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Current interdisciplinary approaches to the diagnosis of stress-related disorders: designing a study and developing the protocol for an experiment with the EyeLink 1000 Plus eye tracker

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Purpose: *First, to develop a combination design for a psychodiagnostic study with the formation of two experimental groups, individuals with and without stress-related disorders (SRD), and, second, to develop a design and protocol for a study that will use the EyeLink 1000 Plus eye tracker for recording eye movement parameters and assessing pupil size.*

Methods: *The EyeLink 1000 Plus eye tracker provides highly accurate recording with a wide field of view at up to 2000 Hz. The experiment protocol includes the prosaccade task to assess the saccade latency, fixation duration, peak saccade velocity, and error rate. Screening psychodiagnostic questionnaires (the OPANA, IMZ-38 and PCL-5) and valid professional psychodiagnostic methods of Integral Instrumental Psychodynamic Diagnosis (IIPD) technology are used to form the experimental groups. Data Viewer software (SR Research) qre used for analysis of the gaze data recorded with the eye tracker.*

Results: *We developed a combination design for a psychodiagnostic study with the formation of two experimental groups, individuals with and without SRD. In addition, we developed a detailed design for an interdisciplinary study aiming to examine eye movement parameters in the context of SRD verified by professional psychodiagnosis tools. The protocol proposed integrates the prosaccade paradigm and current eye-tracking technology, providing objective measurements and standardized conditions for the experiment.*

Conclusion: *Conducting a study according to the design and protocol developed on the basis of an interdisciplinary approach with the use of current eye-tracking technology and psychodiagnostic methods creates the conditions for better understanding of stress-related cognitive and emotional processes, and can be useful for providing a rationale for new objective instrumental methods for the diagnosis of SRD.*

Keywords:
eye tracking, eye movements, stress-related disorders, psychodynamic diagnostics, ophthalmology, psychology, eye

Introduction

Stress-related disorders (SRD) such as posttraumatic stress disorder (PTSD), anxiety and depressive conditions are a major issue in current psychology and psychiatry and substantially affect patients' quality of life (QoL) and social functions. Traditional methods for the diagnosis of these disorders are often based on subjective judgments, which may result in inaccuracy and delay in diagnosis [1].

Eye tracking is a technology that records eye movements over time and provides the possibility of objectively assessing stress-related cognitive and emotional processes. Studies have demonstrated that, anxious individuals were characterized by increased fixation on negative stimuli [2], whereas depressed subjects demonstrated avoidance of positive stimuli [3]. However, the accuracy and practical value of eye tracking in the diagnosis of SRD remains a subject of active discussion. The use of eye-tracking allows quantitative measurement and identification of potential biomarkers of stress-related conditions [3].

This work is part of a project on the development of a technology for objective instrumental diagnosis of SRD. It is expected that the output of this study will contribute to better understanding of stress-related cognitive and emotional processes, and could be used for the development of new approaches to SRD diagnosis and therapy.

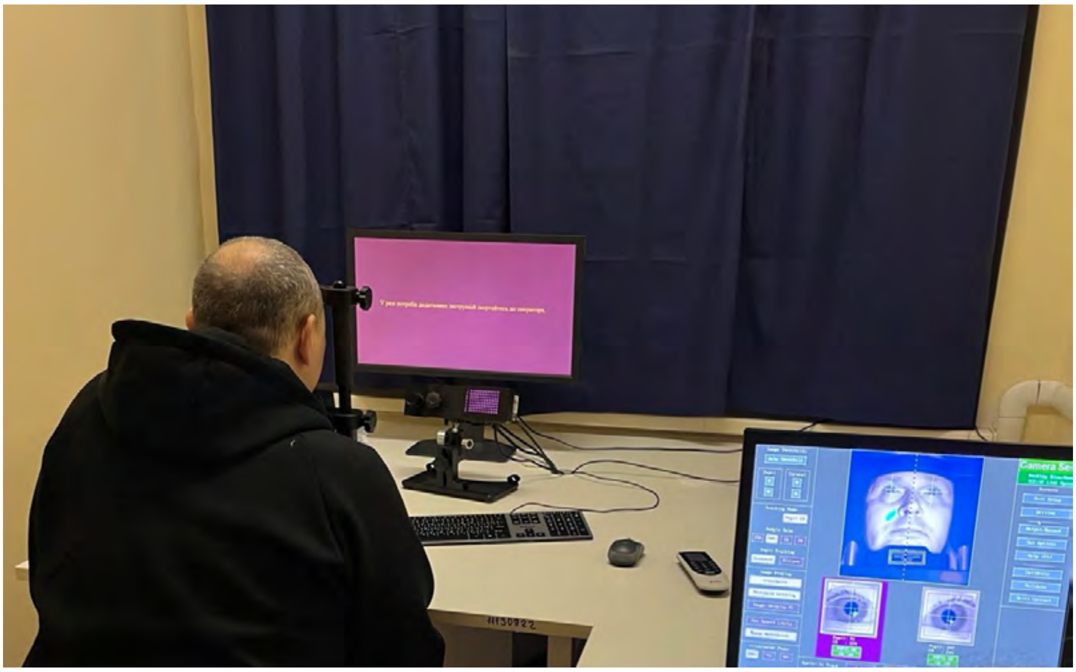

Fig. 1. EyeLink 1000 Plus eye tracker (SR Research Ltd; Mississauga, Ontario, Canada)

The purpose of this work is, first, to develop a combination design for a psychodiagnostic study with the formation of two experimental groups, individuals with and without SRD, and, second, to develop a design and protocol for a study that will use the EyeLink 1000 Plus eye tracker for recording eye movement parameters and assessing pupil size.

Material and Methods

A prospective, single-center, open-label non-interventional study will be conducted at SI "The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine". A combinational design of the psychodiagnostic study was developed to form two experimental groups, individuals without and individuals with SRD. Systemic and meta-analysis allowed us to integrate data from different works on the efficacy of different approaches and psychodiagnostic tools in order to enable informed choice of the most reliable and valid techniques with a high prognostic value for SRD identification.

Particularly, we selected a combination of screening questionnaires includes the OPANA (Positive and Negative Affect Questionnaire) [4], IMZ-38 (Mental Health Index-38) [5], the 2024 Ukrainian version of the Veit and Wares' Mental Health Inventory (MHI) translated and adapted by Fokin [6], and PTSD Checklist for the Diagnostic and Statistical Manual of Mental Disorders, fifth Edition (DSM-5) (PCL-5) [7].

These screening questionnaires were selected due to their ability to detect various stress aspects as well as stress impact on subject's mental health. The OPANA questionnaire allows assessing the level of positive and negative effect, a key characteristic of the emotional state. The IMZ-38 provides a general assessment of mental health, which is important for assessing general stress-resilience. PCL-5 is a specific measure that assesses PTSD symptoms; this makes it possible to identify the features of the reaction to stressful events. In addition, we have proposed a technology of Integral Instrumental Psychodynamic Diagnosis (IIPD; namely, professionally valid psychodiagnosis methods) to be used for identifying personal conscious and unconscious distinctions of examinees. This involves Dodomu package 10 involving the following methods: Aktsent 2-90, MBDO (an adapted version of the Minnesota Multiphasic Personality Inventory (MMPI)), Szondi Picture Selection Test and Lüscher 8-color test. It is with the application of innovative IIPD technology for SRD verification and assessment of the psychic condition of examinees that the interpretation of obtained psychological diagnostic data on examinees substantially improves, which is beneficial for explaining and predicting the behavior of examinee groups and developing psychotherapeutic care programs in future studies.

The EyeLink 1000 Plus eye tracker (SR Research Ltd; Mississauga, Ontario, Canada) is a multipurpose real-time processing system and is planned to be used for collecting eye movement data (Fig. 1). It has several mount combinations (e.g., Desktop Mount, Tower Mount and Long Range Mount), allowing experimenters to adapt it to specific requirements. In addition, a unique protocol

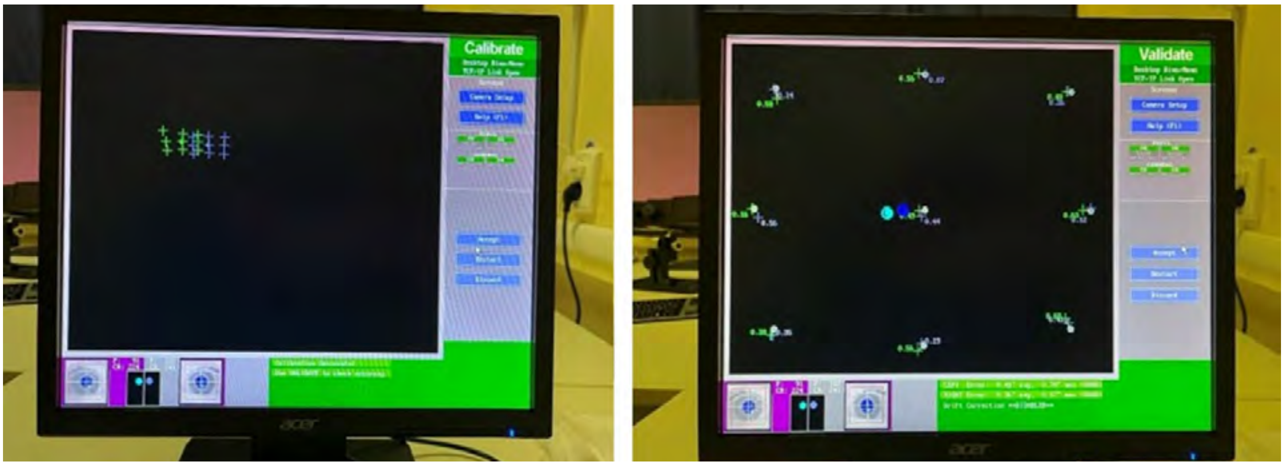

Fig. 2. Standard nine-point calibration and validation of the EyeLink 1000 Plus

should be developed for each experiment to take into account the examined parameters and targets. It enables flexible and accurate data collection, which is critically important for basic science and clinical studies. According to the manufacturer, this system provides highly accurate monocular recording with a wide field of view at up to 2000 Hz, spatial resolution of 0.01° of visual angle (which is especially important for studies of small changes in eye movement) and accuracy of 0.25° (to minimize errors in the analysis of fixation and saccades).

Each session begins with a standard nine-point calibration and validation of the EyeLink 1000 Plus (Fig. 2). A nine-point calibration is selected to enable even coverage of the entire screen for accurate measurements throughout the field of view. To avoid mistakes and enable data stability, participants are instructed before the start of the experiment, and the head is stabilized in a chin/head support.

The eye-tracking experiment was built in SR Research Experiment Builder, a graphical programming environment for creating computer-based psychology and neuroscience experiments. This software has numerous preference settings to modify various aspects of the entire range of experimental process components from stimulus presentation to data collection and analysis. Experiment Builder provides a flexible interface, works well with various hardware (e.g., EyeLink eye trackers), and allows for a wide range of experimental paradigms to be created. Stimulus material consists of simple dots that appear at peripheral locations of the screen.

Results

The methodological criteria for the selection of participants were formed given the further purpose of the project Developing a Technology for Objective Instrumental Diagnosis of Stress-Related Psychological Disorders in individuals that were exposed to stress-inducing factors.

Subject selection

Inclusion criteria for the group of individuals with SRD:

1) Age ≥18 years and <60 years (as per the criteria of the study)

2) Psychological status: stress-related disorder confirmed by: the OPANA (NA > PA); the IMZ-38 (a distress score > 83.1 and a total positive affect score < 31.6); the PTSD Checklist for DSM-5 (the PCL-5) (a total PCL-5 score > 32); the IIPD; integral coefficients of the psychoemotional status as measured by the Dodomu psychodiagnostic technology (social adaptation coefficient (CSA) < 4, neuroticism coefficient (Cneur) > 7, psychosomatic risk coefficient (Cpsr) > 7, suicidal risk coefficient (Csr) > 7; coefficient of risk for PTSD (Cpsdr) > 7, coefficient of risk for antisocial behavior (Casbr) > 7, coefficient of resistance to psychological correction (Cpcr) > 7, conflict proneness coefficient (Ccp) > 7) .

The list of possible SRD includes: PTSD (a total PCL-5 score > 32, Cpsdr > 7); generalized anxiety disorder (GAD) (an anxiety score, as assessed by the IMZ-38, > 28.5; total positive affect as assessed by the IMZ-38, > 31.6; Cneur > 7, Cpsr > 7); stress-related depressive disorder (NA > PA as assessed by the OPANA; a depression score, as assessed by the IMZ-38, > 11.7; a well-being score, as assessed by the IMZ-38, < 44.3; Cneur > 7, Cpsr > 7; Csr > 7); and maladaptive stress response (NA > PA as assessed by the OPANA; loss of behavioral or emotional control, as assessed by the IMZ-38, > 29.8; psychological distress, as assessed by the IMZ-38, > 83.1; CSA < 4).

3) Social functioning: individuals self-reporting on their significantly impaired everyday functioning via symptoms (difficulties in work, education, and social life are identified via the questionnaire developed for participants)

4) Subjective assessment (subjectively high stress that affects physical and mental health is identified via the questionnaire developed for participants)

5) Signed informed consent and readiness for undergoing all study procedures

6) Somatic health status (individuals without serious physical limitations that would prevent them from participating in the study)

Exclusion criteria for the group of individuals with SRD:

1) Presence of serious mental disorders not related to stress (schizophrenia, bipolar affective disorder, obsessive compulsive disorder (OCD), or significant cognitive impairment (dementia))

2) Uncooperative individuals exhibiting antisocial and/or conflict-prone behavior, or resistance to psychological correction (Casbr > 7, Cpcr > 7, Ccp > 7)

3) Somatic abnormalities: serious disorders affecting the nervous system (multiple sclerosis or epilepsy) and chronic somatic conditions that can affect the symptoms (e.g., uncontrolled diabetes, cardiac insufficiency)

4) Substance abuse or taking medications that can influence psychoemotional status (antidepressants, antipsychotics) within the last 30 days or irregularly

5) An eye disease causing a decrease in best-corrected visual acuity (BCVA) to less than 0.3 and/or impaired binocular vision.

Inclusion criteria for the group of individuals without SRD:

1) Age ≥18 years and <60 years (as per the criteria of the study)

2) Psychological status: the absence of stress-related disorder confirmed by: the OPANA (PA > NA); the IMZ-38 (a distress score < 83.2 and a total positive affect score < > 31.5); a total PCL-5 score < 33; the IIPD; integral coefficients of the psychoemotional status as measured by the Dodomu psychodiagnostic technology (social adaptation coefficient (CSA) > 6, neuroticism coefficient (Cneur) < 5, psychosomatic risk coefficient (Cpsr) < 5, suicidal risk coefficient (Csr) < 4; coefficient of risk for PTSD (Cpsdr) < 5, coefficient of risk for antisocial behavior (Casbr) < 4, conflict proneness coefficient (Ccp) < 4)

3) Social functioning: No substantial difficulties in everyday life (assessed on the basis of self-assessment and identified via the questionnaire developed for participants) and involvement in professional and social activities (identified via the questionnaire developed for participants)

4) Signed informed consent

5) General health status: No serious somatic or chronic disorder that can affect the mental status (e.g., diabetes and/or cancer) and no neurologic disorder (epilepsy and/or dementia)

Exclusion criteria for the group of individuals without SRD:

1) Presence of mental disorders related to stress (PTSD, GAD, stress-related depressive disorder, maladaptive stress response)

2) Somatic or neurologic abnormalities: Chronic disorders affecting the sense of physical well-being (e.g., essential hypertension, cardiac insufficiency) or serious central nervous system disorders (e.g., multiple sclerosis)

3) Substance abuse

4) An eye disease causing a decrease in best-corrected visual acuity (BCVA) to less than 0.3 and/or impaired binocular vision.

Psychological questionnaire study

A psychological questionnaire study within the framework of this research will be conducted to collect primary data on the social and demographic characteristics and emotional status of responders, impact of stress on personality, and level of social and emotional support. The questionnaire includes questions that enable (1) an assessment of gender, education level, marriage status, presence of minor children, professional employment, financial circumstances, impact of stress on their life, and availability of emotional support from the social environment, and (2) identification of the most important positive and negative events in the past and future. It also includes questions on somatic and eye diseases.

Developing EyeLink 1000 Plus study design and protocol

To perform the prosaccade task, participants are required to make a saccade toward (i.e., fixate the location of) an abruptly appearing peripheral stimulus onset as quickly and accurately as possible. This allows assessing the saccade latency, fixation duration, peak saccade velocity, and error rate.

The protocol makes it possible to standardize the conditions for participants and provides accuracy and comparability of the data. The requirement for the provision of high-quality data for further analysis is taken into account during the experiment. The exclusion criteria for irrelevant data were defined for this purpose. Data of the intervals related to attentional disengagement, loss of focus, and change in head position were excluded from the analysis. Attentional disengagement was defined as a significant gaze point deviation from the target stimulus or missed peripheral stimulus. Data including technical errors (e.g., loss of eye tracker signal due to hardware failure) were also excluded.

Protocol for experiment using the EyeLink 1000 Plus eye tracker

Participant's preparation

The participant sits in front of the monitor, with the head stabilized in a chin/head support.

The eye tracker camera is set up for the corneal light reflex centered in the pupil.

For better understanding of the task, the participants are initially provided with the following visual and verbal instruction: "Please, fixate on the dot as stably and precisely as possible".

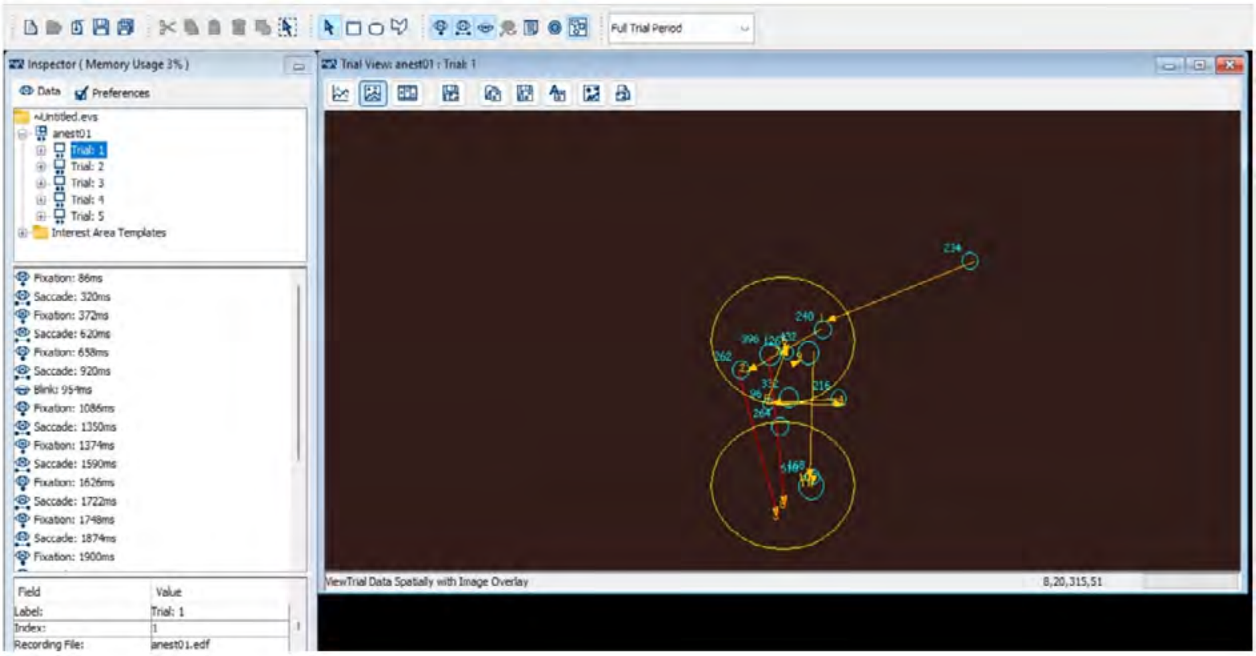

Fig. 3. Data Viewer software (SR Research Ltd; Mississauga, Ontario, Canada) for analysis of the gaze data recorded with EyeLink eye trackers

Sequence of stimuli presented

A central dot is presented on the screen for 3000 ms; thereafter, a peripheral dot stimulus is presented for 3000 ms. Stimuli replace each other automatically to exclude the experimenter's impact.

The total stimulation time is 40 sec. This time period was selected to enable the collection of sufficient data and avoid fatigue compromising the results.

To examine differences in eye movement parameters between the groups with and without SRD, we used the prosaccade paradigm that enables assessing the cognitive and neurophysiological aspects of eye movement control. The paradigm was selected due to several reasons. First, it provides objective measurements (the data obtained during task performance do not depend on the participant's subjective self-assessment). Second, it is easy to perform (the task is universal and can be undertaken by a participant of any age, gender or educational background because it does not require verbal communication or special knowledge). Third, the impact of cognitive and emotional context is minimized (the dots are neutral and do not produce additional cognitive and/or emotional load on participants [14]). Last, it is universal (stimuli are understandable for a participant of any age, educational background or language competence).

The hypothesis of the study is that there would be significant differences in saccade latency, fixation duration, peak saccade velocity, and error rate between the groups with and without SRD.

In the EyeLink 1000 Plus, fixation of eye movements is performed with the help of infrared technology that combines pupil position tracking and corneal reflection tracking.

During the experiment, the eye tracker emits infrared light which is reflected by the corneal surface; corneal reflection is recorded by a high-speed camera. The reflection creates a unique visual pattern which is processed in real time by the software, and gaze coordinates are determined accurately and indicated on the screen.

Data Viewer software (SR Research) for analysis of the gaze data recorded with EyeLink eye trackers is used to form the data base and create the output reports (Fig. 3).

The software provides real-time analysis of eye movements, reflects changes in the gaze and pupil parameters during the experiment, and allows multiple data files to be loaded into a single viewing session. Data Viewer has flexibility to work with large data sets, and provides a range of analysis tools that can be used to generate tab-delimited summary reports based on interest areas, fixations, saccades, time bins or samples. All Data Viewer reports can be exported directly into Excel or statistical analysis packages. Another feature of Data Viewer is that is highly integrated with other SR Research products (e.g., Experiment Builder) to cover a continuous working process from experiment building to gaze data analysis.

Discussion

Findings of recent studies indicate that it is questionable whether screening for individuals at risk for psychological distress can be performed sufficiently with the included instruments due to low number of studies per instrument and the low methodological quality [8]. In the opinion of Vasylchenko and Zhdanova [9], mental health care workers "… use mainly the screening questionnaires which have been designed not as professional diagnostic tools; this essentially means that, although the world faces the challenge of the exponentially growing rate of psychic disorders, psychology has been practically left without relevant diagnostic tools" [9].

Findings of IIPD studies by Vygrochyk, the founder of the Ukrainian school of IIPD, and his followers (coping behavior studies by Rodina [10], studies by Biron [11] on proactive coping in stressful situations, studies by Vasylchenko and Zhdanova [9] on the technological psychodynamic approach to the assessment of the psychological state and the development and introduction of modern psychological technologies) have demonstrated that the psychodynamic paradigm is a comprehensive approach that takes into account conscious and unconscious psychological mechanisms of the examinee to identify their personality distinctions that actually cause the development of SRD. That is, based on the clinical picture of SRD, a professional psychologist experienced in using IIPD can determine which consequences of imbalanced unconscious processes have resulted in the development of SRD in individuals with adverse experiences. It is the use of the psychodynamic approach to psychodiagnostic studies than can explain and predict the behavior of the examinee. This is important not only for dividing examinees into two experimental groups (the main group and the control group), but also for solving the problem of scalable, fast and accurate diagnosis of the psychoemotional status in the setting of growing rates of psychic disorders in Ukraine and globally.

The design developed is based on the available evidence that eye movement parameters (such as saccade latency, fixation duration, and error rate) reflect cognitive and emotional changes. It was found that saccade latency can increase under conditions of increased cognitive load or increased anxiety, because these conditions affect decision-making speed and attention [12, 13]. Changes in fixation duration were found in studies in which shorter fixations were associated with decreased ability to concentrate attention under stressful conditions [14]. High error rate during task performance indicates impaired cognitive control, which was reported in studies on emotional tension and anxiety [15]. Therefore, the hypothesis that these eye movement parameters may reflect cognitive and emotional changes caused by SRD is substantiated by the findings of previous experimental studies.

The prosaccade paradigm used in the study provides for the analysis of cognitive control through the increased saccade latency, which might indicate slowing of cognitive processes secondary to increased stress. Changes in fixation duration indicate difficulties with the ability to concentrate attention which is common in anxiety and depressive conditions. High error rate during task performance reflects impaired emotional regulation or cognitive control, which may be associated with increased emotional tension and anxiety level. The use of eye tracking in this context provides objective measurement of the above changes, since this method excludes the impact of participant's subjective assessment, which is especially important for the investigation of the psychoemotional status.

The study design proposed is unique since it integrates the current eye-tracking technology with the paradigm aiming to assess cognitive and emotional changes in the context of SRD. Previous eye-tracking studies focused mostly on particular cognitive functions or emotional reactions [12,13]. The design of our study, however, takes into the requirement for the comprehensive assessment of eye movement parameters (such as saccade latency, fixation duration, and error rate), which, taken together, reflect multidimensional aspects of the psychoemotional status [14]. A substantial advantage of the proposed approach is standardization of the protocol, which minimizes the impact of subjective factors and creates conditions for reproducibility of results. Additionally, we focus on the use of simple dot stimuli for presentation, making the experiment easy-to-perform by a wide range of participants irrespective of their cognitive and language characteristics [15].

In the context of modern research, the approach proposed allows improving our understanding of the mechanisms of the impact of SRD on cognitive and emotional processes, and forms the basis for further research aiming to develop new diagnostic and therapeutic tools. Although the proposed study has a distinctive design, it also has some limitations which should be taken into account. A key limitation is that the eye-tracking application is focused only on objective eye-movement parameters, but not on other important aspects of the psychoemotional status (e.g., verbal of physiological responses). This may limit interpretation of the data obtained within a wide context of behavioral changes. In addition, a standard eye tracker calibration and validation protocol may affect the measurement accuracy when the participant has difficulties in keeping the head stabilized in a chin/head support or due to individual features of the eyes. Another potential limitation is the universality of the stimulus material. Although the application of simple dots provides for standardization of experimental conditions, it may not take into account cognitive or emotional triggers specific for different groups of participants. In spite of these limitations, the design proposed here forms the basis for reproducible and standardized studies that may be adapted to other contexts or expanded for integration with other analysis methods.

The study design proposed here opens up new perspectives for the investigation of the psychoemotional status of individuals with SRD. The integration of the prosaccade paradigm with eye tracking provides a unique possibility to identify objective indicators of cognitive and emotional changes. In future studies, this approach may be expanded for the analysis of the impact of specific triggers (such as emotional and cognitive stimuli) on eye movement parameters. In addition, the protocol proposed may be integrated with other methods (e.g., neuroimaging) or physiological measurements (e.g., measurement of heart rhythm variability) to obtain a multidimensional picture of the status of participants.

Results of such studies may contribute to the development of new approaches to the diagnosis of SRD. The objectivity of eye-tracking allows for potential early detection of abnormalities and monitoring changes in patient status during therapy. This approach seems especially promising for assessing the efficacy of psychotherapeutic and pharmacological interventions.

In further research, it is important to focus on the assessment of characteristics (such as gender, age or stress level) that may impact the parameters of eye movement. This will make it possible to determine the diagnostic accuracy of the method and to develop personalized assessment protocols.

Conclusion

Therefore, the paper presents the developed detailed design of the study aiming to examine eye movement parameters in individuals with versus without SRD. Screening psychodiagnostic questionnaires (the OPANA, IMZ-38 and PCL-5) and valid professional psychodiagnostic methods of IIPD technology will be used to form two experimental groups (individuals with and without SRD). The protocol proposed for the experiment for collecting eye movement data with the EyeLink 1000 Plus eye tracker integrates the prosaccade paradigm and current eye-tracking technology and provides objective measurements and standardized conditions for the experiment. It forms the basis for further research that may improve our understanding of the cognitive and emotional changes typical of individuals with SRD. In addition, results of these studies may potentially contribute to the development of new therapeutic and psychotherapeutic approaches to the diagnosis of and therapy for SRD in clinical practice.

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Disclosures

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Author Contributions: *All authors have met the criteria for authorship and state that each author (1) has made an important scientific contribution to the study including conceptualization/ design and data analysis, (2) participated in the writing, review and editing of the manuscript, and (3) is responsible for the content of the entire manuscript.*

Ethics statement. *Clinical observations have been planned to be conducted at SI "The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine" within the framework of the National Research Fund of Ukraine Grant Project Developing a Technology for Objective Instrumental Diagnosis of Stress-Related Psychological Disorders (grant 2023.04/0008).*

The study will be conducted in accordance with the principles expressed in the Declaration of Helsinki and informed consent will be signed prior to subject enrollment (approved by the bioethics committee of SI "The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine", committee minutes dated September 12, 2024).

Disclaimer: *The opinions presented in this article are those of the authors and do not necessarily represent those of their institutions.*

Conflict of Interest: *Authors state that the study was conducted within the framework of the National Research Fund of Ukraine Grant Project Developing a Technology for Objective Instrumental Diagnosis of Stress-Related Psychological Disorders (grant 2023.04/0008).*

Data Availability Declaration: *All the data obtained or examined during this study has been incorporated into this published article.*

Abbreviations: *DSM-5, the Diagnostic and Statistical Manual of Mental Disorders, fifth Edition; IMZ-38, MHI-38 (Mental Health Index-38); IIPD, Integral Instrumental Psychodynamic Diagnosis; MHI, Mental Health Inventory; OPANA, Positive and Negative Affect Questionnaire (based on the Positive and Negative Affect Schedule (PANAS)); PCL-5, PTSD Checklist for DSM-5; PTSD, posttraumatic stress disorder.*