







Research Article

Exploratory eye movement patterns in schizophrenia and their potential as biomarker

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Summary

Eye movements represent an objective, quantitative indicator of the integrity of cognitive and perceptual processes. Since the beginning of the 20th century, research has shown that individuals with schizophrenia demonstrate characteristic deviations in smooth pursuit, -regulation, and visual exploration behaviour. These oculomotor alterations are linked to dysfunctions in attention, executive control, and perceptual organization, and have been discussed as potential biomarkers of impaired neural network regulation. More recent work further implicates disturbances in visual attention and integration, as well as reduced executive control over oculomotor activity, which may manifest in altered gaze behaviour.

Building on this literature, the present study examined whether free-viewing eye-movement patterns capture markers of restricted exploration and altered scanpath organization under ecologically valid conditions. We recorded eye movements during passive viewing of landscape and abstract images in three groups: patients with schizophrenia ($n = 30$), healthy controls ($n = 30$), and close relatives ($n = 21$). Visual exploration was quantified using integrative indices of fixation number and duration (mean/median/total), scanpath length, coverage fraction, spatial dispersion (mean/median; dispersion_x and dispersion_y), center bias, fixations per second, gaze entropy (bits), and saccade metrics. Group and image type were tested in 2×2 mixed ANOVA models with FDR correction across metrics.

In the patient-control analysis ($N = 60$), a significant main effect of group was observed across multiple exploration and oculomotor parameters after FDR correction (partial $\eta^2 \approx .12-.21$; $pFDR \leq .032$), with no main effect of image type and no group \times image type interaction surviving correction, supporting a stimulus-nonspecific alteration of visual exploration in schizophrenia. In the relatives-controls analysis ($N = 51$), uncorrected trends suggested a more compact scan pattern (reduced dispersion and saccade amplitude). However, no effects remained significant after FDR correction. Overall, free-viewing eye-movement metrics showed medium-to-large, stimulus-nonspecific group differences in schizophrenia, consistent with a restricted and altered exploration mode, whereas potential vulnerability-related signals in first-degree relatives were weaker and did not survive correction, indicating the need for larger samples and/or targeted paradigms with predefined core metrics in familial-risk designs.



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Introduction

Schizophrenia is a chronic, severe, and heterogeneous psychiatric disorder characterized by disturbances in thinking, perception, emotion, and behavior. It affects core cognitive and affective processes, leading to a distorted perception of reality, social isolation, and reduced occupational and interpersonal functioning (Sadock et al. 2023). The disorder typically begins in late adolescence or early adulthood and follows a relapsing-remitting or progressively deteriorating course. The global burden of schizophrenia is substantial: its lifetime prevalence is approximately 1%, and its disabling effect is high (Charlson et al. 2018).

Despite more than a century of research since the first descriptions by Kraepelin and Bleuler, the pathophysiology of schizophrenia remains incompletely understood, making it one of the most complex conditions in psychiatry. Diagnosis still relies primarily on clinical assessment: recognizing characteristic symptoms and interpreting the patient's subjective reports, within the frameworks of DSM-5-TR and ICD-10/11.

In recent years, however, schizophrenia is increasingly conceptualized as a neurodevelopmental disorder, with pathological processes unfolding long before the clinical onset of psychosis, which represents a late and potentially preventable stage of the disorder (Insel 2010; Notaras et al. 2022).

On the other hand, beyond its personal and social significance, schizophrenia also continues to pose a challenge in the search for reliable biological markers that could improve diagnostic accuracy, prognosis, and therapeutic decision-making.

Despite significant advances in neuroimaging, electrophysiology, and molecular genetics, no biomarker has yet demonstrated sufficient specificity, sensitivity, and reproducibility for routine clinical use. Yet, several candidate biomarkers have been proposed, among which the following stand out:

- Immune-inflammatory abnormalities, including reproducible changes in cytokine levels (Miller et al. 2011);
- Metabolic and neuroendocrine dysregulation, with impaired glucose metabolism evident even at the first episode (Pillinger et al. 2017);
- Dysfunction of neurotransmitter and neuroplastic pathways, particularly the dopamine hypothesis (Howes and Kapur 2009);
- Abnormalities in neural oscillations and functional connectivity, including deficits in beta/gamma synchrony (Uhlhaas and Singer 2010).

Among these approaches, the study of eye movements offers a direct, noninvasive window into neural functioning. Control of oculomotor activity depends on distributed brain networks involving the frontal eye fields, parietal cortex, basal ganglia, cerebellum, and superior colliculi (Leigh and Zee 2015).

Since eye movements are an integral part of visual perception and closely related to attention and cognition, their quantification may allow indirect assessment of disorders in perception, executive control, and sensorimotor integration in psychiatric populations, as discussed by Morita et al. (2017).

Historical background of the study of eye movements

The scientific study of eye movements dates back to the late 19th century. In 1879, Louis Émile Javal observed (using a mirror technique) that reading is carried out through a series of saccades separated by fixations, demonstrating that visual information is perceived discretely rather than continuously (Wade and Tatler 2005; Wolf et al. 2021).

At the beginning of the 20th century, Buswell conducted the first systematic experiments on image viewing, showing that fixations cluster over informative areas (Buswell 1935; Wade 2020; Wolf et al. 2021).

Three decades later, Yarbus demonstrated that task demands and cognitive set shape gaze patterns. His classical demonstrations are presented in *Eye Movements and Vision* (Yarbus 1967; Tatler et al. 2010; Wolf et al. 2021).

Clinical application followed soon after: Diefendorf and Dodge (1908) recorded oculomotor behavior in individuals with *dementia praecox* and manic-depressive illness (corresponding to the modern diagnoses of schizophrenia and bipolar affective disorder), identifying atypical smooth pursuit and unstable fixations (Diefendorf and Dodge 1908; Wolf et al. 2021).

Between 1970 and 1990, Holzman and colleagues formulated the concept of Eye-Tracking Dysfunction (ETD) in schizophrenia, describing reduced smooth pursuit gain and an increased number of corrective saccades (Holzman et al. 1976), as well as the associated familial traits of the tracking deficit. Subsequent neurophysiological studies linked these disturbances to dysfunction within the frontal eye fields and related neural circuits (Sweeney et al. 1998; Wolf et al. 2021).

With the advent of digital high-resolution eye-tracking systems, research has shifted from descriptive observation to computational quantitative analysis of oculomotor behavior. These systems have enabled precise assessment of parameters such as the number and duration of fixations, scanpath length, spatial dispersion, and entropy - metrics that are now regarded as potential biomarkers of schizophrenia (Kojima et al. 2001; Wolf et al. 2021).

Classical and modern experimental paradigms in the study of schizophrenia

Smooth pursuit and saccadic movement paradigms

The earliest controlled studies of oculomotor abnormalities in schizophrenia used smooth pursuit and saccadic task paradigms. In smooth pursuit tasks, typically using sinusoidal or step-ramp targets, patients with schizophrenia exhibit reduced pursuit gain, increased catch-up saccades, and greater phase lag, reflecting impaired prediction and sensorimotor integration. Both classical and contemporary findings confirm these effects and their trait-like nature, including their presence in first-degree relatives (Holzman et al. 1976).

Deficits in the antisaccade task, which require suppressing a reflexive gaze shift and executing a voluntary saccade in the opposite direction, are among the most consistently replicated findings in the field. Patients exhibit higher error rates and prolonged latencies. Large multicenter studies and meta-analyses demonstrate intermediate performance in relatives, supporting

the endophenotypic nature of this marker. Taken together, the abnormalities in smooth pursuit and antisaccadic eye movements point to disrupted communication among the frontal eye fields, parietal cortex, basal ganglia, and cerebellum—networks critically involved in temporal prediction, attention, and motor precision. Neurophysiological and neuroimaging studies link these oculomotor deficits to dysfunction within the frontal oculomotor circuits (Lencer et al. 2010).

Exploratory Eye Movement, EEM paradigm

A significant conceptual advancement in the study of oculomotor abnormalities in schizophrenia is the Exploratory Eye Movement (EEM) test, developed by Kojima and colleagues. In this paradigm, participants view a geometric “table-like” figure. They are then asked to compare two similar versions to identify the differences between them. The main measured parameters include the number and duration of fixations, scanpath length, and the Responsive Search Score (RSS) – an index reflecting the flexibility and adaptability of visual exploration.

Initial clinical studies identified abnormalities in EEM performance among patients with schizophrenia and described their cognitive correlates. Subsequent multicenter investigations confirmed the stability and diagnostic utility of the RSS measure as a sensitive and reliable marker of the disorder (Kojima et al. 1992, 2001).

Neuroanatomical studies using voxel-based morphometry have shown that lower EEM and RSS values are associated with reduced gray matter density in the prefrontal and parietal cortices, further supporting the biological relevance of this test (Qiu et al. 2011).

Free-viewing and naturalistic paradigms

Because structured tasks limit behavior, free-viewing paradigms, i.e., unsupervised viewing of complex visual scenes, allow spontaneous visual exploration to be recorded.

In one of the landmark studies, Benson et al. (2012) demonstrated that simple metrics from free-viewing tests, such as fixation distribution and scan dynamics, can distinguish patients with schizophrenia with high accuracy from healthy controls, including in independent samples (Beedie et al. 2011).

Modern research using free-viewing eye-movement paradigms includes quantitative analyses of the number and duration of fixations, scan length, degree of coverage, spatial dispersion (x/y-axis variability), and gaze entropy.

In patients with schizophrenia, lower entropy and reduced spatial variance were consistently observed, reflecting more stereotyped and less adaptive visual examination strategies. These findings have been systematically reviewed by Beedie et al. (2011).

Integrated and machine learning-based approaches

In recent years, research on oculomotor parameters in schizophrenia has increasingly focused on integrating metrics from various tasks—smooth pursuit, saccadic movements, fixations, and free-viewing exploration—through

machine learning models. Benson et al. (2012) were the first to demonstrate that even simple metrics derived from free-viewing tests can distinguish patients with schizophrenia from healthy controls with high accuracy. Building on this approach, Morita et al. (2017) proposed the Integrated Eye Movement Score (IEMS). This composite index combines multiple eye movement parameters and shows high diagnostic sensitivity.

Subsequent multicenter studies have reported that multifactorial models can differentiate schizophrenia from major affective disorders and healthy controls with a predictive accuracy of around 80%, including in independent samples.

These approaches illustrate the transition from isolated deficit models to multidimensional oculomotor profiles, conceptualized as data-driven biomarkers of schizophrenia (St Clair et al. 2022).

Free visual exploration in modern research

Characteristics of free visual exploration in schizophrenia

Recent studies confirm that, under free-viewing conditions, patients with schizophrenia consistently demonstrate atypical patterns of visual exploration. Commonly observed findings include:

- a smaller number of fixations and shorter scanpaths, reflecting reduced exploratory motivation and diminished visual sampling (Benson et al. 2012);
- longer fixation durations, corresponding to slowed cognitive processing and difficulty disengaging attention (Minassian et al. 2005);
- reduced spatial dispersion and a more pronounced central fixation bias, indicating restricted spatial scanning of attention (Morita et al. 2019);
- lower gaze entropy, reflecting more stereotyped and predictable fixation sequences (Beedie et al. 2011; Benson et al. 2012).

These deviations are associated with dysfunction in the dorsal attention network and prefrontal executive systems, which in healthy individuals exert top-down control over oculomotor behavior (Beedie et al. 2011; Dowiasch et al. 2016).

Studies applying machine learning models to such oculomotor metrics have achieved high classification accuracy in distinguishing patients with schizophrenia from healthy controls (Benson et al. 2012; St. Clair et al. 2022), which further highlights the diagnostic potential of metrics from free-viewing paradigms.

Current study

Purpose of the study

This study aims to compare free-viewing eye-movement parameters between patients with schizophrenia, their first-degree relatives, and healthy controls; to identify significant between-group differences; and to evaluate whether these metrics show potential as candidate biomarkers (trait-like markers) for schizophrenia and familial risk.

Methods of participant selection

The participants were divided into three groups:

1. Individuals with schizophrenia
2. First-degree relatives
3. Healthy controls

Recruitment was conducted under strict inclusion and exclusion criteria to achieve sample homogeneity: (1) age 18–65 years; (2) normal or corrected-to-normal vision. In cases of any doubt, participants were evaluated by an ophthalmologist; (3) no current substance use disorder and no substance use/misuse during the two weeks before the procedure; (4) no evidence of neurological or neurodegenerative disease.

Participants were recruited from inpatient and outpatient psychiatric services. Patients were clinically diagnosed with schizophrenia according to both ICD-10 (F20) and DSM-5 criteria. Diagnostic confirmation was established using a structured clinical interview (Mini International Neuropsychiatric Interview, MINI), validated by using medical records and direct clinical observation. Symptom severity was assessed with the Positive and Negative Syndrome Scale (PANSS), administered by trained psychiatrists, which measures three core domains: positive symptoms, negative symptoms, and general psychopathology.

Only patients with a stable clinical status, without an acute psychotic exacerbation at the time of testing, were included to minimize the effects of agitation, sedation, or motor restlessness on oculomotor outcomes. The patient group (N = 16 men, N = 14 women) ranged in age from 20 to 65 years, with a mean age of 38 ± 10.57 years. The mean duration of illness among patients was 8.61 years (SD = ± 8.03). Patients showed PANSS positive *Mean* = 18.02, PANSS negative *Mean* = 22.69, PANSS general psychopathology *Mean* = 32.56, and PANSS total *Mean* = 73.33. All patients were receiving antipsychotic medication, and some (N = 7) were on combination antipsychotic therapy (amisulpride N = 4, aripiprazole N = 4, cariprazine N = 1, chlorprotixene N = 3, clozapine N = 3, haloperidol N = 6, olanzapine N = 3, paliperidone N = 3, quetiapine N = 3, risperidone N = 6, zuclopentixole N = 2). Some participants additionally received mood stabilizers (valproate, N = 4) and benzodiazepines (clonazepam 0.5 mg, N = 2). The daily antipsychotic doses at the time of testing were converted to chlorpromazine equivalents (CPZ-eq) according to the Maudsley Prescribing Guidelines in Psychiatry (Taylor et al. 2025) to allow comparison of cumulative antipsychotic load across participants. All patients were off benzodiazepines and mood stabilizers for at least 24 h before testing.

The control group comprised 30 clinically healthy volunteers (N = 14 men, N = 16 women), aged 19–65 years, with a mean age of 36 ± 15.15 years. All controls were screened with the MINI to exclude any current or past clinically significant psychiatric disorder.

The third group comprised twenty-one participants who were close relatives of individuals with schizophrenia (N = 15 men, N = 6 women), aged 27–65 years, with a mean age of $M \pm SD = 36 \pm 12.38$, with no evidence of a clinically significant psychiatric or neurological disorder.

Ethical considerations

All participants provided written informed consent after receiving a detailed explanation of the study procedure.

The study protocol was reviewed and approved by the Ethics Committee of the Medical University – Pleven, and all procedures were conducted in accordance with institutional ethical standards and the principles of the Declaration of Helsinki.

Stimuli and procedure

The study focused exclusively on free exploratory gaze behavior, which records spontaneous visual activity without any predefined task. Each participant was presented with two visual stimuli:

- a landscape scene (Fig. 1);
- an abstract painting (Fig. 2).



Figure 1. Landscape scene.



Figure 2. Abstract painting.

Participants were seated comfortably 85 cm from a 69 cm (27-inch) monitor and instructed to remain still in a relaxed, natural posture, avoiding head movements. The stimulus resolution was 5059 × 3352 pixels, image DPI 72 pixels/inch, sRGB color space for the landscape scene, and 2594 × 2479 pixels, image DPI 300 pixels/inch, sRGB color space for the abstract painting. Each stimulus was presented for 25 seconds under free-viewing conditions, without instructions or assigned tasks.

The stimuli were commercially licensed images purchased from a paid database of visual stimuli, with full rights to use and publish. The selected images were balanced for visual complexity, non-fatiguing, and emotionally neutral, with no pre-defined areas of interest (AOIs), to ensure that oculomotor behavior reflected intrinsic exploratory tendencies rather than task-driven attention or visual salience.

Eye-movement recordings and tracking of the true gaze position were performed using the Pupil Core device (Pupil Labs GmbH, Berlin, Germany). Before each recording, a 2D calibration with 9, 15, or 21 points was conducted using Pupil Core. Extended calibration modes, available as optional plug-ins, were integrated into the software to improve spatial accuracy. The number of calibration points was adjusted to each participant's level of cooperation and stability to ensure high spatial accuracy and reliable gaze mapping across the entire display area. In patients with schizophrenia, 9-point (N = 2), 15-point (N = 2), and 21-point (N = 26) calibration modes were used. In healthy controls and close relatives of individuals with schizophrenia, the 21-point calibration mode was used (N = 30 for controls; N = 21 for relatives).

Registration and processing data

Eye movements were recorded using the Pupil Core system—a binocular, high-resolution, portable eye-tracking device operating at a sampling rate of 200 Hz. We set the minimum recording confidence to 0.95 (maximum 1.00). During the experiment, the system continuously recorded gaze coordinates and pupil position throughout the 25-s interval. During post-hoc calibration, we set the minimum confidence for the pupil signal to 0.95 (maximum 1.00) to ensure high data quality. Within the same calibration procedure, we also assessed the accuracy and precision of the recorded gaze. Mean accuracy was approximately 0.65° in patients, 0.40° in the control group, and 0.45° in relatives; precision ranged from a minimum of 0.00 to a maximum of 0.20, with a mean of ~0.10° across all groups, which falls within the acceptable range for high-resolution eye trackers.

In Pupil Core, a saccade is defined as the transition between two consecutive fixations after removing blinks, noise, and samples with low confidence. Fixations were detected using the I-DT (dispersion-threshold identification) algorithm implemented in Pupil Player (Pupil Labs). The algorithm was manually configured with the following parameters: maximum dispersion = 1.01°, minimum duration = 80 ms, and maximum duration = 800 ms to ignore artifacts and microsaccades. To check the robustness of the method, we repeated fixation detection with maximum dispersion set to 0.7° and 1.2°, and the results remained stable.

The resulting data were exported for processing in a purpose-built computational analysis module within a semi-automated software pipeline developed in Colab using MATLAB and Python. The module integrates raw coordinates with spatiotemporal event-detection algorithms. This analytical procedure enables

quantification of the following parameters: fixation number; mean, median, and total fixation duration; scanpath length; coverage fraction; spatial dispersion (mean and median dispersion, dispersion x, and dispersion y); center bias; fixations per second; gaze entropy (bits); and saccade metrics. Together, these features constitute a multidimensional oculomotor profile integrating the spatial, temporal, and dynamic aspects of visual exploration.

By comparing profiles of patients with schizophrenia and healthy controls, the study aimed to identify distinctive markers of cognitive rigidity, narrowed attentional scope, and perceptual disorganization that may serve as reliable biomarkers of neural dysfunction (Beedie et al. 2011; Benson et al. 2012; Morita et al. 2019; Wolf et al. 2021).

Statistical analysis

To compare groups at the metric level of the data (e.g., eye-movement parameters), analyses of variance (ANOVA) were used. Two-way repeated-measures ANOVAs (image \times group) were conducted to test within-subject effects (differences between images) as well as between-group effects on eye-movement parameters. The results of the two-way ANOVAs (image \times group) are presented. We report corrected *p*-values and effect sizes, expressed as partial eta squared (η^2), for the ANOVAs.

Specifications and performance of Pupil Core – binocular, high-resolution, and portable eye-tracking device

Eye Tracking Technology: Dark pupil technique + 3D model. Binocular Eye Tracking: Binocular or monocular Calibration: 5-point calibration. Multiple calibration methods available as plug-in. Scene Camera: Multiple resolutions and frequencies. Select in the Pupil Core software. 1080p @30 Hz, 720p @60 Hz, 480p @120 Hz. Eye Cameras: 2 \times IR eye cameras 192 \times 192 px @200 Hz. Gaze Measurements: 3D: 3D gaze rays + 3D gaze point through binocular vergence, 2D: 2D gaze position

Results

Aggregated oculomotor profiles of the studied groups (Table 1)

Table 1. Aggregated oculomotor profiles of studied groups.

Parameters	Control-abstract	Control-landscape	Patient-abstract	Patient-landscape	Family member-abstract	Family member-landscape
Fixations, n	71.1 (13.1)	73.6 (13.8)	59.6 (17.3)	61.2 (20.0)	67.5 (13.9)	67.2 (8.0)
Mean fixation duration, ms	299.9 (55.0)	292.9 (55.8)	321.4 (52.5)	310.4 (74.3)	288.3 (78.7)	283.7 (61.9)
Median fixation duration, ms	269.2 (53.0)	264.3 (56.3)	264.3 (44.9)	264.5 (59.2)	254.6 (70.6)	256.8 (60.7)
Total fixation time, ms	20909 (3022)	21169 (3836)	18919 (5141)	18463 (5646)	19475 (5709)	19322 (5523)
Scanpath length (normalized)	11.58 (4.02)	10.24 (2.94)	7.34 (3.29)	7.50 (4.37)	12.25 (3.04)	12.53 (3.32)
Spatial coverage (fraction)	0.0260 (0.0054)	0.0261 (0.0061)	0.0197 (0.0064)	0.0196 (0.0097)	0.0244 (0.0036)	0.0248 (0.0030)
Scanpath entropy, bits	5.93 (0.34)	5.92 (0.41)	5.39 (0.75)	5.12 (1.40)	5.87 (0.20)	5.91 (0.19)
Saccade amplitude (mean, norm.)	0.165 (0.050)	0.141 (0.030)	0.127 (0.048)	0.120 (0.053)	0.197 (0.054)	0.192 (0.054)
Saccade amplitude (median, norm.)	0.131 (0.051)	0.113 (0.031)	0.091 (0.049)	0.083 (0.048)	0.158 (0.084)	0.157 (0.038)
Fixations per second	3.44 (0.61)	3.53 (0.64)	3.19 (0.53)	3.45 (1.07)	3.71 (1.08)	3.74 (1.21)
Center bias	0.273 (0.064)	0.265 (0.073)	0.278 (0.131)	0.300 (0.152)	0.322 (0.074)	0.296 (0.065)

*Results in Mean (SD).

2 × 2 Mixed ANOVA

A 2 × 2 mixed analysis of variance (ANOVA) (group: patients vs. controls; image type: landscape vs. abstract), $N = 60$ (patients $n = 30$, controls $n = 30$), revealed a significant main effect of group across multiple oculomotor and visual-exploration parameters after FDR correction (partial $\eta^2 \approx 0.12$ – 0.21), with no main effect of image type and no group × image interaction surviving correction.

Significant group effects were observed for normalized scanpath length (scanpath length_norm), $F(1, 60) = 12.76$, $pFDR = .00967$, $\eta^2 = 0.214$; coverage fraction (coverage frac), $F(1, 60) = 11.37$, $pFDR = .00967$, $\eta^2 = 0.195$; entropy (entropy bits), $F(1, 60) = 10.63$, $pFDR = 0.00967$, $\eta^2 = 0.184$; normalized saccade median (saccade median norm), $F(1, 60) = 9.80$, $pFDR = 0.01049$, $\eta^2 = 0.173$; number of fixations (n fixations), $F(1, 60) = 7.31$, $pFDR = 0.02659$, $\eta^2 = 0.135$; and normalized mean saccade amplitude (saccade mean norm), $F(1, 60) = 6.54$, $pFDR = 0.03235$, $\eta^2 = 0.122$.

We also conducted a 2 × 2 mixed ANOVA (group: first-degree relatives vs. controls; image type: landscape vs. abstract), $N = 51$ (relatives $n = 21$, controls $n = 30$), across multiple free-viewing scan metrics (number of fixations, duration metrics, dispersion and saccade amplitude indices, image coverage, entropy, etc.). At the uncorrected p -value level, trends suggested group differences in fixation spatial dispersion and saccade amplitude. Relatives showed lower horizontal and vertical dispersion (dispersion_x: $F(1, 51) = 4.77$, $p = 0.038$, $\eta^2 = 0.15$; dispersion_y: $F(1, 51) = 4.48$, $p = 0.044$, $\eta^2 = 0.14$), as well as lower mean dispersion (mean_dispersion: $F(1, 51) = 4.66$, $p = 0.039$, $\eta^2 = 0.15$) compared with controls, consistent with a more compact, more constrained scanpath. A similar trend was observed for normalized mean saccade amplitude (saccade mean norm: $F(1, 51) = 4.28$, $p = 0.049$, $\eta^2 = 0.14$) as well as a borderline image type × group interaction for horizontal dispersion (dispersion_x: $F(1, 51) = 4.25$, $p = 0.049$, $\eta^2 = 0.14$). However, none of these effects remained statistically significant after FDR correction.

Discussion

Summary of the main findings

The present study demonstrated a consistent and robust main effect of group on key parameters of the oculomotor profile and visual exploration when comparing patients versus controls. These effects remained significant after FDR correction and were of medium to large magnitude ($\eta^2 \approx 0.12$ – 0.21). The clearest group separation was observed in metrics capturing “how broadly, diversely, and efficiently” the image was explored: normalized scanpath length, coverage, and entropy, as well as median/mean saccade amplitude and the number of fixations. In contrast, no main effect of image type was found, and no group × image type interaction survived FDR correction, pointing to a generalized (stimulus-nonspecific) profile of alteration.

In the relatives-versus-controls analysis, trends (uncorrected p values) suggested a more compact scanpath and lower fixation dispersion in relatives; however, no difference remained significant after FDR correction.

This observation raises the question of whether relatives exhibit a weak trait-like signal that requires greater statistical power and more precise stratification, or whether a true effect is absent.

What does “shorter scanpath, lower coverage, and lower entropy” mean?

The combination of a lower normalized scanpath length, lower spatial coverage, and lower fixation entropy in patients is consistent with a pattern of restricted visual exploration: gaze samples a smaller portion of the scene, the scanning route is less diverse, and the distribution of fixations is more stereotyped. Within the classical framework proposed by Yarbus (1967), according to which high-acuity visual processing is restricted to the fovea and efficient perception depends on selective gaze allocation, this pattern can be interpreted as a suboptimal deployment of foveal vision toward behaviorally relevant regions of the scene.

In practical behavioral terms, this may reflect reduced exploratory drive (a diminished tendency to actively seek new information), impaired executive guidance (less strategic shifting between informative regions), or increased inertia within local regions of interest (a narrower effective attentional window).

The fact that these differences emerge in integrative metrics (coverage, entropy, and scanpath length), rather than in stimulus-specific effects or interactions, supports the interpretation that they reflect a generalized alteration in the control of visual search rather than a selective deficit tied to a particular class of visual stimuli.

Challenges and limitations

The use of eye tracking in clinical populations with schizophrenia is associated with substantial practical and methodological limitations that may affect both data quality and sample representativeness. Patients often have difficulty maintaining a stable head position and may show disengagement and fluctuating concentration during the task, which can compromise calibration precision and fixation-detection accuracy; accordingly, participants in similar studies are frequently excluded due to excessive calibration error.

Variability in symptom severity, as indexed by PANSS scores, represents an additional confounding factor. Differences across positive, negative, and general psychopathology dimensions may differentially affect task engagement, attention, psychomotor speed, and the ability to comply with basic instructions (e.g., maintaining head stability and following the calibration target with the eyes only). Consequently, some patients fail to meet the minimal criteria for reliable measurement and discontinue participation already at the calibration stage, increasing within-group heterogeneity and reducing sensitivity to detect trait-like effects.

Furthermore, a subset of patients declines participation after being informed about the procedure, typically due to mistrust, suspiciousness, or delusional interpretations, such as fears of being monitored, recorded, or having their thoughts “read.” These reactions are consistent with paranoid ideation and passivity-related delusions commonly observed in schizophrenia. Also, they

may introduce selection bias, as participants who consent may systematically differ from non-participants in terms of insight, cognitive functioning, and symptom severity (Morita et al. 2019).

A further methodological challenge concerns the effects of antipsychotic medication. We cannot exclude the possibility that the observed alterations in visual exploration in patients were influenced by pharmacological treatment.

Finally, limited cooperation from close relatives constitutes an additional challenge, as relatives often refuse to participate, show little interest, or distance themselves from the research process, regardless of its relevance to understanding the disorder, thus limiting statistical power to detect subtler effects and complicates the evaluation of a potential familial component.

Conclusion

In the present study, we observed a robust main effect of group (patients vs. controls) on integrative indices of visual exploration and scanpath organization (normalized scanpath length, coverage, entropy, saccade parameters, and number of fixations), with effects surviving FDR correction and reaching medium-to-large magnitudes. Also, this profile is conceptually consistent with the work of Beedie et al. (2011), which reports atypical (more restricted) scanpaths in schizophrenia in “simple/free viewing” paradigms and discusses whether they reflect a trait- or state-dependent phenomenon. In addition, our data showed no robust main effect of image type and no group \times image type interaction after correction, supporting the interpretation of a stimulus-nonspecific exploration deficit (i.e., a generalized scanning mode), in line with the broader argument in this literature for more general mechanisms of disrupted visual–cognitive control (Beedie et al. 2011).

In the relatives-versus-controls contrast, no reliable group effects were detected after FDR correction, despite uncorrected trends and moderate-to-large effect sizes for some metrics. This places our findings closer to the conclusion that, in the “free viewing” configuration used here, the atypical scanning profile is more clearly expressed in the clinical group. In contrast, a potential endophenotypic signal in relatives may be weaker, more heterogeneous, or dependent on statistical power and metric selection. In this context, the classic eye-movement (EEM) line by Kojima et al. (1992, 2001) is relevant: stable and informative markers such as NEF and RSS have been validated in multicenter frameworks, but in different tasks and using different exploration indices, suggesting that the familial/vulnerability component may require a more targeted paradigm or a predefined core set of metrics.

The differences observed in visual-exploration parameters (fixation/scanpath length, coverage, entropy, and related indices of saccadic organization) in patients relative to controls support the concept of restricted free visual scanning in schizophrenia and are consistent with evidence that simple-viewing metrics can discriminate clinical cases from healthy controls (Beedie et al. 2011; Benson et al. 2012). Accordingly, these measures may be considered candidate oculomotor markers. Future studies with greater statistical power, a predefined core set of metrics, and family/genetic analyses (e.g., heritability/PRS) are needed to clarify the extent to which the observed deviations reflect current clinical-state effects versus a stable risk-related trait.

Additional information

Conflict of interest

The authors have declared that no competing interests exist.

Ethical statements

Clinical trials: Department of acute psychotic disorders of First Psychiatric Clinic of UMHAT-Dr Georgi Stranski - EAD.

The authors declared that experiments on humans or human tissues were performed for the present study.

Informed consent from the humans, donors or donors' representatives: Ethics Committee of the Medical University – Pleven.

The authors declared that no experiments on animals were performed for the present study.

The authors declared that no commercially available immortalised human and animal cell lines were used in the present study.

Use of AI

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Author contributions

Conceptualization: GDY. Data curation: GDY. Formal analysis: IIV, KS, GDY. Investigation: SK, IIV, GB, KS, AAT, GDY, EDI, SM. Methodology: GDY. Project administration: GDY, PCT. Supervision: PCT. Writing - original draft: GDY. Writing - review and editing: PCT.

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Data availability

All of the data that support the findings of this study are available in the main text.

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