Verification of virtual reality to evaluate deficiencies in cognitive function among patients with schizophrenia in the remission stage: a cross-sectional study

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Abstract

Background: Schizophrenia is associated with widespread cognitive impairments. The MATRICS Consensus Cognitive Battery (MCCB) is most frequently used to assess cognitive function. However, the MCCB test can be time consuming for the clinician. Virtual reality (VR) has emerged as an adjunctive tool to overcome this limitation, which provides a new means of assessing cognitive function.

Methods: The study is to explore the validity and safety of using VR technology to assess cognitive function in Han Chinese patients with schizophrenia. The virtual reality supermarket training system (VRSTS), which simulates real-life supermarkets, was used to assess cognitive function. Thirty-two patients with schizophrenia (SZs) and 25 healthy controls (HCs) received the VRSTS and MCCB assessments. A diagnosis model was created based on the outcomes of VRSTS to classify SZs and HCs by cognitive impairment.

Results: Significant differences in completion time between the SZs and HCs were detected on the VRSTS. SZs spent more time completing tasks than HCs. The outcome of VRSTS was significantly correlated with the MCCB. Moreover, the diagnosis model has a sensitivity of 88.89% and a specificity of 88.89%.

Conclusions: These results provide support for VR technology in the assessment of cognitive impairment in schizophrenia among Han Chinese patients.

Trial registration: China Clinical Trial Registry, ChiVTR1800016121. Registered 13 May 2018, http://www.chictr.org.cn/showproj.aspx?proj=27233

Background

Schizophrenia is a complex, heterogeneous behavioral and cognitive syndrome characterized by positive symptoms, negative symptoms and cognitive impairment [1, 2]. Patients with schizophrenia (SZs) exhibit damaged cognitive function, including reduced attention and memory, and difficulties with executive functioning[3]. The MATRICS Consensus Cognitive Battery (MCCB), which includes 10 different cognitive subtests, is an accepted standard for measuring cognitive change in schizophrenia and has been recommended by the United States Food and Drug Administration (FDA) to assess cognitive impairment in schizophrenia [4, 5]. It demonstrates excellent reliability and practicality. Recently, studies have shown that the MCCB is both applicable for first-episode schizophrenia and chronic schizophrenia [6]and investigations using the MCCB have focused on different cognitive domains in patients with schizophrenia. A study showed that SZs' parents have conspicuous dysfunction in domains of working memory, problem reasoning and visual learning compared with HCs' parents[7]. However, the MCCB requires a well-trained psychiatrist, and it takes approximately one hour to evaluate cognitive function. Moreover, the MCCB sometimes is complicated for some patients with schizophrenia. And some patients may feel bored and exhausted to a point where they cannot complete the assessment. Thus, it is necessary to find an easier and more attractive method to evaluate cognitive function.

Virtual reality (VR) has emerged as a tool to overcome this limitation of the MCCB, providing a new means of assessing cognitive function. VR is a powerful tool that creates interactive computer-generated worlds that produces a sensation of being in life-sized environments[8]. It has already been used in psychiatry. The present evidence suggests that the use of virtual reality among patients with schizophrenia has great advantages. Some studies have focused on assessing cognitive function using VR technology. A virtual reality navigation task (VRNT) study reported that schizophrenia patients were significantly impaired on memory compared with normal subjects[9]. Thirty-nine patients with schizophrenia and 21 healthy comparison subjects experienced a virtual maze, and the SZs exhibited a higher rate of error [10]. Another study showed that patients with schizophrenia were deficient in life activities, medication management skills, and virtual characters recognition [11–13].

Although studies have reported the application of VR in psychiatry, there is limited literature focusing on VR applied to Han Chinese people, a study in Hong Kong showed VR was a sensitive assessment of prospective memory deficits in people with schizophrenia[14], but the efficiency and safety of VR technology are still not clear enough. Furthermore, the association between the VR method and the MCCB to assess the cognitive function of SZs lacks evidence. To date, two studies in the USA have demonstrated that the completion time of the VR task to assess functional capacity was correlated with the MCCB composite scores [15, 16].

The present study explored the performance of VR technology in assessing cognitive function and the reliability of distinguishing HCs and SZs of Han Chinese descent by cognitive function.

Methods

Participants

Thirty-five patients with schizophrenia in the Ningbo Psychiatric Hospital were recruited under the supervision of Dr. Sun Bin and 25 healthy control (HCs) volunteers, were recruited from society under the supervision of Dr. Li Shangda. All the participants entered the virtual reality environment, named virtual reality supermarket training system (VRSTS) and received the MCCB test. The outcomes of VRSTS in two groups were compared and a diagnosis model was created based on the outcomes of VRSTS to classify SZs and HCs using a method named support vector machine (SVM). Another nine SZs and 9 HCs were recruited for verification of the diagnosis model

The inclusion criteria were as follows: between 18 and 55 years old; met the ICD-10 criteria for schizophrenia; on remission stage: Positive and Negative Syndrome Scale item scores of ≤ 3 or SAPS and SANS item scores of ≤ 2 for at least 6 months according to Andreasen's criteria[17]; only received atypical antipsychotics; normal vision and right-handedness. Exclusion criteria: a history of brain trauma, epilepsy and other neurological diseases or serious physical diseases; a diagnosis of a history of mental retardation and a history of substance abuse in the past 30 days (except smoking); received electroconvulsive therapy in the past year; a history of using typical antipsychotics; and pregnant women or those who planned to get pregnant.

Three people with schizophrenia were declined because they cannot understand the instructions of MCCB so that they cannot complete it. All SZs and HCs were matched by gender and age.

After description of the study to the subjects, written informed consent was obtained before the study were conducted and were offered an incentive of ￥50 per session. The study was approved by the ethics committee of the First Affiliated Hospital of the Medical School of Zhejiang University, in accordance with the Helsinki Declaration (No. 2018533) and was already registered in China Clinical Trial Registry and registration number is No.ChiVTR1800016121

Virtual Reality Procedure

VRSTS was designed to assess cognitive function, performing different shopping tasks with different lists. The VRSTS simulates a supermarket with a variety of shopping goods such as drinks, tea sets, kitchen ware, fruits and vegetables. There is also a shopping cart. Unity 5.3.5f1 (https://unity3d.com) and visual studio 2015 (Microsoft) were used to design and create the VRSTS.

The VRSTS included two tasks (task a and task b) and each task consisted of 4 different levels. Before each task started, there was a practice task which was used to bring all participants up to their best level of performance and the outcome of practice task was not included in statistical analysis.

In the practice task, participants become familiar with the procedures as follows:

The participants took the helmet to enter the VRSTS task;

A list of shopping goods appeared in the VR device and participant read the list and close it after remember the list;

The participants caught the good accordingly to put in the shopping cart in the virtual supermarket by using joysticks;

If the participant forgot the content of the list, he could press the button in the joysticks and the list would occur again.

The VR situation is presented as follows. (see Fig. 1)

Task a asked participants to find goods of certain kind and put them into the shopping carts, such as fruits, vegetables and drinks, while task b instructed participants to catch specific goods such as apples, tomatoes and cola. The number of goods ranged from 3 to 6 as the levels of task increased. While the good number increased, the working memory span needed is increased. As a result, different levels represented different difficulty levels.

When the participant caught all the goods of the list to the shopping cart, Computers automatically recorded the correct numbers, errors, and completion time of every task and calculated the accuracy. The accuracy is equal to the correct numbers divided by the number of goods.

If the accuracy was less than 100 percent for the first time, the participant would enter the present level and repeat again. The second accuracy would be statistically analyzed.

Completion time and accuracy are major outcomes of the VR task, used for evaluating cognitive function. The experiment would not limit the completion time of the task so that every participant made the accuracy as high as possible.

Cognitive Assessment

Cognitive functioning was assessed by a trained psychiatrist using the MCCB. The MCCB includes 10 neurophysiologic tests clustered in 7 cognitive domains: speed of processing (SP), attention/vigilance (AV), working memory (WM), verbal learning (VeL), visual learning (ViL), reasoning/problem solving (RPS), and social cognition (SC)[18]. Each domain score was standardized to a T score using the MCCB computer scoring program (Psychological Assessment Resources, Inc., version 2.1.1). Furthermore, the overall composite T score was calculated by averaging the standardized value of each test's T score.

Diagnosis Model And Verification

We constructed a SVM-based cognitive impairment diagnosis model for patients with schizophrenia based on outcomes from 57 subjects (32 SZs and twenty five HCs), and outcomes from 18 additional subjects (9 SZs and nine HCs) were analyzed for verification of diagnostic effect.

Statistical analysis

The data are expressed as the mean ± SD for continuous variables. T-tests were used to compare age, education year of the schizophrenia patients and healthy controls. The T scores of the MCCB and outcomes of VRSTS were analyzed by covariance analysis (covariates: years of education). Correlation of T scores of the MCCB and outcomes of VRSTS was analyzed by Pearson correlation. Statistical analyses were performed using SPSS version 19.0 (IBM, Chicago, IL, USA) for windows. As for verification of diagnostic model, DTREG (https://www.dtreg.com/) was used to test the diagnosis model.

Results

Characteristics of SZs and HCs

We recruited 35 SZs and 25 HCs. Three out of the 35 SZs were withdrawn because they could not finish the MCCB. Thirty-two SZs and 25 HCs completed both the VRSTS and the MCCB. Five SZs and 4 HCs felt dizzy during the VR tasks, but they finished all tasks because it was tolerable. No other uncomfortable feeling was reported both in SZs and HCs. The age of SZs ranged from 24 to 54 (mean age = 42.69, SD = 9.01), while the age of HCs ranged from 28 to 51 (mean age = 38.84 SD = 5.56). Subject demographic and clinical characteristics are provided in Table 1. The duration of disease of SZs ranged from 12 to 384 months (217.87 ± 108.11). SZs received second generation antipsychotics (SGA) for treatment. There were no significant differences in age and gender between groups (all $P > 0.05$). However, patients with

SZ had fewer years of education (10.50 ± 3.14) than the healthy controls (16.28 ± 1.72) ($P < 0.001$) (see Table 1).

Table 1
demographic and clinical characteristics of schizophrenic patients and healthy controls

group	SZ (n = 32)	HC (n = 25)	t/χ^2	*p*
Age (years)	42.69 ± 9.01	38.84 ± 5.56	1.873[a]	0.066
Gender (male/female)	16/16	8/17	1.865[b]	0.172
Education (years)	10.50 ± 3.14	16.28 ± 1.72	-8.270[a]	< 0.001**
Age of first onset (year)	24.63 ± 6.89			
Duration (months)	217.88 ± 108.11			

Cognitive function of patients with schizophrenia and healthy controls

It took each participant approximately one hour to finish the MCCB. Covariance analysis (education) showed that SZs were significantly impaired in SP, AV, VeL, ViL, RPS, and SC compared to HCs (all $P > 0.003$) (see Table 2).

Table 2
MCCB results of schizophrenic patients and healthy controls

Category	SZ(n = 32)	HC(n = 25)	F	*p*
SP	23.38 ± 11.22	52.38 ± 8.58	57.970	< 0.001**
AV	31.53 ± 8.60	51.90 ± 7.90	23.262	< 0.001**
WM	41.94 ± 12.11	51.38 ± 18.72	0.312	0.579
VeL	32.63 ± 6.54	46.67 ± 8.15	9.680	0.003*
ViL	32.69 ± 11.71	54.90 ± 8.62	19.584	< 0.001**
RPS	35.84 ± 5.46	49.90 ± 10.67	23.233	< 0.001**
SC	21.50 ± 7.25	43.50 ± 10.02	26.096	< 0.001**
CC	31.38 ± 5.21	50.14 ± 6.37	49.788	< 0.001**
Note				
*P < 0.05, **P < 0.001				
Abbreviation				
SZ:patients with schizophrenia; HC:health controls; SP:speed of processing; AV:attention-vigilance; WM:working memory; VeL:verbal learning; ViL:visual learning; RPS:reasoning/problem solving; SC:social cognition; CC:Cognitive Composite				

Comparison of performance on the VRSTS between SZs and HCs

The average total competition time of the VRSTS in SZs (1061 ± 427 s) was significantly higher than that in HCs (389 ± 226 s). Specifically, SZs spent significantly more time completing the different levels compared to HCs in Task a level 1, level 2 and level 3 as well as in Task b level 2 and level 3 (Bonferroni correction, all P < 0.0125). However, the accuracy of every task showed no difference between patients with schizophrenia and healthy controls (see Table 3).

Table 3
VRSTS outcome of patients with schizophrenia and healthy controls

Tasks		SZ (n = 32)	HC (n = 25)	*p*
Task a level 1	Time to complete	88.15 ± 55.30	31.75 ± 26.40	< 0.001**
	Accuracy	0.97 ± 0.10	0.96 ± 0.11	0.296
Task a level 2	Time to complete	117.04 ± 81.57	29.91 ± 11.62	0.008*
	Accuracy	0.95 ± 0.12	0.95 ± 0.10	0.481
Task a level 3	Time to complete	139.81 ± 76.51	37.32 ± 17.62	0.006*
	Accuracy	0.93 ± 0.12	0.95 ± 0.09	0.297
Task a level 4	Time to complete	152.13 ± 121.55	44.10 ± 18.21	0.057
	Accuracy	0.93 ± 0.09	0.96 ± 0.09	0.325
Task b level 1	Time to complete	72.36 ± 78.00	43.26 ± 50.90	0.351
	Accuracy	0.94 ± 0.13	0.89 ± 0.19	0.183
Task b level 2	Time to complete	106.97 ± 60.92	44.21 ± 34.56	0.012*
	Accuracy	0.89 ± 0.17	0.86 ± 0.19	0.825
Task b level 3	Time to complete	132.98 ± 71.84	54.69 ± 41.16	0.010*
	Accuracy	0.88 ± 0.15	0.87 ± 0.11	0.950
Task b level 4	Time to complete	179.83 ± 117.25	95.28 ± 131.59	0.211
	Accuracy	0.90 ± 0.13	0.87 ± 0.16	0.132
Note				
Bonferroni correction *P < 0.0125,**P < 0.001				
Abbreviation				
SZ:patients with schizophrenia; HC:health controls				

Correlations of VRSTS outcome with the MCCB

In this analysis, we selected the completion time of every task as well as the average completion time that discriminated between the HCs and schizophrenia patients and correlated them with the MCCB cognitive composite. These correlations are presented in Table 4 and Fig. 2. As shown in the Table 4, the average completion time of task a, task b and many tasks were significantly negatively correlated with the MCCB cognitive composite.(Bonferroni correction, all P < 0.0125) .

Table 4
Pearson correlations between VRSTS and MCCB in patients with schizophrenia

Time to complete	MCCB Cognitive Composite	p
Task a level 1	-0.487	< 0.001**
Task a level 2	-0.604	< 0.001**
Task a level 3	-0.723	< 0.001**
Task a level 4	-0.493	< 0.001**
Average of task a	-0.699	< 0.001**
Task b level 1	-0.310	0.032
Task b level 2	-0.468	0.001*
Task b level 3	-0.382	0.007*
Task b level 4	-0.12	0.415
Average of task b	-0.441	0.002*
Average of all	-0.625	< 0.001**

Using the VRSTS to identify cognitive impairment

Our results showed the cognitive impairment diagnosis model correctly classified SZs and HCs by cognitive impairment. The competition time of VRSTS in classifying cognitive impairment was 92.98% accuracy, 90.63% sensitivity, and 96% specificity. The area under the ROC curve was 0.9325 (see Fig. 3). And verification based on another 18 subjects showed 88.89% accuracy, 88.89% sensitivity, 88.89% specificity, 88.89% positive predictive value and 88.89% negative predictive value.

Discussion

The present study built a virtual situation called VRSTS, simulating a real supermarket to assess cognitive function and explored the validity and safety of VR technology used in the cognitive function of Han Chinese patients with schizophrenia. It took SZs nearly 18 minutes and HCs 6 minutes to complete the VRSTS, which is less than the completion time of the MCCB.

The VRSTS was divided into two tasks and each tasks consisted of 4 levels reflecting increasing working memory span. Task a was used to evaluate the processing of information related to certain categories, while task b was used to assess the processing of specific information. We designed different levels for each task, such as task a level 1 and level 2. The number of goods needed to catch ranged from 3 to 6 as

the levels of task increased. The outcome was measured by two variables: accuracy of performance and the time to complete the task. Because the accuracy of tasks showed no difference between SZs and HCs, it is meaningful to compare the completion time of the two groups.

Our results showed that the completion time of task a and task b of SZs was both significantly higher than that of HCs, which was likely due to the cognitive impairment of patients with schizophrenia. These findings coincide with some studies. Thirty-three SZs and 39 HCs performed ten trials of a virtual radial arm maze task, and the results showed that SZs took more time to finish the task[19]. Other studies also showed that SZs performed worse than HCs in the Virtual Action Planning-Supermarket (VAP-S) study and a Virtual Reality Functional Skills Assessment (VRFAS)[20, 21]. Furthermore, using virtual reality could assess the severity of theory of mind (ToM) impairment of SZs[22].

In addition, there is a significantly negative correlation between the average completion time of each task and the MCCB composite score, which support our hypothesis that the VRSTS outcome may reflect the cognitive impairment of patients with schizophrenia in the remission stage.

Furthermore, our results showed that the VRSTS could distinguish patients with schizophrenia and healthy controls with high accuracy (88.89%), sensitivity (88.89%) and specificity (88.89%). This means that patients with schizophrenia can be separated from healthy people based on their performance in the VRSTS. This result is consistent with a study of a virtual reality prospective memory test demonstrating that the VR test could examine prospective memory deficits in patients with schizophrenia with high sensitivity (92.9%) and specificity (75%) [14].

In summary, the present study demonstrates that virtual reality technology, such as the VRSTS, is a time-saving, efficient and attractive method to evaluate cognitive function. It builds a virtual situation applicable to Han Chinese people to evaluate cognitive function and its outcome has a significant correlation with the MCCB. Moreover, it could precisely distinguish patients with schizophrenia and healthy people by cognitive impairment, indicating that it might be a new adjunctive examination to evaluate cognitive impairment in patients with schizophrenia in the remission stage, especially in those of Han Chinese descent.

This study had some limitations. Firstly, the sample size of participants is small. Secondly, we did not ask participants to assess their preference for MCCB vs VRSTS. So it lacks the feedback of participants after they finish VRSTS; as a result, it is difficult to rate the satisfaction and pleasantness the participants experienced. Moreover, the SCs received different types of second-generation antipsychotics, which may interfere with the patients' cognitive function. Furthermore, the two groups were not education matched, it may influence their performance in virtual supermarket. So we used covariance analysis (covariates: years of education) to compare the outcome between patients with schizophrenia and healthy controls. Last but not the least, VRSTS is an assessment to evaluate cognitive function deficit but as it simulated a daily activity, choosing goods in a supermarket, the task involves many domains of cognitive function such as attention, verbal learning, visual learning and working memory span. As a result it was not closely related with a specific cognitive domain except working memory span.

Conclusions

The VRSTS is a highly sensitive measure of cognitive function associated with the MCCB test. These results provide support for VR technology in the assessment of cognitive function in schizophrenia among Han Chinese patients.

Abbreviations

SZ: patients with schizophrenia

HC: health controls

Declarations

Ethical Approval and Consent to participate

All participants provided informed consent prior to participation in the study.

The study was approved by the ethics committee of the First Affiliated Hospital of the Medical School of Zhejiang University in accordance with the Declaration of Helsinki

Consent for publication

All participants provided consent for publication of their data prior to participation in the study.

Availability of supporting data

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

YX and MH contributed to the study design and concept and wrote the protocol. SL managed the literature searches, statistical analysis and manuscript writing. Bin Sun contributed to data acquisition.

HL and WX helped with the statistical analysis. JJ, FP, JH, JC and YC assisted with the experiment. All authors were involved in the preparation and review of the manuscript and approved the final version to be submitted.

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Figures

Figure 1

Screenshots showing different views within the virtual reality supermarket. The shopping cart (upper) and the goods (lower).

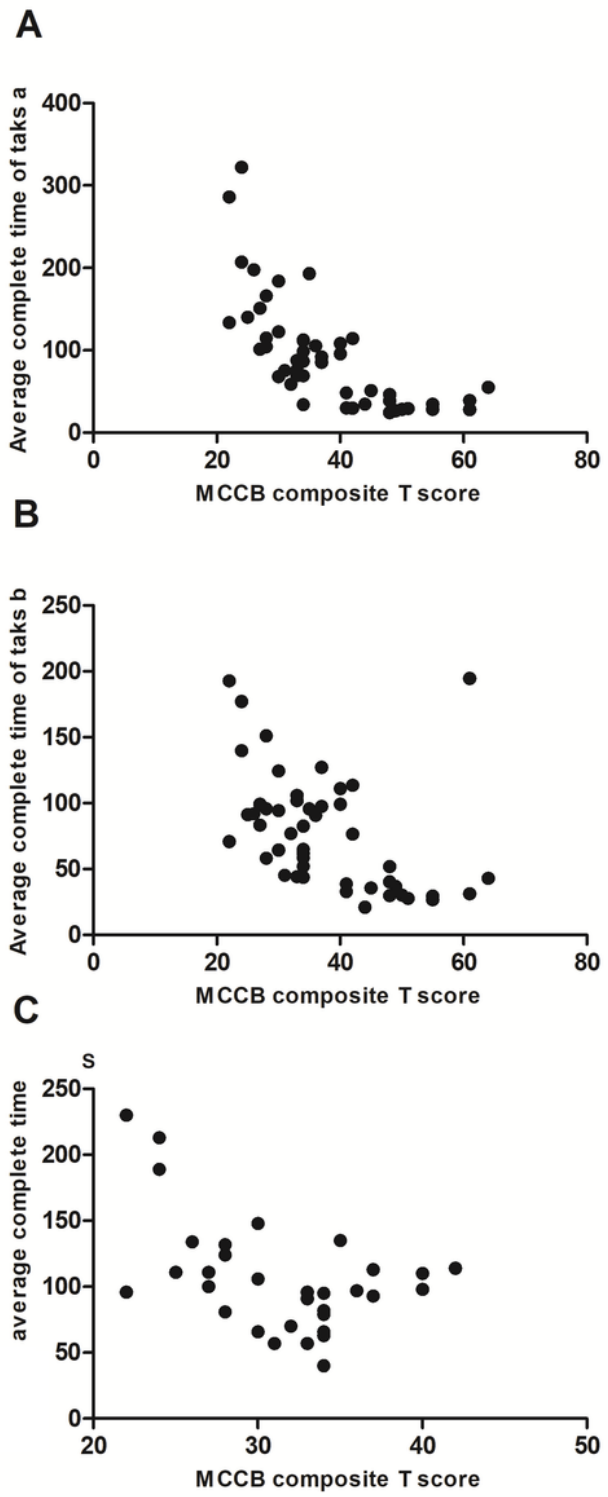

Figure 2

Scatter plots showing the correlation between the complete time of the VRSTS and the MCCB T scores. Completion time of Task a and MCCB T scores (A), completion time of Task b and MCCB T scores (B) average completion time of VRSTS and MCCB T scores (C).

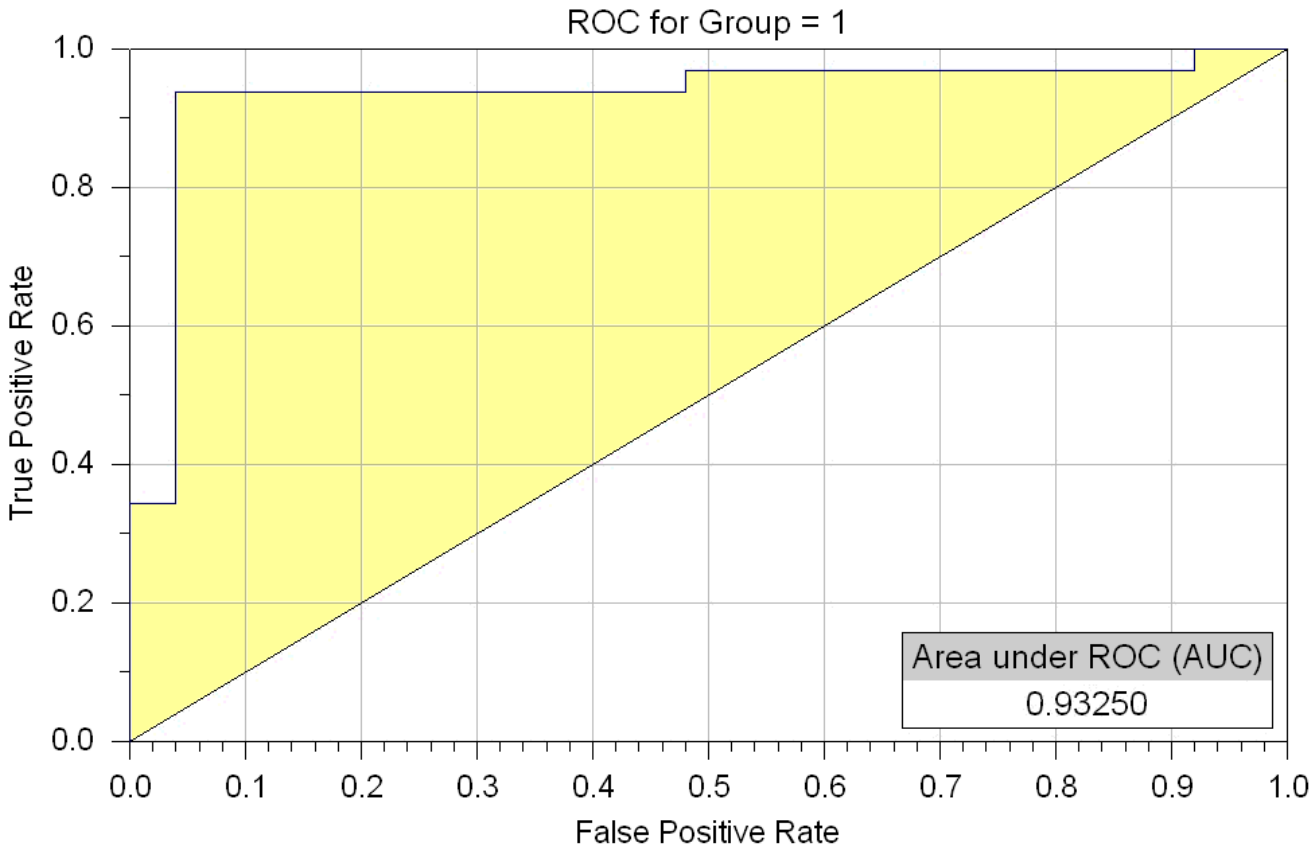

Figure 3

ROC curve to distinguish HCs and SZs.