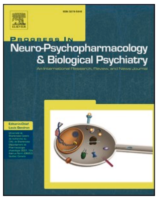
Progress in Neuropsychopharmacology & Biological Psychiatry 118 (2022) 110578

Contents lists available at ScienceDirect

Progress in Neuropsychopharmacology & Biological Psychiatry

journal homepage: www.elsevier.com/locate/pnp



The impact of COVID-19 pandemic on individuals at clinical high-risk for psychosis: Evidence from eye-tracking measures

Dan Zhang [a], Qian Guo [a,d,*], Lihua Xu [a], Xu Liu [a], TianHong Zhang [a], Xiaohua Liu [d], Haiying Chen [d], Guanjun Li [a,**], Jijun Wang [a,b,c,*]

[a] *Shanghai Key Laboratory of Psychotic Disorders, Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, Shanghai 200030, PR China*
[b] *CAS Center for Excellence in Brain Science and Intelligence Technology (CEBSIT), Chinese Academy of Science, Shanghai 201203, PR China*
[c] *Institute of Psychology and Behavioral Science, Shanghai Jiao Tong University, Shanghai 200030, PR China*
[d] *Department of Early Psychotic Disorders, Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, Shanghai 200030, PR China*

ARTICLE INFO

Keywords:
Clinical high-risk for psychosis
COVID-19
Psychological distress
Eye movement

ABSTRACT

Emerging evidence suggested that people with severe mental disorders were more vulnerable to the negative effects of the COVID-19 pandemic. However, few researches investigated the influence of global pandemics on people at clinical high risk (CHR) for psychosis. This study aimed to investigate the impact of the COVID-19 pandemic on clinical symptoms, psychological distress, and eye-tracking characteristics in CHR individuals and healthy participants. Forty-nine CHR individuals and 50 healthy controls (HC) were assessed by PTSD Checklist for DSM-5 (PCL-5), Perceived Stress Scale, 10-item version (PSS-10), and Coronavirus Impact Scale (CIS). Eye movement performances were measured by the tests of fixation stability, free-viewing, and anti-saccade. According to the mean score of CIS, participants were stratified into high-impact ($n = 35$) and low-impact ($n = 64$) subgroups. Compared with the HC group, CHR participants reported significantly higher levels of post-traumatic symptoms caused by the COVID-19 pandemic and showed abnormalities in most of the eye movement indexes. Among the altered indexes, the saccade amplitude of fixation stability test (far distractor), the scan path length of free-viewing test, and the accuracy of anti-saccade test were negatively affected by the severity of impact level in the CHR group. Moreover, the altered eye movement indexes were significantly associated with the total scores of CIS, PCL-5, and subscales of the Scale of Prodromal Syndromes (SOPS) among CHR individuals. Overall, our findings suggested the negative impact of the COVID-19 pandemic on the eye movement characteristics of CHR individuals. The present study provides valuable information on physiological distress related to the COVID-19 pandemic and sensitive neuropsychological biomarkers that interacted with social and environment stress in the CHR population.

1. Introduction

The ongoing coronavirus disease −19 (COVID-19) pandemic has caused a profound impact on mental health issues across the world (Shahrour and Dardas, 2020). Of note, people with psychotic disorders may suffer more from the impact of the pandemic (Kozloff et al., 2020; Yao et al., 2020). It is reported that many factors could cause the progression of symptoms and relapse in patients with psychiatric disorders, including social distancing (Kozloff et al., 2020), inadequate awareness of risk, reduced access to health care, and restrictive conditions in psychiatric wards (Yao et al., 2020). In addition, months of real-time isolation could significantly increase psychiatric morbidity and hospital admissions (O'Donoghue et al., 2021). Although emerging evidence indicated that COVID-19 might have a profound negative impact

---

Abbreviations: CHR, clinical high-risk for psychosis; HC, healthy control; PTSD, posttraumatic stress disorder; PCL-5, PTSD Checklist for DSM-5; PSS-10, Perceived Stress Scale, 10-item version; CIS, Coronavirus Impact Scale; SHARP, ShangHai-At-Risk-for-Psychosis; SIPS/SOPS, Prodromal Symptoms/Scale of Prodromal Syndromes.

[*] Corresponding authors at: Shanghai Key Laboratory of Psychotic Disorders, Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, Shanghai 200030, PR China.

[**] Corresponding author at: Department of Early Psychotic Disorders, Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, Shanghai 200030, PR China.

E-mail addresses: guoqian1205@vip.163.com (Q. Guo), liguanjun66@126.com (G. Li), jijunwang27@163.com (J. Wang).

https://doi.org/10.1016/j.pnpbp.2022.110578
Received 30 November 2021; Received in revised form 18 May 2022; Accepted 19 May 2022

on patients with schizophrenia (Kozloff et al., 2020), there has been no research investigating this impact in people at clinical high risk (CHR) for psychosis so far.

It's proposed that the onset of psychosis is caused by a series of risk factors, including epigenetics (Richetto and Meyer, 2021), stress (Bentley et al., 2016), and environmental factors during the prenatal stage, childhood, adolescence, and early adulthood. A previous study reported that the incidence of schizophrenia among Caribbean migrants in Europe was nearly seven times higher than that of non-migrants in Europe, indicating that apparent social stress, such as acute life events and chronic social adversity, might play a crucial role in the onset of psychosis (Harrison et al., 1997). Conversely, the conversion to schizophrenia was significantly lower than expected in areas with robust family support systems (Menezes et al., 2007). In line with the above findings, it's posited that social support is associated with the symptoms and COVID-19 impact in patients with schizophrenia. For example, patients with poor social support were more susceptible to social distancing during the COVID-19 pandemic and showed further progression in paranoid thinking, depression, and suicide ideation (Hamada and Fan, 2020), indicating an increased stress level in schizophrenia during the pandemic. Other negative factors such as surfeit information about COVID-19 infection and fear of acquiring infection have also been proposed as potential triggers for the progression of psychotic symptoms (Zhand and Joober, 2021). However, there has been rare study investigating the related neurophysiological changes in the schizophrenia spectrum during the pandemic. And the biological mechanisms underlie this increased stress level are still unrevealed.

In recent two decades, researches have been focusing on individuals at clinical high risk (CHR) for psychosis, which are characterized by subthreshold psychotic symptoms and impairment in social function (Cannon, 2015). Accumulated evidence indicated that CHR individuals were particularly vulnerable to stress (Palmier-Claus et al., 2012). The abnormal responses to stress could indicate the onset of psychosis (Pruessner et al., 2011) and predict the 6-month conversion (Yung et al., 2005). However, there is still debate about whether social distancing might serve as a buffer or a pressure for CHR during the COVID-19 pandemic (Mittal et al., 2021).

Eye movement abnormalities have been identified as an "endophenotype" in schizophrenia (Kacur et al., 2020). Schizophrenia patients manifested abnormal performances in multiple eye movement tasks, comprising fixation stability, free-viewing, smooth pursuit, and saccadic tests (Benson et al., 2012; Morita et al., 2017; Wolf et al., 2021). Evidence suggested that aberrant performances of eye movement were also observed prior to the onset of psychosis. For instance, altered indicators, including increased error rates of the anti-saccade (Nieman et al., 2007; Obyedkov et al., 2019), pro-saccade (Obyedkov et al., 2019), and memory-guided saccade tests (Caldani et al., 2017) along with prolonged anti-saccade latency (Kleineidam et al., 2019), were frequently reported in CHR population. Additionally, eye movement indexes were observed to be associated with levels of psychological stress in intensive care unit nurses (Ahmadi et al., 2022) and were also altered in the individuals diagnosed with posttraumatic stress disorder (PTSD) (Coll et al., 2022), suggesting the potential of eye movement metrics as markers of psychological stress (Skaramagkas et al., 2021). As a measure with advantages in both convenience and non-invasion, the eye-tracking technique could be a promising approach for identifying the neuropsychological status of CHR individuals during the COVID-19 pandemic.

In the present study, we aimed to investigate the impact of the COVID-19 pandemic on clinical symptoms, psychological distress, and eye-movement characteristics in CHR individuals and healthy controls (HCs). We hypothesized that 1) CHR individuals would show significant abnormalities in eye movement characteristics; 2) compared with HCs, CHR individuals would be more susceptible to the impact of the COVID-19 pandemic, both on the levels of psychological status and eye movement indicators. As an additional analysis, we also explored the linear associations between eye movement, psychological and clinical characteristics in both groups.

2. Methods

2.1. Study design and participants

Participants were recruited from August 2020 to September 2021 at the Shanghai Mental Health Center as a part of the Shanghai At-Risk for Psychosis (SHARP) Extending program (Zhang et al., 2014; Zhang et al., 2017). This study was approved by the local ethics committees at the Shanghai Mental Health Center. All participants or their legal guardians (those younger than 18) signed the informed consent documents prior to study participation.

Forty-nine CHR individuals participated in the study. All patients fulfilled the diagnostic criteria for CHR for psychosis based on the Chinese version of the Structured Interview for Prodromal Syndromes (SIPS) and the Scale of Prodromal Symptoms (SOPS) as identified by a senior psychiatrist (Miller et al., 2003; Miller et al., 2002). CHR individuals included in the study met at least one of the following criteria: (1) attenuated positive symptom syndrome, (2) brief limited intermittent psychotic syndrome, and (3) genetic risk and deterioration syndrome. All participants were between the ages of 15 and 45 years and received at least six years of formal education. Exclusion criteria included: 1) diagnosed with organic mental disorders or other serious physical diseases, 2) taking any drugs that may affect their mental and cognitive functions, 3) being treated with antipsychotics, and 4) diagnosed with any ophthalmological disease that severely affects vision.

Fifty HCs joined our study through online advertisement. HCs were screened by a professional psychiatrist with the Chinese version of the Mini International Neuropsychiatric Interview, Version 5.0 (Sheehan et al., 1998; Si et al., 2009) to exclude any psychiatric disorder. HCs with any mental illness history, family history of mental illness, or ophthalmological disease affecting vision were excluded.

2.2. Psychological assessments

Psychological assessments were performed by the panel consisting of the PTSD Checklist for DSM-5 (PCL-5) (Wortmann et al., 2016), Perceived Stress Scale, 10-item version (PSS-10) (Barbosa-Leiker et al., 2013), and Coronavirus Impact Scale (CIS) and detailed as follow: 1) PCL-5 was a 20-item scale scored at 5 points [0 (none at all) to 4 (very much)], which assessed PTSD symptoms in the DSM-5. PCL-5 was used to determine the levels of psychological distress among CHR individuals and to compare the rate of probable PTSD symptoms between CHR and HC groups. The Cronbach α reliability coefficient of PCL-5 in our study was 0.93. 2) PSS-10, consisting of ten items, was employed to assess how uncontrollable, unpredictable, or overloaded an individual has felt in their life in the past month. The Cronbach α reliability coefficient of the PSS-10 scale was 0.70. 3) CIS (https://www.nlm.nih.gov/dr2/Coronavirus_Impact_Scale.pdf) was used to investigate the overall impact of COVID-19 on people, including aspects of employment, food access, medical health care access, mental health treatment access, social supports, experiences of stress, and the status of COVID-19 diagnosis. The scoring items included 11 questions, with the first nine items scored at 4 points (0: No change/None to 3: Severe), and the 10th and 11th items scored at 5 points (0: None to 4: died from coronavirus) (Supplementary materials Table S1). The Cronbach α reliability coefficient of the CIS scale was 0.69. The reliability and validity of Chinese translations of PSS-10 (Wang et al., 2011) and PCL-5 (Guo et al., 2020; Li et al., 2019) have been verified by early studies.

2.3. Eye-tracking measurements

2.3.1. Fixation stability test

In the beginning, participants were instructed to look at a black "+" in the center of the white screen. When the stimulus (a solid black dot) appeared, they were asked to keep their eyes on the solid black dot and ignore the distracting stimulus nearby. The test comprised two paradigms with a near distractor and a far distractor, including five trials in each. Distractors in the shape of starflowers were about the same size as the target fixation point (size 0.5°), appearing at the left or right of the target fixation point at different distances (one distractor appeared at a random position each time). Average fixation duration and average saccade amplitude were calculated to measure the fixation stability of participants.

2.3.2. Free-viewing test

The participants were required to freely view different types of images. The test consisted of 35 black and white images, including social scenes, natural landscapes, stationary objects (rabbits, bicycles, shoes, etc.), and meaningless images (rows of stripes, blurred noises, etc.). Each image was presented randomly for 10 s. Among those images, participants were asked to look at the black "+" in the center of the screen for 1.5 s. Three indicators were analyzed, including average fixation duration, average saccade amplitude, and scan path length.

2.3.3. Anti-saccade test

Participants were asked to firstly look at a "+" (black) in the center of the screen for 1.5 s. When the target stimulus (hollow dot) appeared, and the "+" disappeared, the participants were required to look to the opposite side of the target position (mirror position) as quickly and accurately as possible. A total of 8 trials were completed, and each stimulus was presented for 1000 ms. The stimulus was displayed in random directions to avoid anticipatory saccadic interference. The accuracy and mean latency of the correct anti-saccades were collected.

2.4. Data collection and procedures

EYE LINK 2000 Desktop (SR Research, Ottawa, Canada) was used for eye-tracking data detection. A 9-point calibration mode was adopted to collect the dominant eye data at a sampling frequency of 1000 Hz. The subject's eyes were positioned at the same height as the center of the screen and 50 cm away from the screen. The subject's head was fixed on the jaw rest, and the eye movements were tracked in a horizontal position (±30°) and vertical position (±30°). The screen was a 17-in. monitor with a 1024 × 768 pixels resolution. The experiment was conducted in a quiet, independent room without bright light stimulation.

2.5. Statistical analysis

Statistical analyses were conducted using R (Version 3.6.0), with package "psych" and package "ggplot2" (Team, 2018). Prior to the analysis, we identified and removed flicker artifacts, fixations under 20 milliseconds or outside the screen, and saccades out of the screen or from outside the screen for data cleaning (Morita et al., 2017). Univariate extreme outliers were identified by histograms and box plots. The outliers were replaced with the next lowest or highest observed value via the winsorization method (Tabachnick and Fidell, 2019) to reduce the influence of the outliers on the statistical test. Demographics and clinical characteristics were analyzed by χ^2 test and independent-sample t-test. Participants were divided into two subgroups (high CIS level and low CIS level) based on the mean score of CIS. One-way MANOVA was performed in each eye movement measure of all three paradigms, with group and impact level of CIS as fixed factors. For the eye movement indicators with significant between-group differences, partial correlation analysis was performed to detect the relationship between those indicators and clinical characteristics, with age, education, and gender as covariates.

3. Results

3.1. Demographic and clinical characteristics

The CHR group and HC group didn't show significant difference in age ($t = -1.849$, $p = 0.067$), gender ($\chi^2 = 0.857$, $p = 0.355$), or education level ($\chi^2 = 1.656$, $p = 0.198$). Compared with HCs, CHR group demonstrated significantly elevated total scores of PCL-5 ($t = 8.178$, $p < 0.001$), with six CHR individuals scored equal to or more than 33, while no HC scored equal to or more than 33. No significant differences were observed in PSS-10 ($t = 1.000$, $p = 0.320$) and CIS scales ($t = 1.085$, $p = 0.281$) between two groups. Since the average CIS score of all participants was 3.49, subjects with a score greater than 4 were defined as the high-level impact group (CHR: $n = 20$; HCs: $n = 15$), while those with a score less than or equal to 4 were defined as the low-level impact group (CHR: $n = 29$; HCs: $n = 35$). Detailed demographics and clinical characteristics were illustrated in Table 1.

3.2. Group comparisons and the effects of the COVID-19 pandemic on eye movement indicators

3.2.1. Fixation stability test

Examples of the anti-saccade, free-viewing, and fixation stability tests are illustrated in Fig. 1. In the near distractor paradigm, only the average saccade amplitude showed significant group difference ($F = 6.129$, $p = 0.015$, $\eta_p^2 = 0.061$). There was no significant group effect in average fixation duration, and neither were any interaction effects between group and COVID-19 impact levels in the average saccade amplitude or average fixation duration (Table 2).

Under the far distractor condition, significant group effect ($F = 7.037$, $p = 0.009$, $\eta_p^2 = 0.069$) and group × impact interaction ($F = 6.176$, $p = 0.015$, $\eta_p^2 = 0.061$) were observed in average saccade amplitude (Fig. 2, Table 2). CHR individuals exhibited greater average saccade amplitude compared to HCs. For the interaction effect, the simple effect analysis demonstrated that CHR individuals with high-impact level of CIS showed significantly increased average saccade amplitude ($F = 4.294$, $p = 0.041$, $\eta_p^2 = 0.043$) than those with low-impact level of CIS, while HCs with different levels of CIS showed no

Table 1

Demographic, psychological, and clinical characteristics.

	CHR ($n = 49$)	HC ($n = 50$)	t/χ^2	p value	Cohen d
Age (years)	19.80 (4.16)	21.08 (2.58)	−1.849	0.067	0.370
Gender (male/female)	30/19	26/24	0.857	0.355	–
Education (primary school/middle school/ bachelor degree)	0/43/6	0/39/ 11	1.656	0.198	–
PCL-5 Total Score	17.12 (12.59)	2.36 (2.08)	8.178	< 0.001	1.636
PSS-10 Total Score	19.22 (5.23)	18.14 (5.56)	1.000	0.320	0.200
CIS Total Score	3.80 (3.08)	3.20 (2.34)	1.085	0.281	0.219
SOPS Positive Score	7.12 (3.36)	–	–	–	–
SOPS Negative Score	9.51 (5.46)	–	–	–	–
SOPS Disorganized Score	3.82 (2.78)	–	–	–	–
SOPS General Score	5.96 (3.38)	–	–	–	–
SOPS Total Score	26.41 (11.88)	–	–	–	–

Note: Continuous variables are shown using Mean (SD).

Abbreviations: PCL-5, PTSD Checklist for DSM-5; PSS-10, Perceived Stress Scale, 10-item version; CIS, Coronavirus Impact Scale; SOPS, Scale of Prodromal Syndromes; SD, Standard Deviation.

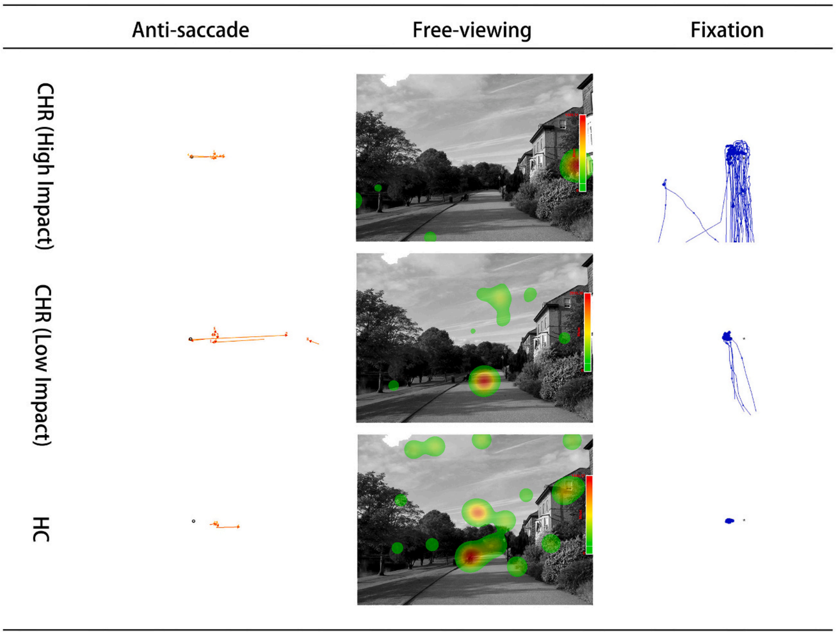


Fig. 1. An example of temporal graph views of the anti-saccade test, fixation heat map of the free-viewing test, and trace plots of the fixation stability test. Each row indicated the performance of one individual (CHR with high-level impact, CHR with low-level impact, and HC, respectively). Abbreviations: CHR, clinical high risk for psychosis; HC, healthy control.

difference ($F = 2.138$, $p = 0.147$, $\eta_p^2 = 0.022$). No statistical group effect or group × impact interaction was discovered in average fixation duration (Table 2).

3.2.2. *Free-viewing test*

Compared with HCs, CHR group exhibited a strong trend of reduced average saccade amplitude ($F = 3.926$, $p = 0.050$, $\eta_p^2 = 0.040$), significantly shortened scan path length ($F = 7.423$, $p = 0.008$, $\eta_p^2 = 0.072$) and increased average fixation duration ($F = 5.667$, $p = 0.019$, $\eta_p^2 = 0.057$) (Table 2). However, only the scan path length showed significant group × impact interaction ($F = 4.980$, $p = 0.028$, $\eta_p^2 = 0.050$) (Fig. 2, Table 2.). The simple effect analysis implicated that CHR individuals with high-impact level of CIS had more diminished scan path length than those with low-impact level of CIS ($F = 6.976$, $p = 0.010$, $\eta_p^2 = 0.068$). On the contrary, the effect of the CIS impact level was not significant in HCs ($F = 0.334$, $p = 0.565$, $\eta_p^2 = 0.004$) (Table 2).

3.2.3. *Anti-saccade test*

There were significant group difference in latency ($F = 4.387$, $p = 0.039$; $\eta_p^2 = 0.044$) and trending difference in accuracy ($F = 3.684$, $p = 0.058$; $\eta_p^2 = 0.037$). Significant effect in group × impact interaction ($F = 8.028$, $p = 0.006$; $\eta_p^2 = 0.078$) was observed in accuracy (Fig. 2, Table 2.). CHR participants with high-impact level of CIS exhibited significantly lower accuracy than those with low-impact level ($F = 4.428$, $p = 0.038$; $\eta_p^2 = 0.045$), while HCs with different levels of CIS showed no difference in accuracy ($F = 3.650$, $p = 0.059$; $\eta_p^2 = 0.037$). No significant group × impact interaction was discovered in latency (Table 2).

3.3. *Associations between eye movement, psychological, and clinical characteristics*

In the CHR group, CIS scores were remarkably correlated with the scan path length of the free-viewing test ($r = -0.329$, $p = 0.026$), and PCL-5 scores were positively correlated with the average saccade amplitude of the fixation stability test (near distractor) ($r = 0.302$, $p = 0.041$). The negative symptoms of SOPS were negatively associated with the average saccade amplitude of the free-viewing test ($r = -0.306$, $p = 0.039$). The disorganized symptoms of SOPS were positively correlated with the average saccade amplitude of the fixation stability test (near distractor) ($r = 0.294$, $p = 0.047$) while negatively associated with the accuracy of the anti-saccade test ($r = -0.310$, $p = 0.036$). The general symptoms of SOPS were positively correlated with average fixation duration of the free-viewing test ($r = 0.315$, $p = 0.033$). Moreover, PCL-5 scores were positively associated with total sores of PSS-10 ($r = 0.601$, $p < 0.001$) among CHR individuals (Table 3).

Additionally, in the HC group, significant correlations were also observed in PCL-5 scores with CIS scores ($r = 0.338$, $p = 0.022$) and PSS-10 scores ($r = 0.425$, $p = 0.003$). Meanwhile, there was no correlation between the eye movement indexes and any psychological scales (Supplementary materials Table S2).

4. Discussion

To our knowledge, our study is the first to investigate the impact of the COVID-19 pandemic on the eye movement characteristics of CHR individuals. Compared with HCs, CHR individuals presented higher post-traumatic symptoms related to the COVID-19 pandemic. Compared with those with lower impact level of the COVID-19 pandemic, CHR individuals with higher impact level exhibited severer deficits in the average saccade amplitude of the fixation stability test (far distractor), the scan path length of the free-viewing test, and the accuracy of the anti-saccade test. While the COVID-19 pandemic showed no impact on the above parameters in HCs. Furthermore, altered eye movement characteristics were associated with the PTSD, negative, general, and disorganized symptoms in the CHR group. Overall, our results suggested that the vulnerability to COVID-19 pandemic-related stress might manifest in the eye movement features in CHR individuals.

Given the profound influence of the COVID-19 outbreak, it was not surprising that CHR individuals experienced higher levels of post-traumatic symptoms. As reported, a considerable proportion of individuals experienced emotional impact or mental trauma due to the psychological sequelae of disasters (Benight and Harper, 2002). Due to the medical inconvenience caused by social isolation, individuals might be more prone to psychological stress reactions, including depression, anxiety, anger, and even violent impulse. Unlike individual-level traumatic events, the COVID-19 outbreak could act as a continuing crisis

Table. 2
Group comparison and COVID-19 impact on eye-movement characteristics: MANOVA results for each paradigms.

	CHR [Mean (SD)]	HC [Mean (SD)]	*F value*	*p value*
Fixation stability test (near distractor)				
Average saccade amplitude (degree)	1.91 (1.23)	1.44 (0.81)	**$F_{Group} = 6.129$** $F_{impact} = 0.082$ $F_{Interaction} = 1.536$	**$p = 0.015$*** $p = 0.775$ $p = 0.218$
Average fixation duration (ms)	925.65 (564.14)	1001.50 (628.64)	$F_{Group} = 0.141$ $F_{impact} = 0.087$ $F_{Interaction} = 0.407$	$p = 0.708$ $p = 0.769$ $p = 0.525$
Fixation stability test (far distractor)				
Average saccade amplitude (degree)	2.10 (1.01)	1.74 (0.72)	**$F_{Group} = 7.037$** $F_{impact} = 0.127$ **$F_{Interaction} = 6.176$**	**$p = 0.009$*** $p = 0.722$ **$p = 0.015$***
Average fixation duration (ms)	896.04 (519.10)	980.20 (648.04)	$F_{Group} = 0.401$ $F_{impact} = 0.040$ $F_{Interaction} = 0.002$	$p = 0.528$ $p = 0.842$ $p = 0.963$
Free-viewing test				
Average saccade amplitude (degree)	4.96 (1.22)	5.42 (1.01)	$F_{Group} = 3.926$ $F_{impact} = 0.004$ $F_{Interaction} = 0.058$	$p = 0.050$ $p = 0.949$ $p = 0.810$
Average fixation duration (ms)	409.29 (244.17)	313.94 (95.76)	**$F_{Group} = 5.667$** $F_{impact} = 0.056$ $F_{Interaction} = 0.019$	**$p = 0.019$*** $p = 0.814$ $p = 0.891$
Scan path length (degree)	118.83 (39.67)	135.11 (30.78)	**$F_{Group} = 7.423$** $F_{impact} = 1.933$ **$F_{Interaction} = 4.980$**	**$p = 0.008$*** $p = 0.168$ **$p = 0.028$***
Anti-saccade test				
Accuracy	0.46 (0.10)	0.48 (0.08)	$F_{Group} = 3.684$ $F_{impact} = 0.003$ **$F_{Interaction} = 8.028$**	$p = 0.058$ $p = 0.959$ **$p = 0.006$***
Latency (ms)	507.19 (113.62)	475.28 (73.29)	**$F_{Group} = 4.387$** $F_{impact} = 0.213$ $F_{Interaction} = 3.569$	**$p = 0.039$*** $p = 0.645$ $p = 0.062$

Note: Parts marked in bold and "*" indicated significant results ($p < 0.05$).

that profoundly affected every member of society. Evidence suggested that the PTSD symptoms not only occurred shortly after the sudden outbreak of COVID-19 (González-Sanguino et al., 2020; Liu et al., 2020; Tang et al., 2020) but also existed in the general population for a long time (Benfante et al., 2022), even after controlling the spread of COVID-19 in China (Shen et al., 2021). In the current study, 12.24% of CHR individuals scored higher than 33 in PCL-5 and were identified as experiencing obvious PTSD symptoms, while no HC scored equal to or more than 33. Further, our results demonstrated that the scores of PCL-5 were positively correlated with scores of PSS-10 in CHR and HC groups while paralleled with scores of CIS in HC group. Such findings implicated that the PTSD symptoms were paralleled with the levels of perceived stress and COVID-19 pandemic-related stress in our study. Taken together, from the perspectives of epidemiology and health economics, it calls for bringing more concerns to the PTSD symptoms in CHR individuals instead of the whole general population.

Our results demonstrated similar stress and impact level caused by COVID-19 in CHR and HC groups. A relatively small sample size might account for this. Besides, our findings might support a theory that the impact of the COVID-19 pandemic on CHR could be heterogeneous (de Figueiredo et al., 2021). For example, CHR individuals with pronounced distress during social interactions or experiencing social pressure-triggered delusions and hallucinations might contrarily benefit from social isolation during the pandemic. Recent research revealed increased asociality among CHR individuals during the pandemic compared to pre-pandemic levels but no decline in global negative symptoms or functioning (Strauss et al., 2022). Nevertheless, the divergent patterns of eye-tracking performances observed in subgroups reflected the neurobiological abnormalities in CHR, suggesting subtle neurobiological examinations might be valuable to detect the COVID-19 impact on the schizophrenia spectrum.

Among the impaired eye movement indexes in the CHR group, we observed a strong effect of COVID-19 impact on the average saccade amplitude of the fixation stability (far distractor), the scan path length of free-viewing, and the accuracy of the anti-saccade tests. In the fixation stability task, the average saccade amplitude evaluates the degree of fixation convergence (Gooding et al., 2000). Poor fixation stability might be related to the impairment of the dorsal prefrontal cortex, colliculus (Pretegiani and Optican, 2017), and visual cortex (V2 and V4) (Pirdankar and Das, 2016). As for the performance of free-viewing in CHR group, the restricted scanning path pattern characterized by longer fixation duration, decreased saccade amplitude, and shorter scan path length found in our study was also in line with the findings in schizophrenia patients (Huang et al., 2020; Oh et al., 2014). Of note, the scan path length of free-viewing was the most prominent feature affected by COVID-19 impact among CHR individuals and was highly correlated with the severity of the impact level. This index represented a common deficit in schizophrenia and served as the most robust discriminator between schizophrenia patients and HCs (Benson et al., 2012). Moreover, as we reported, the average saccade amplitude was negatively related to negative symptoms of SOPS, while the average fixation duration was positively correlated with general symptoms. This suggested an altered free-viewing pattern as a stable trait associated with clinical features and could serve as potential biomarkers for stress response in CHR individuals during the pandemic period (Huang et al., 2021). With regard to the anti-saccade test, the current study revealed longer latency and marginally reduced accuracy in the CHR group, with the accuracy being more sensitive to the level of COVID-19 impact. The performance of the anti-saccade test represented executive inhibition, which corresponded to the function of the prefrontal system (Curtis and Connolly, 2008). An earlier study has demonstrated that patients with impairment of the VLPFC brain region exhibited difficulty inhibiting eye movement and showed a lower accuracy in anti-saccades (Hodgson et al., 2007; Leung and Cai, 2007). In general, our findings implicated that the impact of the COVID-19 pandemic might, to some extent, aggravate the existing vulnerability of neural regulation to stress in CHR individuals.

Emerging studies have investigated the psychological illness of patients with COVID-19 (Guo et al., 2020). Preliminary studies also suggested a compromised psychological status in the general population due to the long-time exposure to the COVID-19 outbreak (Wang et al., 2020). On top of this, our study further suggested that the COVID-19 pandemic could cause more neuropsychological distress in CHR

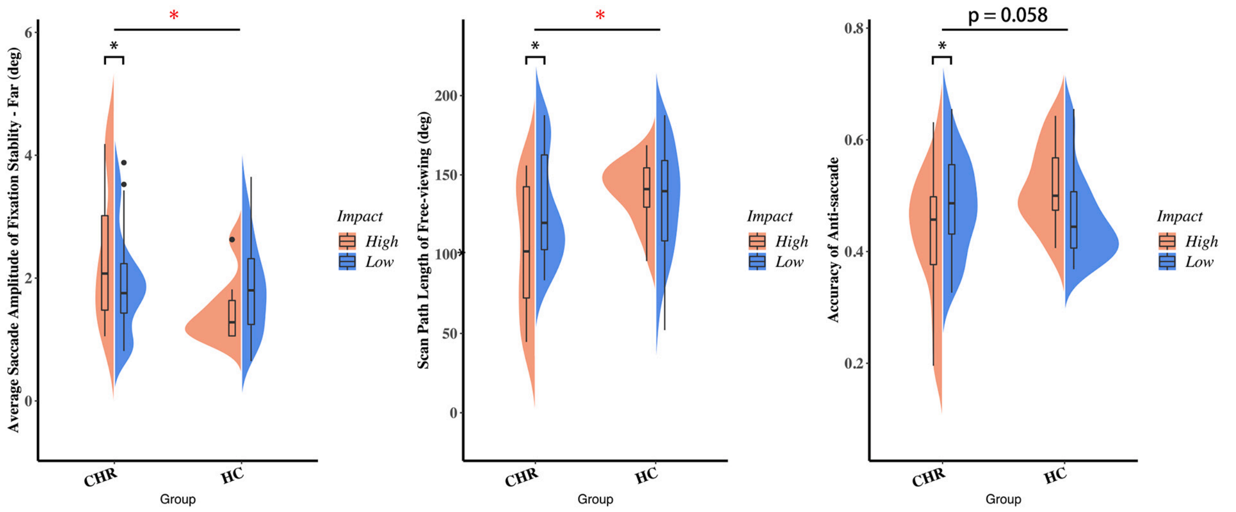


Fig. 2. Significant interaction effects of the group by the impact level on the eye movement indicators. Red "*" indicated significant group effects in MANOVA analysis, while black "*" represented significant simple effects on subgroup analysis within CHR group. Abbreviations: CHR, clinical high risk for psychosis; HC, healthy control. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 3
Associations between eye movement, psychological, and clinical characteristics in the CHR group.

	CIS Total Score	PSS-10 Total Score	PCL-5 Total Score	SacAmp_FS (N) *r* (*p*)	SacAmp_FS (F) *r* (*p*)	SacAmp_FV *r* (*p*)	FixDur_FV *r* (*p*)	ScanPath_FV*r* (*p*)	Accuracy_AS *r* (*p*)	Latency _AS *r* (*p*)
CIS Total Score	1	–	–	0.135 (0.370)	0.279 (0.060)	−0.089 (0.556)	−0.124 (0.413)	**−0.329 (0.026*)**	−0.147 (0.329)	0.061 (0.689)
PSS-10 Total Score	0.177 (0.240)	1	–	−0.125 (0.409)	−0.229 (0.126)	−0.058 (0.702)	−0.145 (0.337)	0.031 (0.838)	0.183 (0.224)	0.089 (0.557)
PCL-5 Total Score	0.228 (0.127)	**0.601 (<0.001*)**	1	**0.302 (0.041*)**	0.186 (0.215)	0.039 (0.795)	−0.088 (0.562)	0.128 (0.396)	0.068 (0.652)	0.194 (0.196)
SOPS Total Score	0.013 (0.933)	−0.125 (0.408)	−0.037 (0.807)	0.051 (0.736)	0.030 (0.845)	0.039 (0.795)	0.214 (0.152)	−0.223 (0.136)	−0.085 (0.574)	0.008 (0.956)
SOPS Positive Score	0.232 (0.121)	−0.003 (0.986)	0.054 (0.722)	0.042 (0.780)	−0.015 (0.923)	−0.072 (0.637)	0.069 (0.647)	−0.227 (0.130)	−0.104 (0.490)	0.101 (0.506)
SOPS Negative Score	0.003 (0.985)	−0.041 (0.788)	−0.012 (0.935)	0.013 (0.933)	0.023 (0.881)	**−0.306 (0.039*)**	0.170 (0.259)	−0.216 (0.149)	0.026 (0.864)	−0.189 (0.210)
SOPS Disorganized Score	−0.010 (0.947)	−0.194 (0.198)	0.022 (0.884)	**0.294 (0.047*)**	0.258 (0.083)	−0.110 (0.467)	0.125 (0.408)	−0.110 (0.466)	**−0.310 (0.036*)**	0.235 (0.116)
SOPS General Score	−0.181 (0.228)	−0.218 (0.145)	−0.182 (0.226)	−0.118 (0.434)	−0.124 (0.410)	−0.274 (0.066)	**0.315 (0.033*)**	−0.127 (0.402)	0.009 (0.951)	0.046 (0.762)

Note: Data marked in bold indicated significant correlations ($p < 0.05$).
Abbreviations: SacAmp, average saccade amplitude; ScanPath, scan path length; FixDur, average fixation duration; FS (N), fixation stability test (near distractor); FS (F), fixation stability test (far distractor); FV, free-viewing test; AS, anti-saccade test; CIS, Coronavirus Impact Scale; PCL-5, PTSD Checklist for DSM-5; PSS-10, Perceived Stress Scale, 10-item version; SOPS, Scale of Prodromal Syndromes.

individuals. Previous research revealed that neural maladaptation was significantly associated with more tremendous psychological stress during public speaking among CHR individuals (Appiah-Kusi et al., 2020). This result was partly in line with our work, which showed poorer eye-tracking performances among those CHR participants who endured more psychological distress during the pandemic. Further, neuropsychological responses to stress could be individualized. The evidence suggested that malfunctions in hippocampal activation and neuroendocrine level might be observed only in "stress-responsive" individuals (Pruessner et al., 2008). It echoed our findings in the high-level impacted CHR individuals, indicating the increased vulnerability in the CHR population when encountering elevated stress. Moreover, sustained social stress could predict poorer long-term global functional outcomes among CHR patients with social anxiety than others without (Deng et al., 2022). Such results highlighted the importance of longitudinal follow-up and assessments for CHR individuals who reported higher distress from the COVID-19 pandemic. In light of our study, two comments should be noted in future clinical practice: (a) it is of prospective significance to regularly assess the CHR individuals with the high-level impact of the pandemic, and (b) the psychological distress of CHR individuals should be detected and intervened as early as possible, especially the symptoms of post-traumatic stress caused by the pandemic.

Several limitations need to be taken into account. First, this study is a cross-sectional study. Thus, longitudinal research is required to explore the dynamic change of stress and eye movement performances during the pandemic. Such concern might be addressed by our ongoing SHARP extending project. Second, this study found some marginally significant results on psychological distress between CHR and HC groups, which might be due to the small sample size or heterogeneous response to COVID-19 impact among CHR individuals. Future research with a large sample is needed to validate our findings. Third, since other social or environmental stressors on the individual level were not assessed simultaneously, the results should be rendered with caution, and other stressful events except the COVID-19 pandemic should be recorded in future research. Finally, other advanced techniques such as neuroimaging could be used to further investigate the underlying neuropsychological mechanism caused by COVID 19 pandemic.

5. Conclusion

In summary, our study found that eye movement characteristics in CHR individuals were associated with psychological distress related to the COVID-19 pandemic. Moreover, CHR individuals with the high-level impact of the COVID-19 pandemic manifested more pronounced eye movement abnormalities than those with low-level influence. Our results provided insight into the influence of social and environmental stress on the neuropsychological status of CHR. More attention should be paid to the effects of the COVID-19 pandemic on CHR individuals in aspects of traumatic stress and neuropsychological performance to early predict and intervene in the risk of conversion.

Contributions of authors

G. Li, Q. Guo, J. Wang, and T. Zhang elaborated on the research project; X. Liu and H. Chen were responsible for recruiting patients and healthy participants. D. Zhang, L. Xu, and X. Liu carried out the data collection; D. Zhang and Q. Guo contributed to statistical analyses and the conceptualization of the manuscript. All authors were responsible for reviewing and approving the final manuscript.

Funding

This study is supported by the Excellent Talents Training Project of Shanghai Municipal Commission of Health (GVW-10.2-YQ44); Shanghai Clinical Research Center for Mental Health (19MC1911100); Key Project of Shanghai Mental Health Center (2019-zd01); Science and Technology Commission of Shanghai Municipality (21S31903100 and 20ZR1448600); Shanghai Jiao Tong University Foundation (ZH2018QNB19); National Natural Science Foundation of China under Grant No.62171269.

Ethical statement

This study was approved by the local ethics committee of the Shanghai Mental Health Center (smhcirb@163.com). The authors claimed that all procedures during this work were in accordance with the ethical standards of human experimentation and with the Hel- sinki Declaration of 1975, as revised in 2008.

Declaration of Competing Interest

The authors declare no conflict of interest.

Data availability

The data that has been used is confidential.

Acknowledgments

The authors thank all the volunteers and participants who took part in the study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pnpbp.2022.110578.

References

Ahmadi, N., Sasangohar, F., Yang, J., Yu, D., Danesh, V., Klahn, S., Masud, F., 2022. Quantifying workload and stress in intensive care unit nurses: preliminary evaluation using continuous eye-tracking. Hum. Factors 187208221085335. https://doi.org/10.1177/00187208221085335.

Appiah-Kusi, E., Petros, N., Wilson, R., Colizzi, M., Bossong, M.G., Valmaggia, L., Mondelli, V., McGuire, P., Bhattacharyya, S., 2020. Effects of short-term cannabidiol treatment on response to social stress in subjects at clinical high risk of developing psychosis. Psychopharmacology 237 (4), 1121–1130. https://doi.org/10.1007/s00213-019-05442-6.

Barbosa-Leiker, C., Kostick, M., Lei, M., McPherson, S., Roper, V., Hoekstra, T., Wright, B., 2013. Measurement invariance of the perceived stress scale and latent mean differences across gender and time. Stress. Health 29 (3), 253–260. https://doi.org/10.1002/smi.2463.

Benfante, A., Tesio, V., Di Tella, M., Romeo, A., Castelli, L., 2022. From the first to the second wave of COVID-19: anxiety, de-pressive, and post-traumatic stress symptoms in the Italian population. Int. J. Environ. Res. Public Health 19 (3). https://doi.org/10.3390/ijerph19031239.

Benight, C.C., Harper, M.L., 2002. Coping self-efficacy perceptions as a mediator between acute stress response and long-term distress following natural disasters. J. Trauma. Stress. 15 (3), 177–186. https://doi.org/10.1023/a:1015295025950.

Benson, P.J., Beedie, S.A., Shephard, E., Giegling, I., Rujescu, D., St Clair, D., 2012. Simple viewing tests can detect eye movement abnormalities that distinguish schizophrenia cases from controls with exceptional accuracy. Biol. Psychiatry 72 (9), 716–724. https://doi.org/10.1016/j.biopsych.2012.04.019.

Bentley, E., Millman, Z.B., Thompson, E., Demro, C., Kline, E., Pitts, S.C., DeVylder, J.E., Smith, M.E., Reeves, G., Schiffman, J., 2016. High-risk diagnosis, social stress, and parent-child relationships: a moderation model. Schizophr. Res. 174 (1–3), 65–70. https://doi.org/10.1016/j.schres.2016.04.014.

Caldani, S., Bucci, M.P., Lamy, J.C., Seassau, M., Bendjemaa, N., Gadel, R., Gaillard, R., Krebs, M.O., Amado, I., 2017. Saccadic eye movements as markers of schizophrenia spectrum: exploration in at-risk mental states. Schizophr. Res. 181, 30–37. https://doi.org/10.1016/j.schres.2016.09.003.

Cannon, T.D., 2015. How schizophrenia develops: cognitive and brain mechanisms underlying onset of psychosis. Trends Cogn. Sci. 19 (12), 744–756. https://doi.org/10.1016/j.tics.2015.09.009.

Coll, S.Y., Eustache, F., Doidy, F., Fraisse, F., Peschanski, D., Dayan, J., Gagnepain, P., Laisney, M., 2022. Avoidance behaviour generalizes to eye processing in posttraumatic stress disorder. Eur. J. Psychotraumatol. 13 (1), 2044661. https://doi.org/10.1080/20008198.2022.2044661.

Curtis, C.E., Connolly, J.D., 2008. Saccade preparation signals in the human frontal and parietal cortices. J. Neurophysiol. 99 (1), 133–145. https://doi.org/10.1152/jn.00899.2007.

de Figueiredo, C.S., Sandre, P.C., Portugal, L.C.L., Mázala-de-Oliveira, T., da Silva Chagas, L., Raony, Í., Ferreira, E.S., Giestal-de-Araujo, E., Dos Santos, A.A., Bomfim, P.O., 2021. COVID-19 pandemic impact on children and adolescents' mental health: biological, environmental, and social factors. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 106, 110171. https://doi.org/10.1016/j.pnpbp.2020.110171.

Deng, W., Addington, J., Bearden, C.E., Cadenhead, K.S., Cornblatt, B.A., Mathalon, D.H., Perkins, D.O., Seidman, L.J., Tsuang, M.T., Woods, S.W., Walker, E.F., Cannon, T.D., 2022. Characterizing sustained social anxiety in individuals at clinical high risk for psychosis: trajectory, risk factors, and functional outcomes. Psychol. Med. 1-8 https://doi.org/10.1017/s0033291722000277.

González-Sanguino, C., Ausín, B., Castellanos, M., Saiz, J., López-Gómez, A., Ugidos, C., Muñoz, M., 2020. Mental health consequences during the initial stage of the 2020 coronavirus pandemic (COVID-19) in Spain. Brain Behav. Immun. 87, 172–176. https://doi.org/10.1016/j.bbi.2020.05.040.

Gooding, D.C., Grabowski, J.A., Hendershot, C.S., 2000. Fixation stability in schizophrenia, bipolar, and control subjects. Psychiatry Res. 97 (2–3), 119–128. https://doi.org/10.1016/s0165-1781(00)00226-2.

Guo, Q., Zheng, Y., Shi, J., Wang, J., Li, G., Li, C., Fromson, J.A., Xu, Y., Liu, X., Xu, H., Zhang, T., Lu, Y., Chen, X., Hu, H., Tang, Y., Yang, S., Zhou, H., Wang, X., Chen, H., Wang, Z., Yang, Z., 2020. Immediate psychological distress in quarantined patients with COVID-19 and its association with peripheral inflammation: a mixed-method study. Brain Behav. Immun. 88, 17–27. https://doi.org/10.1016/j.bbi.2020.05.038.

Hamada, K., Fan, X., 2020. The impact of COVID-19 on individuals living with serious mental illness. Schizophr. Res. 222, 3–5. https://doi.org/10.1016/j.schres.2020.05.054.

Harrison, G., Glazebrook, C., Brewin, J., Cantwell, R., Dalkin, T., Fox, R., Jones, P., Medley, I., 1997. Increased incidence of psychotic disorders in migrants from the Caribbean to the United Kingdom. Psychol. Med. 27 (4), 799–806. https://doi.org/10.1017/s0033291796004643.

Hodgson, T., Chamberlain, M., Parris, B., James, M., Gutowski, N., Husain, M., Kennard, C., 2007. The role of the ventrolateral frontal cortex in inhibitory oculomotor control. Brain 130 (Pt 6), 1525–1537. https://doi.org/10.1093/brain/awm064.

Huang, L., Wei, W., Liu, Z., Zhang, T., Meur, O.L., 2020. Effective schizophrenia recognition using discriminative eye movement features and model-metric based features. Pattern Recogn. Lett. 138 (3), 608–616. https://doi.org/10.1016/j.patrec.2020.09.017.

Huang, W., Chen, C., Chen, X., Chen, X., Gan, J., Zhu, X., Xu, J., Zhao, L., Zhou, J., Yang, R., Lv, J., Liu, X., Li, H., 2021. Association between global visual scanning and cognitive function in schizophrenia. Asian J. Psychiatr. 56, 102559 https://doi.org/10.1016/j.ajp.2021.102559.

Kacur, J., Polec, J., Smolejova, E., Heretik, A., 2020. An analysis of eye-tracking features and modelling methods for free-viewed standard stimulus: application for schizophrenia detection. IEEE J. Biomed. Health Inform. 24 (11), 3055–3065. https://doi.org/10.1109/jbhi.2020.3002097.

Kleineidam, L., Frommann, I., Ruhrmann, S., Klosterkötter, J., Brockhaus-Dumke, A., Wölwer, W., Gaebel, W., Maier, W., Wagner, M., Ettinger, U., 2019. Antisaccade and prosaccade eye movements in individuals clinically at risk for psychosis: comparison with first-episode schizophrenia and prediction of conversion. Eur. Arch. Psychiatry Clin. Neurosci. 269 (8), 921–930. https://doi.org/10.1007/s00406-018-0973-4.

Kozloff, N., Mulsant, B.H., Stergiopoulos, V., Voineskos, A.N., 2020. The COVID-19 global pandemic: implications for people with schizophrenia and related disorders. Schizophr. Bull. 46 (4), 752–757. https://doi.org/10.1093/schbul/sbaa051.

Leung, H.C., Cai, W., 2007. Common and differential ventrolateral prefrontal activity during inhibition of hand and eye movements. J. Neurosci. 27 (37), 9893–9900. https://doi.org/10.1523/jneurosci.2837-07.2007.

Li, J., Zhang, W., Chen, W., Yuan, H., Zhang, S., Tian, M., Qu, Z., 2019. Applications of the Chinese version of the primary care PTSD screen for DSM-5 (PC-PTSD-5) for children. J. Affect. Disord. 254, 109–114. https://doi.org/10.1016/j.jad.2019.05.021.

Liu, C.H., Zhang, E., Wong, G.T.F., Hyun, S., Hahm, H.C., 2020. Factors associated with depression, anxiety, and PTSD symptomatology during the COVID-19 pandemic: clinical implications for U.S. young adult mental health. Psychiatry Res. 290, 113172 https://doi.org/10.1016/j.psychres.2020.113172.

Menezes, P.R., Scazufca, M., Busatto, G., Coutinho, L.M., McGuire, P.K., Murray, R.M., 2007. Incidence of first-contact psychosis in São Paulo, Brazil. Br. J. Psychiatry Suppl. 51, s102–s106. https://doi.org/10.1192/bjp.191.51.s102.

Miller, T.J., McGlashan, T.H., Rosen, J.L., Somjee, L., Markovich, P.J., Stein, K., Woods, S.W., 2002. Prospective diagnosis of the initial prodrome for schizophrenia based on the structured interview for prodromal syndromes: preliminary evidence of interrater reliability and predictive validity. Am. J. Psychiatry 159 (5), 863–865. https://doi.org/10.1176/appi.ajp.159.5.863.

Miller, T.J., McGlashan, T.H., Rosen, J.L., Cadenhead, K., Cannon, T., Ventura, J., McFarlane, W., Perkins, D.O., Pearlson, G.D., Woods, S.W., 2003. Prodromal assessment with the structured interview for prodromal syndromes and the scale of prodromal symptoms: predictive validity, interrater reliability, and training to reliability. Schizophr. Bull. 29 (4), 703–715. https://doi.org/10.1093/oxfordjournals.schbul.a007040.

Mittal, V.A., Walker, E.F., Strauss, G.P., 2021. The COVID-19 pandemic introduces diagnostic and treatment planning complexity for individuals at clinical high risk for psychosis. Schizophr. Bull. 47 (6), 1518–1523. https://doi.org/10.1093/schbul/sbab083.

Morita, K., Miura, K., Fujimoto, M., Yamamori, H., Yasuda, Y., Iwase, M., Kasai, K., Hashimoto, R., 2017. Eye movement as a biomarker of schizophrenia: using an integrated eye movement score. Psychiatry Clin. Neurosci. 71 (2), 104–114. https://doi.org/10.1111/pcn.12460.

Nieman, D., Becker, H., van de Fliert, R., Plat, N., Bour, L., Koelman, H., Klaassen, M., Dingemans, P., Niessen, M., Linszen, D., 2007. Antisaccade task performance in patients at ultra high risk for developing psychosis. Schizophr. Res. 95 (1–3), 54–60. https://doi.org/10.1016/j.schres.2007.06.022.

Obyedkov, I., Skuhareuskaya, M., Skugarevsky, O., Obyedkov, V., Buslauski, P., Skuhareuskaya, T., Waszkiewicz, N., 2019. Saccadic eye movements in different dimensions of schizophrenia and in clinical high-risk state for psychosis. BMC Psychiatry 19 (1), 110. https://doi.org/10.1186/s12888-019-2093-8.

O'Donoghue, B., Collett, H., Boyd, S., Zhou, Y., Castagnini, E., Brown, E., Street, R., Nelson, B., Thompson, A., McGorry, P., 2021. The incidence and admission rate for first-episode psychosis in young people before and during the COVID-19 pandemic in Melbourne, Australia. Aust. N Z J. Psychiatry 48674211053578. https://doi.org/10.1177/00048674211053578.

Oh, J., Chun, J.W., Lee, J.S., Kim, J.J., 2014. Relationship between abstract thinking and eye gaze pattern in patients with schizophrenia. Behav. Brain Funct. 10, 13. https://doi.org/10.1186/1744-9081-10-13.

Palmier-Claus, J.E., Dunn, G., Lewis, S.W., 2012. Emotional and symptomatic reactivity to stress in individuals at ultra-high risk of developing psychosis. Psychol. Med. 42 (5), 1003–1012. https://doi.org/10.1017/s0033291711001929.

Pirdankar, O.H., Das, V.E., 2016. Influence of target parameters on fixation stability in normal and strabismic monkeys. Invest. Ophthalmol. Vis. Sci. 57 (3), 1087–1095. https://doi.org/10.1167/iovs.15-17896.

Pretegiani, E., Optican, L.M., 2017. Eye movements in Parkinson's disease and inherited Parkinsonian syndromes. Front. Neurol. 8, 592. https://doi.org/10.3389/fneur.2017.00592.

Pruessner, J.C., Dedovic, K., Khalili-Mahani, N., Engert, V., Pruessner, M., Buss, C., Renwick, R., Dagher, A., Meaney, M.J., Lupien, S., 2008. Deactivation of the limbic system during acute psychosocial stress: evidence from positron emission tomography and functional magnetic resonance imaging studies. Biol. Psychiatry 63 (2), 234–240. https://doi.org/10.1016/j.biopsych.2007.04.041.

Pruessner, M., Iyer, S.N., Faridi, K., Joober, R., Malla, A.K., 2011. Stress and protective factors in individuals at ultra-high risk for psychosis, first episode psychosis and healthy controls. Schizophr. Res. 129 (1), 29–35. https://doi.org/10.1016/j.schres.2011.03.022.

Richetto, J., Meyer, U., 2021. Epigenetic modifications in schizophrenia and related disorders: molecular scars of environmental exposures and source of phenotypic variability. Biol. Psychiatry 89 (3), 215–226. https://doi.org/10.1016/j.biopsych.2020.03.008.

Shahrour, G., Dardas, L.A., 2020. Acute stress disorder, coping self-efficacy and subsequent psychological distress among nurses amid COVID-19. J. Nurs. Manag. 28 (7), 1686–1695. https://doi.org/10.1111/jonm.13124.

Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G.C., 1998. The mini-international neuropsychiatric interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J. Clin. Psychiatry 59 Suppl 20, 22–33 quiz 34-57.

Shen, X., Yan, S., Jiang, H., Cao, H., Dowling, R., Feng, J., Lei, Z., Li, J., Han, X., Lv, C., Gan, Y., 2021. Post-traumatic stress disorder and associated factors 1 year after the beginning of the COVID-19 pandemic among Chinese residents. Front. Psychiatry 12, 766127. https://doi.org/10.3389/fpsyt.2021.766127.

Si, T.M., Shu, L., Dang, W.M., Su, Y.A., Zhang, W.H., 2009. Evaluation of the reliability and validity of Chinese version of the mini-international neuropsychiatric interview in patients with mental disorders. Chin. Ment. Health J. 23, 493–503.

Skaramagkas, V., Giannakakis, G., Ktistakis, E., Manousos, D., Karatzanis, I., Tachos, N., Tripoliti, E.E., Marias, K., Fotiadis, D.I., Tsiknakis, M., 2021. Review of eye tracking metrics involved in emotional and cognitive processes. IEEE Rev. Biomed. Eng. https://doi.org/10.1109/rbme.2021.3066072.

Strauss, G.P., Macdonald, K.I., Ruiz, I., Raugh, I.M., Bartolomeo, L.A., James, S.H., 2022. The impact of the COVID-19 pandemic on negative symptoms in individuals at clinical high-risk for psychosis and outpatients with chronic schizophrenia. Eur. Arch. Psychiatry Clin. Neurosci. 272 (1), 17–27. https://doi.org/10.1007/s00406-021-01260-0.

Tabachnick, B.G., Fidell, L.S., 2019. Using Multivariate Statistics. Pearson, New York.

Tang, W., Hu, T., Hu, B., Jin, C., Wang, G., Xie, C., Chen, S., Xu, J., 2020. Prevalence and correlates of PTSD and depressive symptoms one month after the outbreak of the COVID-19 epidemic in a sample of home-quarantined Chinese university students. J. Affect. Disord. 274, 1–7. https://doi.org/10.1016/j.jad.2020.05.009.

Team, R.C, 2018. R: A Language and Environment for Statistical Computing. The R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org.

Wang, Z., Chen, J., Boyd, J.E., Zhang, H., Jia, X., Qiu, J., Xiao, Z., 2011. Psychometric properties of the Chinese version of the perceived stress scale in policewomen. PLoS One 6 (12), e28610. https://doi.org/10.1371/journal.pone.0028610.

Wang, C., Pan, R., Wan, X., Tan, Y., Xu, L., Ho, C.S., Ho, R.C., 2020. Immediate psychological responses and associated factors during the initial stage of the 2019 coronavirus disease (COVID-19) epidemic among the general population in China. Int. J. Environ. Res. Public Health 17 (5). https://doi.org/10.3390/ijerph17051729.

Wolf, A., Ueda, K., Hirano, Y., 2021. Recent updates of eye movement abnormalities in patients with schizophrenia: a scoping review. Psychiatry Clin. Neurosci. 75 (3), 82–100. https://doi.org/10.1111/pcn.13188.

Wortmann, J.H., Jordan, A.H., Weathers, F.W., Resick, P.A., Dondanville, K.A., Hall-Clark, B., Foa, E.B., Young-McCaughan, S., Yarvis, J.S., Hembree, E.A., Mintz, J., Peterson, A.L., Litz, B.T., 2016. Psychometric analysis of the PTSD checklist-5 (PCL-5) among treatment-seeking military service members. Psychol. Assess. 28 (11), 1392–1403. https://doi.org/10.1037/pas0000260.

Yao, H., Chen, J.H., Xu, Y.F., 2020. Patients with mental health disorders in the COVID-19 epidemic. Lancet Psychiatry 7 (4), e21. https://doi.org/10.1016/s2215-0366(20)30090-0.

Yung, A.R., Yuen, H.P., McGorry, P.D., Phillips, L.J., Kelly, D., Dell'Olio, M., Francey, S. M., Cosgrave, E.M., Killackey, E., Stanford, C., Godfrey, K., Buckby, J., 2005. Mapping the onset of psychosis: the comprehensive assessment of at-risk mental states. Aust. N Z J. Psychiatry 39 (11–12), 964–971. https://doi.org/10.1080/j.1440-1614.2005.01714.x.

Zhand, N., Joober, R., 2021. Implications of the COVID-19 pandemic for patients with schizophrenia spectrum disorders: narrative review. BJPsych Open 7 (1), e35. https://doi.org/10.1192/bjo.2020.157.

Zhang, T., Li, H., Woodberry, K.A., Seidman, L.J., Zheng, L., Li, H., Zhao, S., Tang, Y., Guo, Q., Lu, X., Zhuo, K., Qian, Z., Chow, A., Li, C., Jiang, K., Xiao, Z., Wang, J., 2014. Prodromal psychosis detection in a counseling center population in China: an epidemiological and clinical study. Schizophr. Res. 152 (2–3), 391–399. https://doi.org/10.1016/j.schres.2013.11.039.

Zhang, T.H., Li, H.J., Woodberry, K.A., Xu, L.H., Tang, Y.Y., Guo, Q., Cui, H.R., Liu, X.H., Chow, A., Li, C.B., Jiang, K.D., Xiao, Z.P., Seidman, L.J., Wang, J.J., 2017. Two-year follow-up of a Chinese sample at clinical high risk for psychosis: timeline of symptoms, help-seeking and conversion. Epidemiol. Psychiatr. Sci. 26 (3), 287–298. https://doi.org/10.1017/s2045796016000184.