-	-
Disintegration of object spatial grounding	47 (74.6%)	-	-	-
Micropsia	43 (68.2%)	-	-	-
Total retinal thickness, μm (52 patients)				
Temporal parafoveal region	267.0 ± 10.5	310.5 ± 9.0	11.271	<0.001
Foveal region	235.5 ± 16.0	270.9 ± 7.9	23.170	<0.001
Nasal parafoveal region	295.5 ± 12.0	330.1 ± 10.0	13.250	<0.001
Total retinal thickness reduction vs. HC, μm				
Temporal parafoveal region	43.5 ± 10.4	-	-	-
Foveal region	35.4 ± 8.8	-	-	-
Nasal parafoveal region	34.6 ± 11.9	-	-	-

Reliability, Validity, and Roc Curve Analysis

The BSABS-VPSES reliably assessed VPDs in the FUSCH sample (Cronbach's α, 0.903; Spearman-Brown coefficient, 0.863). The coefficients of correlation with scale scores were 0.65, 0.84, and 0.88 for severe (32 patients, rank point 3, Fig. 2A), moderate (9 patients, rank point 2, Fig. 2B), and mild (10 patients, rank point 1, Fig. 2C) RTI-grade groups respectively. The associated cutoff set points for severe (AUC, 0.98), moderate (AUC, 0.90), and mild (AUC, 0.76) VPDs were ≥21, ≥16, and ≥5 (Fig. 3).

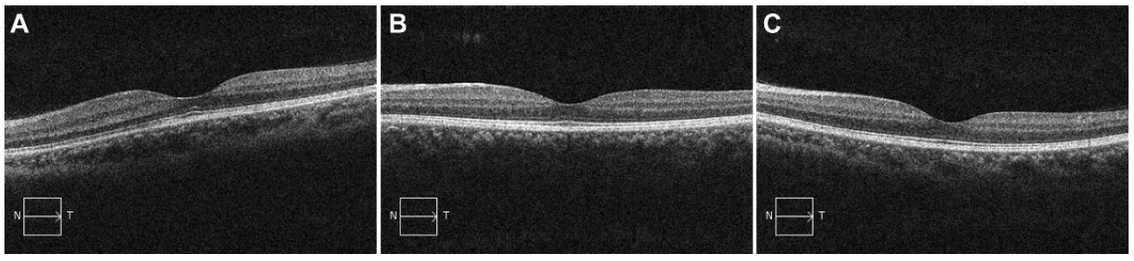

Figure 1. OCT imaging in FUSCH patients and HCs. (A) Representative image of maximum retinal thickness reductions among 52 FUSCH patients with RTIs. (B) Representative image of the minimum thickness among the 52 FUSCH patients with RTIs. (C) Representative image of retinal thickness in a HC subject.

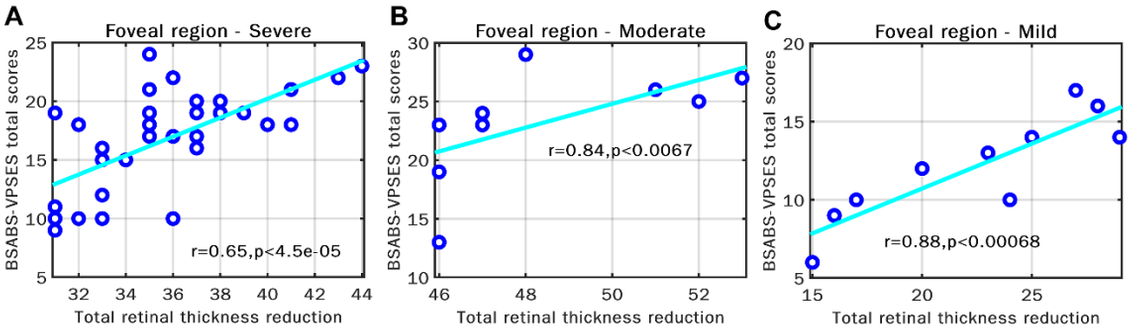

Figure 2. Correlations between BSABS-VPSES scores and RTI. Correlation of scale scores with RTI severity among 32 patients with severe RTI (A), 9 patients with moderate RTI (B), and 10 patients with mild RTI (C).

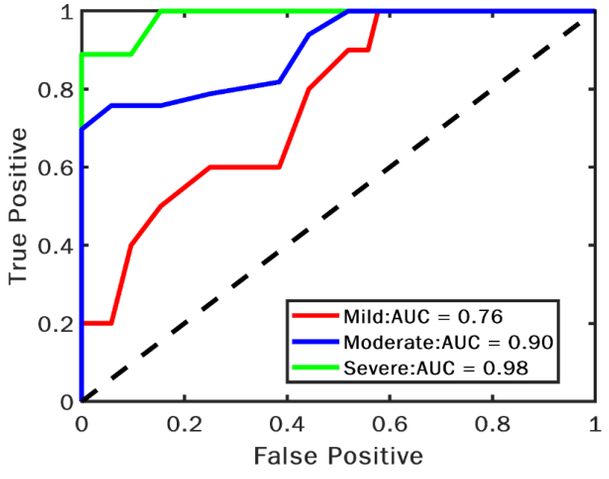

Figure 3. ROC curves of BSABS-VPSES scores (N = 52).

Relationships Among BSABS-VPSES Scores, PANSS Scores, and Total Retinal Thickness

Neither BSABS-VPSES scores nor total retinal thickness was associated with total PANSS scores.

DISCUSSION

This study is the first to our knowledge to investigate the reliability and validity of a BSABS-VPSES instrument and the relationship of VPDs with OCT-determined RTI. Here, we demonstrated that our Chinese-language BSABS-VPSES could be used as a reliable and valid VPD screening tool in Chinese FUSCH patients to discriminate among VPD symptom severities in patients with mild, moderate, or severe RTI. Notably, using the BSABS-VPSES, we detected a 67% prevalence of VPD symptoms in a cohort of 100 FUSCH patients, and 52% of the patients in our sample had total retinal thickness reductions. Remarkably, a majority of FUSCH patients with VPD symptoms had an accompanying RTI, and all 52 patients with an RTI were in the group of FUSCH patients that reported experiencing VPD symptoms. Although the present study sample is not large enough to generalize the prevalence of VPDs and RTIs among all patients with schizophrenia, the data do illustrate the importance of evaluating VPDs and retinal thickness in the

schizophrenia spectrum population at large, especially in the early and prodromal stages of schizophrenia.

Our negative finding with respect to VPD symptoms and RTI not being significantly associated with FUSCH patients' PANSS scores suggests that perhaps the current model of schizophrenia progression and disorder severity should more thoroughly assess specific symptoms of the disease. Although the PANSS may provide a useful index of global schizophrenia severity, other tools may be needed to evaluate specific symptoms properly (e.g., Measurement and Treatment Research to Improve Cognition in Schizophrenia Consensus Cognitive Battery for cognitive impairment [30] and Psychotic Symptom Rating Scale to assess auditory hallucinations [31]). In this context, the BSABS-VPSES could be used to obtain specific information about VPDs.

Finally, because our patient sample consisted of newly diagnosed patients who were not taking any medications, their VPD symptoms and RTIs cannot be attributed to antipsychotic agent effects. Similar to previous research, the documented VPD symptoms reported in the current study likely developed prior to the onset of the patients' first episode of psychosis [1-8, 11-15, 17, 32]. However, further research is necessary to identify the pathogenic course of VPD symptom emergence and RTIs in schizophrenic patients.

Limitations

This study had four notable limitations. First, our sample size was small, and therefore, there may be limited the generalizability of our findings to the broader population of schizophrenic patients. Second, because we conducted a cross-sectional study, the evolution of observed changes within patients was not documented. Longitudinal cohort studies of first-degree relatives of schizophrenic patients and ultra-high-risk populations are needed to identify the pathogeneses of these changes. Third, the clinical applicability of our defined RTI levels based on the magnitude of difference from mean thickness reduction is not known. Fourth, in this pilot study, we did not assess the relationship between VPDs and cognitive impairment because some patients could not complete the MATRICS Consensus Cognitive Battery test due to their acute symptoms. However, our previous studies suggest that VPD symptoms are associated with a worse cognitive impairment in first-episode patients with schizophrenia [33, 34]. Further investigations focused on the relationship between VPDs and cognitive ability are necessary.

CONCLUSION

The current Chinese-language BSABS-VPSES is a reliable and valid tool for assessing VPD symptom severity in Chinese-speaking patients with schizophrenia. Further, the BSABS-VPSES can be used to screen for VPD symptom severity and has the potential to support personalized treatment strategies for patients diagnosed with schizophrenia.

Acknowledgements: We thank Springer Publisher for authorizing our use of the BSABS.

Funding: This work was supported by grants from the National Natural Science Foundation of China (81871052 to C.Z., 81801679 and 81571319 to Y.X.), the Key Projects of the Natural Science Foundation of Tianjin, China (17JCZDJC35700 to C.Z.), the Tianjin Health Bureau Foundation (2014KR02 to C.Z.), the National Key Research and Development Program of China (2016YFC1307004 to Y.X.), the Shanxi Science and Technology Innovation Training Team's Multidisciplinary Team for Cognitive Impairment (201705D131027 to Y.X.), Zhejiang Public Welfare Fund Project (LGF18H090002 to D.J), Tianjin Anding Hospital Outstanding Award rewarding 300000 to C.Z., and the key project of Wenzhou Science and Technology Bureau (ZS2017011 to X.L).

Conflicts of interest: The authors declare that they have no conflicts of interest.

Data availability statement: The datasets generated and analyzed during the present study are available from the corresponding author upon reasonable request.

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