The Objectivization of the Complex PTSD Diagnostic by Identifying Ophthalmological Biomarkers

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Abstract. **Objectives: The purpose of this work is to objectivate the complex PTSD diagnostic by identifying ophthalmological biomarkers. Methods: The ophthalmological markers of PTSD were studied in two groups of volunteers. The main group (45 persons) in which patients had already proven diagnosis PTSD, and control group (30 persons) – healthy volunteers. We estimated features of eye movements recorded via eye tracker. On contrary to the majority of works in this field which rely on visual stimulation, we used verbal stimuli – a dialogue with a psychiatrist. We also assessed pupil reactions, degree of accommodation and convergence and stereoscopic threshold, near visual acuity. Results. The studied indicators of visual functions - convergence, accommodation, visual acuity were worse in patients with PTSD. The pupils were larger, the stereo effect occurrence time were also longer in patients with PTSD. Eye movement disturbances were identified with a use of Eye-Tracker device: the maximum fixation time in a single spot was longer – (3,02s ± 1,75) in the PTSD group versus to the control group – (2,22±1,5)s, (p=0,04). Conclusions: The reduction of visual functions and disturbances in ocular vergent system were stated in patients with PTSD: lower near visual acuity, lower accommodation and convergence rates, pupills diameters enlargement, lower stereo threshold versus to healthy persons. Eye movement disturbances were identified with a use of Eye-Tracker device The maximum fixation time in a single spot was longer – (3,02s ± 1,75) in the PTSD group versus to the control group – (2,22±1,5)s, (p=0,04). The majority of the PTSD patients (80%) fixated their sight at the central and upper central sector on contrary to the healthy persons. In addition to the development of PTSD, disorders of the oculomotor and vergent systems of the eye are in evidence to the hybrid war syndrome. The determined ophthalmological PTSD biomarkers (lower near visual acuity, lower accommodation and convergence rates, pupils diameters enlargement, eye movements disturbances) are suitable for usage in the technology of objective diagnosis, treatment and prevention of PTSD in hybrid war syndromes.**

Keywords **- the hybrid war, PTSD, PTSD ophthalmological biomarkers, eye movements.**

I. INTRODUCTION

The underdiagnosed and undertreated consequences of exposition to stressing factors (such as car accidents, catastrophes, military actions, other forms of violence) have deeply distorting effects on mental, social, professional and frequently physical aspects of an individuum's life. The worldwide statistics represents that one in five physically intact participants of military actions suffer from neuropsychological disorders and one in three among wounded or disabled [1].

Known algorithms for the PTSD diagnostics are semi-quantitative or qualitative, in most of the cases they are built of questionnaires and interviews [2], [3], [4]. The subjectivity of such methods compels them to rely on researcher's mastery and degree of testee involvement. John Krystal, Professor of Psychiatry and of Neurobiology claims that "It would be great if some kind of biological test existed that would tell us if a person has PTSD without checking for symptoms. Generally PTSD is diagnosed by anamnesis retrieving with further studying of every symptom in each case. There are few diagnostic criteria, if you observe a sufficient amount of symptoms you can diagnose PTSD. However there are people whose disorders are not corresponding with the diagnostic criteria, though you can suspect PTSD development by other clinical marks. Sometimes even without a complete diagnosis a medical intervention is needed to help to deal with existing symptoms. [5].

A biomarker is a process, substance or structure that can be found and measured in one's organism, biological fluids or wastes in order to predict an onset of certain disease, diagnose it, assess dynamics and prognosis and predict possible treatment outcomes [6].

There are studies of biological markers for such psychiatric conditions as schizophrenia, bibolar disorder [7], [8], [9], [10], [11]. Currently the lack of diagnostic biomarkers for PTSD is not due to a lack of intensive study, which is likely to be caused by the complexity of PTSD and the complex set of rules by which we classify individuals according to the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [12]. The review article from 2013 mentions the following biomarkers for PTSD diagnostics: hypothalamic-pituitary-adrenal system dysregulation, sympathetic adrenomedullar system hyperreactivity, intensification of quadruplet bodies reflexes, cognitive distortions, "anatomic" markers such as reduction of amygdala, anterior cingulate cortex, prefrontal cortex, hippocampus. Authors emphasize quadruplet bodies reflex as the most reliable biomarker [13]. In addition to the foresaid, the review article from 2015 expands the data on neuroendocrine disorders and also mentions serotoninergic system disruption, inflammatory biomarkers (some interleukins, C-protein, TNF), psychophysiological markers

which estimate a vegetative nervous system responses (heart rate, blood pressure, skin conduction, respiratory rate, body temperature, muscular contractions) [12].

Although ophthalmic markers are absent in these articles we can find solitary works on this topic.

Thus, given the worldwide tendency of shifting from subjective methods to the objectification of conducted surveys, the search for possible PTSD markers is extremely relevant.

II. OBJECTIVE

The purpose of this work is to objectivate the complex PTSD diagnostic by identifying ophthalmological biomarkers.

III. MATERIALS AND METHODS

The ophthalmological studies were provided by SI "Filatov Institute of eye disease and tissue therapy NAMS". The ophthalmological markers of PTSD were studied in two groups of volunteers. The main group (45 persons) which patients already have proven diagnosis PTSD, and control group (30 persons) – healthy volunteers. We estimated features of eye movements recorded via eye tracker, also matched eye tracker data with polygraph data. On contrary to the majority of works in this field which rely on visual stimulation, we used verbal stimuli – a dialogue with a psychiatrist. We also assessed pupil reactions, degree of accommodation and convergence and stereoscopic threshold, near visual acuty.

The study protocol was approved by a local institutional review board and is in compliance with the Helsinki Declaration. A signed informed consent was obtained from all subjects. Studies were conducted through the use of eye tracker and lie detector. During the subject were undergoing the questionnaire for combat PTSD the measures of eye tracker and lie detector were registering simultaneously.

The following specialists were involved in the investigation: eye tracker operator, polygraph examiner, ophthalmologist and psychiatrist.

The research was carried out in the room with definite requirements. It was isolated from disturbing factors and was comfortable for a test-taker subject. During the examination there were four people present in the room: psychiatrist, eye tracker operator, polygraph examiner and a test-taker subject. Another room was suited for ophthalmologist. The nearest convergence point and the nearest point of clear vision (testBERNELLb) were established for assessment of corresponding parameters. Pupils diameters were examined by Bernell OCCLUDE-A-MEASURE BC/7019. The stereoscopic threshold was tested via STEREO FLY TEST (STEREO OPTICAL CO., INC., Vectogram, Chicago) and via LANG STEREOTEST II (Lang – Stereotest PO.Box 19 CH-8127 Forch)

Another equipment used in the research included eye tracker (GP3HD 150Hz), polygraph (Lafayette LX 4000), monitor, notebooks.

Main group: males, 27 to 45 y.o., soldiers and sergeants of Ground Forces of the Armed Forces of Ukraine, who directly participated in military actions on the frontline. They had already been diagnosed with PTSD, had no somatic complaints, denied traumatic brain injury, other psychiatric or neurologic disorders.

Control group: males, 23 to 31 y.o., soldiers, sergeants and junior commanding staff of Ground Forces of the Armed Forces of Ukraine, almost healthy somatically, had never taken action on the frontline and had no diagnosed psychiatric or neurologic diseases.

Participants placement in the room: a test-taker subject sits on a chair and faces the monitor which is placed on a table 50 cm away from eyes of a patient. The eye tracker is mounted below the monitor. There is an eye tracker operator to the right of a test-taker subject following the process with a notebook. To the left of a test-taker subject there is a polygraph examiner who dynamically analizes the data from polygraph via notebook. At the opposite side of the table and to the left of the polygraph operator there is the psychiatrist who instructs a testee and reads verbal stimulating material.

The verbal stimulating material is a test for PTSD diagnostics that is included in the supplement to the order of the Ministry of Health of Ukraine №121 from 23.02.2016 "The unified clinical protocol of primary, secondary (specializied) and tertiary (highly specializied) medical help. Stress reaction and adaptation disorders. Post-traumatic stress disorder" and is recommended to physicians of all specialties for PTSD screening.

We estimated characteristic features of eye movements recorded via eye tracker, matched them with polygraph data of patients with or without PTSD. The following indexes were extracted from each testee's EYE-Tracker session: a question and an answer timings, the maximum single spot fixation time, a number of separate spots of sight fixation, a number of sectors involved (1 to 9), the most and the least engaged sectors, concentration losses.

IV. RESULTS

The data of the state of the visual functions in the main and control groups are presented in Table I.

TABLE I

The State of the Visual Functions in the Groups with and without PTSD (M± SD)

	Without PTSD (n=30)	PTSD (n=45)	P
Visual aculty, near vision	0,7 ± 0,3	0,49±0,27	0,023
The closest convergence point (cm)	5,0 ±1,13	8,5 ±4,6	0,04

The closest point of clear sight (cm)	6,0±0,5	8,64±3,4	0,0001
Pupils diameter	5,2 ± 0,54	7,12 ±1,8	0,00049
Lang's test time	3,9 ± 2,1	12,6 ± 8,7	0,04

The studied indicators of visual functions - convergence, accommodation, visual acuity were worse in patients with PTSD. The pupils were larger, the stereo effect occurrence time were also longer in patients with PTSD. Stereoscopic threshold met the norm in the control group – 200 arc seconds 90%, whereas in the PTSD group normal results were obtained only in 33,1% (χ^2 =4,08, p= 0,04), Stereo-fly test showed normal results in 63,3% of the healthy patients and in 20% of the PTSD patiens only (χ^2 = 4,9, p=0,02).

While assessing the advance EYE-Tracker data we noticed that the majority of the PTSD patients (80%) fixated their sight at the central and upper central sector on contrary to the healthy group in which sight fixation was predominantly in the central, lower central and in 40% in the upper central. The frequency of sector switching varied from 1 to 6 in 70% of the cases however both groups had testees who switched 11 to 14 times. The maximum fixation time in a single spot was averagely longer – (3,02s ± 1,75) in the PTSD group in comparison to the control group – (2,22±1,5)s, (p=0,04). Automatically measured pupils diameters in both groups confirm the data retrieved manually with the same illumination regimen (10 lux). PTSD patients have larger pupils.

Thereby the received data leads us to conclusion that the carried out tests may be transformed into PTSD state objective assessment criteria (ophthalmological biomarkers) as well as screening programs.

V. DISCUSSION

Considering the clinical and biological complexity of PTSD there is a minor to no chance of single biomarker identification. Prognostically, multiple biomarkers will be used as PTSD manifestation attribute, risk assessment factors or objective signs of recovery [14].

It is known that there are anatomic bonds between visual cortex, oculomotor apparatus and brain structures responsible for psychoemotional state [15]. The investigation of eye movements is a good tool for understanding the control of motor functions, both in physiological and in pathological conditions. There are researches on eye movements, particularly saccadic ones in patients with psychiatric disorders – schizophrenia, depression, bipolar disorder [7], [8], [9], [10], [11]. Authors pointed out the significant changes of such movements.

There are few researches on eye tracking in war veterans. The majority of them rely on visual stimuli whereas we used verbal stimuli – a dialogue with a psychiatrist. One research linked PTSD to vigilance on contrary to believed avoidance. In veterans with relatively higher levels of PTSD symptoms more prominent degree of midriasis to negative pictures was observed. They tended to maintain longer fixation times and preferred military-associated content to any other. This data implies that post-traumatic stress is associated to vigilance, not to avoidance. Authors deteremined midriasis in PTSD patients [16]. Another research reviewed a model of vigilance-avoidance. Authors stated an attention shift to a possible threat which was accompanied by specific vegetative excitation [17]. The mentioned papers focus on vigilance-avoidance mechanism studying and present major interest for psychosciences. Our work is accentuated on possible biomarkers detection. We studied the basic functions of the visual analyzer (saccades, pupil reactions, degree of accommodation and convergence and stereoscopic threshold, near vision acuty). Besides that, the stimulus diversity (visual or verbal) has made the key difference in our work. Nevertheless our results correspond to aforecited researches: in addition to midriasis measurement we detected prolonged single spot fixation time in PTSD patiens which can also confirm PTSD connection to vigilance.

As we established in previous works, the hybrid war (hybrid conflict) syndrome is a condition manifested as a complex of characteristic mental, psychosomatic, physiological and cognitive changes that occur to varying degrees in the population of countries involved in a hybrid conflict, subjected to a combination of traumatic influences of various nature and a complex of informational and psychological and cognitive influences, having individual and group manifestations. In this work, we found that in addition to the development of PTSD, disorders of the oculomotor and vergent systems of the eye are in evidence to the hybrid war syndrome.The received data on ophthalmic changes (ophthalmic PTSD markers) is rational to use in complex with "The technology of objective diagnosis, treatment and prevention of PTSD in hybrid war syndromes", which was developed recently by our team. The technology is detailed in the article [18].

The complex of specific ophthalmic data we received provides a great perspective in terms of PTSD diagnostics since multiple biomarkers have been revealed.

VI. CONCLUSIONS

1. The reduction of visual functions and disturbances in ocular vergent system were stated in patients with PTSD: lower near visual acuity, lower accommodation and convergence rates, pupils diameters enlargement, lower stereo threshold versus to healthy persons.
2. Eye movement disturbances were identified with a use of Eye-Tracker device. The maximum fixation time in a single spot was longer – (3,02s ± 1,75) in the PTSD group versus to the control group – (2,22±1,5)s, (p=0,04). The majority of the PTSD patients (80%) fixated their sight at the central and

upper central sector on contrary to the healthy persons.

3. In addition to the development of PTSD, disorders of the oculomotor and vergent systems of the eye are in evidence to the hybrid war syndrome.

4. Determined ophthalmological PTSD biomarkers (lower near visual acuity, lower accommodation and convergence rates, pupils diameters enlargement, eye movements disturbances) are suitable for usage in the technology of objective diagnosis, treatment and prevention of PTSD in hybrid war syndromes.

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