Eye Movement Characteristics in Deficit and Non-deficit Schizophrenia and Their Relationships With Psychiatric Symptoms and Cognitive Function

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Abstract

Background

The cognitive impairment pattern of deficit schizophrenia (DS) is centered on an impaired attention function. Previous studies have suggested that the exploratory eye movement (EEM) tests reflect attention deficits in patients with schizophrenia. However, no study has investigated the characteristics of eye movement in DS in the Chinese Han population. This study aimed to investigate the pattern of eye movement characteristics in DS patients and analyze its clinical correlation.

Methods

A total of 86 male patients (37 DS and 49 NDS) and 80 healthy controls (HC) participated in this study. Clinical symptoms were assessed using the Scale for the Assessment of Positive Symptoms (SAPS) and Scale for the Assessment of Negative Symptoms (SANS). Cognitive function was assessed using the Mattis Dementia Rating Scale (MDRS-2). Eye movement data of subjects were collected using an eye movement tracking analyzer.

Results

There were significant differences in the overall eye movement data and cognitive test scores among the three groups (all $P < 0.001$). Both DS and NDS schizophrenia subgroups showed more severe eye movement and cognitive impairment compared with the control group. The number of eye fixations (NEF), total of eye scanning length (TESL), and cognitive function in DS patients were significantly lower than those in NDS patients. The discriminant analysis (D score) was higher than that of the control group ($P < 0.001$). In the DS group, the inattention factor of SANS was negatively correlated with the attention factor ($r = -0.545$, $P = 0.001$), and structure factor of cognitive ($r = -0.389$, $P = 0.023$), the affective flattening factor of SANS was negatively correlated with TESL ($r = -0.353$, $P = 0.041$) and initiation/retention factor of cognitive ($r = -0.376$, $P = 0.028$). TESL was found to positively correlate with the MDRS-2 total score ($r = 0.427$, $P = 0.012$), attention factor ($r = 0.354$, $P = 0.040$), and memory factor ($r = 0.349$, $P = 0.043$) in the DS group, whereas the mean of eye scanning length (MESL) positively correlated with cognitive impairments in the NDS group. The negative symptoms showed no significant correlation with cognition in the NDS group.

Conclusions

Total of eye scanning length may be a characteristic eye movement symptom in DS patients, which is associated with serious negative symptoms and cognitive impairment in this schizophrenia subtype.

Introduction

Schizophrenia is a common and severe mental disease in clinical practice, which leads to social dysfunction [1], and might be the most disabling of all mental disorders [2]. The treatment of schizophrenia has made considerable progress, but about one-third of patients still have an **unfavorable** prognosis and continue to show decline in social functioning [3]. In 1988, Carpenter et al proposed the concept of Deficit Schizophrenia (DS) subtype [4], characterized by primary and persistent negative symptoms; this classification is stable, with few changes in its core symptoms. However, the cognitive impairment pattern in DS is centered on the impaired attention function [5]. In addition, DS patients are characterized by familial aggregation, high birth rate in summer, poor long-term clinical efficacy, and early decline in social function [6-7].

In 1972, Moriya et al. first reported eye movement abnormalities in schizophrenia patients using the exploratory eye movement (EEM) test [8]. Since then, most studies have consistently reported EEM disorders in schizophrenia patients [9-18]. EEM examination includes observation of NEF, responsive of search scores (RSS), TESL, MESL, and D score [11,19-20]. NEF and RSS have been reported to reflect some characteristics of the cognitive function, including cognition, memory, attention, and other mental states of individuals [9,21]. EEM examination has been regarded as a biological indicator of schizophrenia [12], which can reflect visual cognitive dysfunction and attention deficit in patients with schizophrenia [22-23]. Previous studies have shown that most patients with schizophrenia have abnormal eye trajectories [12], a smaller number of fixations on memory tasks, and a narrower range of eye movements compared with healthy controls [9,17,24-26]. Previous studies have shown that TESL and RSS in patients with schizophrenia are negatively correlated with negative symptoms such as emotional withdrawal and flatness [12].

Previous studies have further reported that patients with DS have more severe impairment in almost all cognitive domains compared with patients with non-DS (NDS) [27]. Negative symptoms are a core component of DS [4], and are associated with a large proportion of long-term morbidity and poor functional outcome cases in DS patients. No study has investigated eye movements in DS in the Chinese Han population. The present study compared EEMs of healthy controls, patients with DS, and patients with NDS. The participants were also assessed by the Revised Mattis Dementia Rating Scale (MDRS-2) for measuring cognitive functions [28], such as sustained attention and memory function. The present study was performed to investigate the characteristics of eye movements in patients with DS and their correlation with clinical psychiatric symptoms and [cognitive impairment](#).

Methods

2.1. Participants

In all, 166 male participants were recruited in this study, including 86 schizophrenia patients who were clinically stable (37 DS and 49 NDS) and 80 HCs. The schizophrenia patients were recruited from the Department of Psychiatry at the Second People's Hospital of Jiangning District in Nanjing, Jiangsu Province, China. The following individuals were included in the analysis: (1) individuals diagnosed with schizophrenia according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), confirmed by the Chinese version of the Structured Clinical Interview for DSM-IV (SCID-I) [29]; (2) male, right-handed, Chinese Han patients aged between 25 and 65 years; and (3) individuals showing stable psychiatric symptoms and taking antipsychotic medication for at least 12 months based on the medical record. The exclusion criteria included the following: neurological disorders, severe comorbid conditions, head trauma, mental retardation, alcoholism or substance abuse disorder, and a history of previous electroconvulsive therapy. All DS and NDS patients were diagnosed according to the Chinese version of the Schedule for the Deficit Syndrome (SDS) [30]. The 80 male HCs were recruited from the local community and matched for age and handedness of the enrolled patients. These healthy subjects were assessed using a neuropsychological assessment scale to rule out individuals with organic brain disorders, mental retardation or severe head trauma, and a personal or family history of mental disorders. The study was approved by the Institutional Ethical Committee for clinical research of the Second People's Hospital of Jiangning District in Nanjing, and written informed consent was obtained from all participants.

2.2. Clinical and neuropsychological assessment

2.2.1. Clinical evaluation

After consistency training, a semi-structured interview that achieved a high inter-rater reliability [intraclass correlation coefficient (ICC) = 0.84] was conducted by two senior attending physicians. The deficit syndrome was determined according to the Chinese version of SDS [31]. The diagnostic criteria for SDS include the presence of two or more of the following negative symptoms: a deficit syndrome that has reached clinical significance, has persisted for more than 12 months, and has persisted during periods of clinical stability. These symptoms were primary or idiopathic and not secondary to depression, anxiety, drug side effects, psychotic symptoms, or mental retardation. Our diagnostic criteria were in line with the DSM-IV diagnosis of schizophrenia. The Scale for the Assessment of Positive Symptoms (SAPS) and the Scale for the Assessment of Negative Symptoms (SANS) was used to evaluate the positive and negative symptoms of patients, respectively, for assessing the severity of schizophrenia symptoms. SANS scale was classified into separate categories including diminished expression, social amotivation, and inattention factors based on the findings of the most comprehensive factor analysis of the 19-item SANS to date [32].

2.2.2. Neurocognitive Assessments

Each participant was assessed using MDRS-2, based on previous reports on cognitive process assessment for each task. These cognitive measures were further divided into five areas of reasonable motivation: continuous vigilance/attention (hereinafter referred to as continuous attention), initiation/retention, concept formation, structure, and memory [28].

2.3. Exploratory Eye Movement (EEM) Recording

The EEM examination was performed in 86 patients with schizophrenia and 80 HCs using DEM-2000 eye movement detection system (Shanghai Dikang, China). The EEM test procedure was based on that reported by Kojima et al. (1992) [10]. A standard 9-point calibration was performed before task initiation. A monocular sampling method was used to track the pupil of the dominant eye. EEM images were recorded on a videotape with an eye-mark recorder based on the reflection of infrared light on the cornea. The numbers of eye fixations (NEF), responsive of search scores (RSS), total eye scanning length (TESL), and mean eye scanning length (MESL) of the patient during the first 15 s of viewing a target figure was analyzed [12,19-20].

2.3.1. Eye movement recording procedure

First, the subject was comfortably seated in the viewing room, an eye camera that detected corneal reflection of infrared light to identify eye movements, and an LCD monitor that displayed target figures for EEM tasks were included in this system. Then, three horizontal S-shaped figures were projected onto a screen positioned at 30 cm directly in front of the subject's eyes. The first S-shaped figure (S1) was displayed on the screen for 15 s. The second and third S-shaped figures (S2, S3), which were slightly different from the first one, were then displayed on the screen, each figure lasting for 15 s. Following this, the subject was asked whether the last two figures differed from the first figure and, if they did, how did they differ.

The gaze point (NEF) is the total number of points in the eye fixation pattern S1 within 15 s, and the duration of a certain point in the eye fixation image should be more than 200 ms. The RSS score is calculated by dividing S2 or S3 into 7 areas. The instrument measures the number of areas that the eyes focus on, for a total of 5 s. As long as the subjects' eyes gaze at a certain area, one point is counted, regardless of how many times this area is looked at. Therefore, the maximum RSS score for each image is 7 points, and the total RSS score for S2 and S3 is 14 points.

The D score is calculated according to the discriminant analysis formula, $D = 10.265 - [(0.065 \times NEF) + (0.871 \times RSS)]$. The extent of the eye fixation point is TESL. MESL is the mean extent of eye movement. In the digital eye-mark recording system, the detected eye movements were automatically analyzed by a digital computerized EEM analyzer [12,19].

2.4. Statistical Analysis

All statistical analyses were performed using the SPSS 26.0 software. The continuous variables of demographics, clinical symptoms, eye movement, and cognitive raw data are presented as mean $\pm$ SD. The qualitative data were analyzed by Chi-square test. EEMs, cognitive function, and psychiatric symptoms were compared using two sample *t*-tests between DS and NDS groups. Age and years of education were used as covariables to conduct covariance analysis on the data of the two groups. $P < 0.05$ was considered statistically significant.

To determine the group differences in eye movement and cognition function, statistical comparisons were performed on eye movement indices (such as NEF, RSS, D score, TESL, and MESL) and cognitive function indices (such as continuous vigilance/attention, initiation/retention, concept formation, structure, and memory) among the three groups via univariate one-way analysis of covariance (ANCOVA), with potential effect factors (e.g., age, education, and duration of disease) as covariates. Partial correlation analysis between eye movements and neurocognitive domain and clinical variables (with age, years of education, and duration of disease as covariate) was conducted in the two patient groups. The significance level was set at $P < 0.05$.

Results

3.1. Demographic and clinical characteristics

Demographic and clinical characteristics of the subjects are presented in Table 1. The ANOVA results showed significant differences in age ($F=9.819$, $P<0.001$) and education ($F=28.024$, $P<0.001$) among the three groups. Least-significant difference (LSD) post-hoc comparisons revealed shorter education periods in the DS ($P<0.001$) and NDS ($P<0.001$) groups relative to those in the HC group, although the two patient subgroups did not differ significantly ($P=0.323$). The DS ($P=0.001$) and NDS ($P=0.009$) patients were older than the HC subjects, but there was no significant difference between the two patient subgroups ($P=0.093$). Chi-square test and *t*-test results indicated that significant differences in family history ($P<0.001$) and marital status ($P<0.001$) among the three groups, but the two patient subgroups had no significant differences in terms of family history ($P=0.209$), marital status ($P=0.754$), the mean age at onset, smoking status, positive symptoms, and antipsychotic medicine dosage (chlorpromazine equivalents), except for duration of disease ($t=3.771$, $P<0.001$) in the DS group. The DS patients showed more severe negative symptoms ($P<0.001$) than the NDS patients.

Table 1. Demographics and clinical characteristics for DS, NDS and HC groups.

	DS(n=37)	NDS(n=49)	HC(n=80)	F/ χ^2 /t	P
Age (years)	50.00±10.509 [△]	45.86±10.809 [#]	40.48±11.842	9.819	<0.001
Education (years)	9.65±2.251 [△]	10.35±3.244 [#]	13.78±3.590	28.024	<0.001
Age at Onset (years)	23.7365±6.76	26.61±9.808		-1.612	0.111
Duration of disease (years)	26.27±9.137 ^{**}	19.04±8.541		3.771	<0.001
CPZ-equivalent daily dose (mg/day)	418.38±201.94	398.2±201.39		0.459	0.647
Marital status [example (%)]				60.169	<0.001
unmarried	30(33.7)	41(46.1)	18(20.2)		
married	7(9.1)	8(10.4)	62(80.5)		
Family history [example (%)]				40.653	<0.001
positive	17(51.5)	16(48.5)	0(0.0)		
negative	20(15.0)	33(24.8)	80(60.2)		
Use rate of anticholinergic drugs [example (%)]	17(54.8)	14(45.2)		2.761	0.097
Smoking ratio (%)	13(18.6)	26(37.1)	31(44.3)	3.518	0.172
SDS total score	13.62±1.846 ^{**}	8.86±2.111		10.927	<0.001
SAPS total score	9.22±2.083	9.67±0.944		-1.364	0.176
Hallucinations	1.57±0.603	1.57±0.500		-0.259	0.796
Delusions	2.08±0.894	2.29±0.540		-1.317	0.191
Bizarre behavior	3.05±0.911	2.98±0.989		0.357	0.722
Positive thought disorder	2.54±0.869	2.84±0.624		-1.840	0.069
SANS total score	44.81±5.929 ^{**}	31.27±4.729		11.786	<0.001
Affective flattening	11.30±1.525 ^{**}	9.12±1.889		5.904	<0.001
Alogia	10.76±2.006 ^{**}	6.90±1.403		10.000	<0.001
Avolition	8.65±1.495 ^{**}	5.53±1.101		10.687	<0.001
Anhedonia	9.81±2.526 ^{**}	6.24±1.164		7.972	<0.001
Inattention	4.41±0.927 ^{**}	3.47±0.68		5.180	<0.001

Note: DS: deficit schizophrenia; NDS: non-deficit schizophrenia; HC: healthy controls; SANS: the Scale for the Assessment of Negative Symptoms; SAPS: the Scale for the Assessment of Positive Symptoms; SDS: schedule for the deficit syndrome; CPZ: chlorpromazine;

^{**} $P < 0.001$ DS vs. NDS;

* $P < 0.05$ DS vs. NDS;

Δ $P < 0.05$ DS vs. HC;

$P < 0.05$ NDS vs. HC.

3.2. Cognitive Characteristics

LSD post-hoc comparisons confirmed that both the DS and NDS patients performed worse than the HC subjects in each of the neuropsychological tests (all $P < 0.05$). Patients with DS, as compared with those with NDS, had significantly more severe impairment in most of the neuropsychological measures (all $P < 0.05$) Table 2.

Table 2. **Eye movement and cognitive function** for DS, NDS and HC groups.

	DS(n=37)	NDS(n=49)	HC(n=80)	<i>F</i>	<i>P</i>
NEF(score)	19.7±10.176**	25.22±9.072#	30.95±3.198 Δ	32.296	<0.001
RSS(score)	3.32±1.684	3.96±2.031#	7.33±1.43 Δ	98.406	<0.001
D score	6.11±1.955*	5.1±2.054#	1.87±1.32 Δ	100.432	<0.001
TESL	130.51±81.527**	193.08±96.211#	281.08±75.14 Δ	45.431	<0.001
MESL	7.97±5.535	8.27±3.684#	12.09±3.82 Δ	18.459	<0.001
MDRS-2 score	83.0±22.44**	108.31±18.517#	138.13±5.01 Δ	183.133	<0.001
continuous vigilance/attention	32.51±4.776*	34.78±2.435#	36.67±0.93 Δ	31.25	<0.001
initiation/retention	15.11±8.235**	23.22±7.267#	35.58±1.64 Δ	185.169	<0.001
concept formation	17.49±9.383**	25.96±7.112#	35.26±2.23 Δ	115.127	<0.001
structure	4.35±1.844*	5.31±1.294#	5.99±0.11 Δ	27.451	<0.001
memory	13.54±5.059**	19.16±4.23#	24.64±0.82 Δ	144.497	<0.001

Note: NEF: The numbers of eye fixations, RSS: responsive of search scores, TESL: total eye scanning length, MESL: mean eye scanning length, MDRS: Dementia Rating Scale.

** $P < 0.001$ DS vs. NDS;

* $P < 0.05$ DS vs. NDS;

Δ $P < 0.05$ DS vs. HC;

$P < 0.05$ NDS vs. HC.

3.3. Characteristics of eye movement parameters

ANOVA showed that there were statistically significant differences in eye movement indices among the three groups (all $P < 0.001$). LSD post-hoc comparisons showed that patients with DS ($P = 0.001$) and NDS ($P = 0.001$) had worse eye

movement parameters than HC subjects. NEF and TESL in the DS group were significantly lower than those in the NDS group (both $P<0.01$). The D value in the DS group was higher than that in the NDS group (all $P<0.05$). There were no statistically significant differences in RSS and MESL between the two groups (both $P<0.05$) Table 2, Fig. 1, 2, 3.

3.4. Relationships between eye movement, clinical features, and cognitive domains

With age, years of education, and duration of disease as covariables, the clinical symptoms, eye movement indices, and cognitive indices in the DS and NDS groups were analyzed by partial correlation. The bizarre behavior factor of SAPS in the DS group was negatively correlated with NEF ($r=-0.545$, $P=0.001$) and memory factor ($r=-0.347$, $P=0.045$) and positively correlated with D value ($r=0.396$, $P=0.020$). The affective flattening factor of SANS was negatively correlated with TESL ($r=-0.353$, $P=0.041$) and initiation/retention factor of cognitive ($r=-0.376$, $P=0.028$). The inattention factor of SANS was negatively correlated with the MDRS-2 total score ($r=-0.468$, $P=0.005$), attention factor ($r=-0.545$, $P=0.001$), and structure factor ($r=-0.389$, $P=0.023$). TESL was positively correlated with MDRS-2 score ($r=0.427$, $P=0.012$), attention factor ($r=0.354$, $P=0.040$), and memory factor ($r=0.349$, $P=0.043$).

MESL was positively correlated with the inattention factor of SANS, MDRS-2 total score ($r=0.401$, $P=0.006$), initiation/retention factor ($r=0.349$, $P=0.018$), and concept formation factor ($r=0.392$, $P=0.007$) in the NDS group. The negative symptoms showed no significant correlation with cognition in the NDS group. Table 3, 4.

Table 3. Correlation of eye movement with cognitive and clinical symptoms in DS

		NEF	TESL	MDRS-2 total score	continuous vigilance/attention	initiation/retention	structure	memory
SAPS	Bizarre behavior	-0.545**						-0.347*
SANS	Affective flattening		-0.353*			-0.376*		
	Inattention			-0.468**	-0.545***		-0.389*	
	TESL			0.427*	0.354*			0.349*

Note:* $P<0.05$ after correction of multiple testing.

** $P< 0.01$ after correction of multiple testing.

*** $P< 0.001$ after correction of multiple testing.

Table 4. Correlation of eye movement with cognitive and clinical symptoms in NDS group.

		NEF	MESL	TESL	MDRS-2 total score	initiation/retention	concept formation
SAPS	Bizarre behavior	0.068					
SANS	Inattention		0.337*	0.308*			
	MESL				0.401**	0.349*	0.392**

Note: * $P < 0.05$ after correction of multiple testing.

** $P < 0.01$ after correction of multiple testing.

Discussion

To the best of our knowledge, this is the first study to investigate eye movement characteristics in patients with DS and their correlation with clinical symptoms and cognition. The main findings of our study were as follows: in the DS group and NDS group, eye movement index and cognitive function were generally low, and the impairment of eye movement index in DS group (i.e., lower NEF and TESL) was greater than that in the NDS group. DS patients showed greater impairments in all cognitive function measures than NDS patients [27]. Both schizophrenia subgroups performed worse than the control group in every area of eye movement measurement and cognition. In addition, NEF was significantly correlated with SAPS bizarre behavior factor in the DS group, whereas TESL was correlated with SANS affective flattening factor, cognitive MDRS total score, attention factor, and memory factor in the DS group.

NEF and RSS reflect cognitive function such as memory and active attention, whereas TESL is associated with emotional withdrawal, and blunted effect and emotional relationship disorder [25]. The previous studies have found the lower the NEF, the shorter the TESL and the narrower the range of eye movement in the patients with schizophrenia, suggesting that limited scanning length may be a characteristic of schizophrenia [12, 17, 26, 33]. Less eye movement was believed to be a sign of impaired visual cognitive function [10, 12–13, 20]. A significant reduction in the scan length may be because of lack of sustained attention [25]. In this study, both DS and NDS patients presented with lower NEF and shorter TESL, which was largely compatible with several previous studies, indicating decreased eye movement in schizophrenia [12, 17, 26]. Ryu et al. observed that individuals with schizophrenia may stare aimlessly at a certain part of the picture rather than properly focusing their attention on that part of the picture [25]. Shakow reported that people with schizophrenia were unable to focus their attention on the external environment or move in a meaningful direction [34]. In terms of face recognition, Williams et al. reported that under more difficult task conditions, schizophrenia patients could not focus their eye gaze on characteristic areas; they thought that these patients could not form the general gestalt of the initial registration, followed by abnormal stress of serial processing. These studies found that patients with schizophrenia in a variety of eye movement task execution process of aberrations [35]. Restricted facial visual scanning may indicate social cognitive impairment or may be a marker of vulnerability associated with disease features [36–37]. These findings indicate that abnormal eye movement may be a common feature in schizophrenia, regardless DS and NDS, but the decrease was more pronounced in DS patients. These gaze points in DS patients were few and also relatively fixed and limited. The eyes of DS patients tend to be fixated at a single point or move within a particularly limited range, which significantly shortens the total eyeball distance. This may be closely related to the disease characteristics of DS patients. In our study, the presence of persistent negative symptoms in DS patients caused the patient to be unable

to concentrate on a particular instruction. DS patients with emotional withdrawal, anhedonia, resulting in patients in interpersonal communication and social interaction on the obstacles.

Schizophrenia patients have cognitive impairments in attention, working memory, language learning, visual learning, social cognition, and other aspects [38–39]. Previous studies have reported that EEM abnormalities in schizophrenia are associated with cognitive impairment [40–43]. Several studies have shown differences in neurocognitive function between patients with DS and NDS [44–45]. Previous studies have found that DS patients had more severe impairment in almost all cognitive domains when compared with NDS patients [27]. A meta-analysis by Cohen et al. reported evidence of moderate widespread cognitive impairment in patients with defect syndrome [46]. Previous studies have found that schizophrenia patients with persistent negative symptoms showed more severe continuous attention impairment in related cognitive assessments [47–49]. A modified version of MDRS was used in this study [28, 50–51]. The present study found that both schizophrenia subgroups performed worse compared with the control group in every cognitive area. These reflected the overall impairment of cognitive function in schizophrenia. Compared with NDS patients, DS patients had more severe impairments in all neurocognitive domains, and it was correlated with the attention factors of SANS: the more severe the negative symptoms, the worse the neurocognitive function. However, negative symptoms were not associated with cognitive function in the NDS group. There were significant differences in the neurocognitive impairment patterns between the two groups, mainly because of the differences in attention and executive function between the two groups. The persistent attention deficit may be the core cognitive impairment module in DS patients [27]. Previous studies have reported that patients with DS had more severe impairments in general cognitive function, executive function [52, 53], and speech fluency [54–58] than patients with NDS. Other studies have reported impaired sustained attention [5, 46–49, 58] and visuospatial memory [30, 59] in DS patients. Patients with DS have been previously reported to have abnormal frontal and parietal lobe function. Recent imaging studies have consistently found that patients with DS have reduced gray [60–63] and white matter volumes [62] in the temporal lobe region compared with patients with NDS. These findings regarding the structural abnormalities in specific brain regions in patients with different schizophrenia subtypes may explain the differences in core cognitive impairment modules between the DS and NDS groups.

Furthermore, the present study found the specific correlations of eye movement and clinical features with cognition in the DS group, which may represent a possible compensatory response to the functional deficit in DS patients. The present study found that the attention factors in the SANS in the DS group were significantly negatively correlated with the total MDRS score, attention factors, and structural factors, whereas the negative symptoms in the NDS group were not correlated with cognition. Previous studies have reported that TESL and RSS in patients with schizophrenia are negatively correlated with negative symptoms such as emotional withdrawal and flatness [8, 12, 25–26, 41–42, 64–66]. However, there was no significant correlation between positive symptoms and TESL and RSS. In the present study, NEF was significantly negatively correlated with the bizarre behavior factor of SAPS. Further, TESL was found to be negatively correlated with affective flattening factor of SANS in the DS group, but not in the NDS group. TESL was also positively associated with the total MDRS score, attention factor, and memory factor. This indicates that the shortening of total fixation distance in DS patients is related to the severity of negative symptoms and cognitive decline. The more severe the negative symptoms, the shorter the total fixation distance and the worse the cognitive function. Recent studies have shown that negative symptoms play a key role in mediating the neurocognitive and social cognitive functions in patients with schizophrenia and in the prognosis of their functional outcomes [67]. Visual cognitive dysfunction in patients with schizophrenia was closely associated with the decline in social function, social status, independent living, working ability, and interpersonal communication ability [68–71], which may be the restrictions that hinder the social and vocational rehabilitation of patients [72]. DS is a subtype of schizophrenia. The characteristic negative symptoms of this subgroup include restriction of emotion,

reduced range of emotion, poor speech, inhibition of interest, poor sense of purpose, and reduced social motivation [31, 45]. Further, patients with DS show more persistent, prominent negative symptoms and are associated with neurocognitive and social cognitive impairments [7]. Tsunoda et al. reported that a number of eye movement parameters were negatively associated with negative symptoms, particularly lack of willpower and blandness or dullness of emotion [65]. These findings suggested that exploratory eye movements are biomarkers for negative symptoms such as emotional withdrawal, emotional dullness, and mannerisms [25]. This clinical correlation suggested that negative effects on eye movement reflect underlying brain dysfunction that leads to communication disorders in relation to the environment and interpersonal relationships [8, 10]. In addition, this study showed that MESL was positively correlated with total MDRS score, onset/retention factor, and concept formation factor in the NDS group. No correlation of TESL and negative symptoms with cognition was found in NDS patients, suggesting significant differences in eye movement characteristics between the two subgroups, which may result from the biological characteristics distinguishing DS from NDS.

Limitations Of The Study

Our study has several limitations. First, all patients were receiving antipsychotics, and although the type and dosage of antipsychotics were consistent between the two groups of patients, their influence on the study results cannot be ruled out. Second, patients in the two subgroups had different disease courses and age. Although the duration of disease and age had been controlled as a covariable in the statistical analysis of this study, it cannot be ruled out that it may have a certain influence on cognition. In addition, because we only recruited male chronic schizophrenia patients, future studies ought to also consider outpatients, female patients, and larger sample sizes.

Conclusions

In summary, our findings provide empirical evidence for association between eye movement and cognitive function in patients with DS and NDS. TESL is significantly associated with negative symptoms and impaired cognitive function. Specifically, abnormalities between the two patient groups emphasize that visuoemotional and social functions were characteristically impaired in DS Patients. Patients with DS have persistent negative symptoms that lead to visual cognitive deficits in novel and complex problem-solving environments, and these deficits are partly related to cognitive indicators of persistent attention and executive dysfunction. These deficits begin to show with a reduced ability to scan complex visual environments effectively and eventually lead to environmental and social impairments. The present study suggests that deficit syndrome may be a specific subtype of schizophrenia.

Abbreviations

ANCOVA: Analysis of covariance; CPZ: chlorpromazine; DS: Deficit schizophrenia; DSM-IV: Diagnostic and statistical manual-IV; EEM: exploratory eye movement; MDRS-2: Mattis Dementia Rating Scale; MESL: mean of eye scanning length; NDS: Non-deficit schizophrenia; NEF: number of eye fixation; RSS: responsive of search scores; SANS: Scale for the assessment of negative symptoms; SAPS: Scale for the assessment of positive symptoms; SCID: Structured clinical interview for DSM-IV; SDS: Schedule for the Deficit Syndrome; SPSS: Statistical package for social sciences; TESL: total of eye scanning length

Declarations

Ethics approval and consent to participate

The Ethics Review Committee of the Second People's Hospital of Jiangning District, Nanjing approved the study (NO. 201910). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed written consent was obtained from all participants prior to the commencement of the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

XRZ was responsible for the analysis and interpretation of the study. LZ drafted the initial manuscript and was responsible for creation and design.

XYF and CZ were all principle investigators and were responsible for creation and design of the study. LW, XMP, JC and FQZ were all involved in study design and interpretation of results. All authors

contributed to and have approved the final manuscript.

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Availability of data and materials

Data available on request from the corresponding author.

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Figures

Figure 1

NEF: 15 TESL: 80.17mm MESL: 7.93 mm

Figure 2

NEF: 24 TESL: 195.20 mm MESL: 8.59 mm

Figure 3

NEF: 32 TESL: 283.40 mm MESL: 12.06 mm