Psychiatria Danubina, 2020; Vol. 32, No. 1, pp 74-75

Commentary

ERG AND OCT AS AN EFFECTIVE SCREENING AND STAGING TOOLS FOR SCHIZOPHRENIA?

Ante Silić[1], Draženka Ostojić[2] & Dalibor Karlović[1]

[1]*Department for Psychiatry, University Clinical Hospital Sestre milosrdnice, Zagreb, Croatia*
[2]*Department for Diagnostics and Intensive Care, University Hospital Vrapče, Zagreb, Croatia*

* * * * *

Article by Jurišić et al. targets a specific area in schizophrenia endophenotype research with an implycation that electroretinography (ERG) and/or optical coherence tomography (OCT) could be used as a specific episode or trait marker by integrating retinal, vascular and perceptual findings (Jurisic et al. 2019).

Out of currently available laboratory and physical (imaging) tests, none provide pathognomonic finding for schizophrenia (Karlovic & Silic 2019). This kind of research, using eletroretinography and optical coherence tomography has opened the door to the study of the central nervous system in living patients with schizophrenia (Balogh et al. 2008, Silverstein et al. 2015, Ascaso et al. 2015, Demmin et al. 2018, Fernandes et al. 2019). In this context, we are dealing with "in vivo" available neurons, which use the same neurotransmitters as neurons in the basal brain structures that are most affected according to the monoamine hypothesis of schizophrenia. Namely, the retina is an integral part of the central nervous system, and is derived from the same tissue as the Telencephalon – the Ectoderma. It does not contain myelin and is available by visualisation using non-invasive methods. It is connected to visual occipital cortex via optical nerve that has its fibers in the retina connected to the ganglion cells. Thus, there is a potential premise of the investigation of the nervous system in living patients, with the possibility of defining specific biological indicators of schizophrenia by non-invasive methods (Kolb et al. 2009, Lee et al. 2013). Using the aforementioned tests with clinical diagnostic criteria of schizophrenia, we can expect to define clear subgroups within schizophrenia as a group of diseases that would have different prognostic and therapeutic specificities. Given the available data, visual impairments should be definitely taken into consideration when organizing schizophrenia into different prognostic and therapeutic subgroups.

ERG and OCT today exceed the use in ophthalmology alone. By examining the studies applying ERG and OCT methods in the field of psychiatry, we can conclude that the results of research conducted in morphologic and functional changes in patients with schizophrenia are not consistent. However, in most studies there is a clear reduction in the size of amplitude and changes in the implicit time in ERG and the thinning of the retinal nerve fiber layer in the OCT. There is obviously the unfulfilled need for longitudinal prospective research in order to define specific biological indicators using these methods for the purpose of early screening, diagnostics, monitoring of patients in certain stages of the disease and therapeutic response in patients (Cimmer et al. 2006, Chu et al. 2012, Silverstein et al. 2015, Doustar et al. 2017. Sago & Babic 2019). Psychiatry today clearly recognizes the need for early detection and early intervention in schizophrenia and spectrum disorders (Kulhara et al. 2008, Radić et al. 2018). The Lancet Commission on global mental health and sustainable development concludes that early identification of risks and vulnerabilities to mental health, as well as delivery of evidence-based interventions, should be applied in all populations (Maric et al. 2018). There is enough evidence from research and clinical practice to justify the implementation of early detection and intervention services for psychosis for all patients. That is why further research in this specific area should, in our opinion be focused on clarification whether those specific changes detectable by ERG and OCT develop in prodromal phase or later in first episode with clear prognostic and therapeutic implications. So far, we have not pinpointed the moment between prodromal phase and first episode psychosis in which a definitive therapeutical intervention starts and are using a watchful waiting approach (Herbert et al. 2010, Dama et al. 2019).

Schizophrenia is characterized by high relapse rates, which eventually lead to therapy resistance. The main goal of treatment should be functional recovery (Karlovic & Silic 2019). This specific area of research could provide us with the tool not only for early detection but as available data suggests, potential application could be in identification and prevention of relapse together with monitoring of treatment response. Further prospective research should be directed to monitoring of ERG and OCT changes with specific treatment. The design should take into consideration age, sex, duration of untreated psychosis (DUP), specific algorithm of treatment (class of antipsychotic drug, mechanism of action, psychotherapy, brain stimulation therapy, possible add on therapy etc.).

We have another consideration regarding Jurišić et al. article. It should be clearer whether changes in ERG and OCT are specific for schizophrenia spectrum disorders alone and in what way are they influenced and linked to other comorbidities in a larger sample. For example, Silverstein et al. 2018, examined the influence of comorbidities in patients with schizophrenia on results obtained using SD-OCT. Compared to a group of healthy subjects, no differences in retinal layer thick-

ness, macula and inner granular layer were obtained, and the determined habitat of the retina structure was associated with associated diseases such as diabetes mellitus and arterial hypertension in both groups of subjects. The study showed changes in the optic nerve head in patients with schizophrenia. It showed an increase in cup-to disk ratio of the excitation with the diameter of the optic nerve papilla which was not associated with comorbidities. Such results indicate the need for further research of the optic nerve head changes as an indicator of specific changes in schizophrenia.

Joe P et al. 2018 also investigated the use of SD-OCT in the pursuit of biomarkers in psychosis. They studied macular thickness and were among the first who studied thickness of the vascular layer that supplied the retina, i.e. choroidea. Six chronic psychiatric patients were involved (three with schizophrenia and three with bipolar disorder), and 18 healthy controls matched by age and gender. As in previous studies, they found thinning of the macula, especially the inner ring of the macula (statistically significant), which they attributed to neurodegenerative changes. They also found thinning of the choroid in individuals with psychosis, but it was not statistically significant, which they attributed to small sample of study participants. The authors point to the need for further research of these changes and their association with inflammation and degenerative changes of the CNS.

Acknowledgements: *None.*

Conflict of interest: *None to declare.*

References

1. *Ascaso FJ, Rodriguez-Jimenez R, Cabezón L, López-Antón R, Santabárbara J, De la Cámara C et al.: Retinal nerve layer and macular thickness in patients with schizophrenia: Influence of recent illness episodes. Psychiatry Res 2015; 229:230-6*
2. *Balogh Z, Benedek G, Kéri S: Retinal dysfunctions in schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry 2008; 32:297-300*
3. *Cimmer C, Szendi I, Csifcsák G, Szekeres G, Ambrus Kovács Z, Somogyi I et al.: Abnormal neurological signs, visual contrast sensitivity, and the deficit syndrome of schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry 2006; 30:1225-30*
4. *Chu EM, Kolappan M, Barnes TRE, Joyce EM, Rona MA: A window into the brain: An in vivo study of the retina in schizophrenia using optical coherence tomography. Psychiatry Res 2012; 203:89-94*
5. *Dama M, Shah J, Norman R, Iyer S, Joober R, Schmitz N et al.: Short duration of untreated psychosis enhances negative symptom remission in extended early intervention service for psychosis. Acta Psychiatr Scand 2019 (E-pub ahead of print)*
6. *Demmin DL, Davis Q, Roché M, Silverstein SM: Electroretinographic anomalies in schizophrenia. J Abnorm Psychol 2018; 127:417-28*
7. *Doustar J, Torbati T, Black KL, Koronyo Y, Koronyo-Hamaoui M: Optical Coherence Tomography in Alzheimer's Disease and Other Neurodegenerative Diseases. Front Neurol 2017; 8:701*
8. *Fernandes TMP, Silverstein SM, Butler PD, Kéri S, Santos LG, Nogueira RL et al.: Color vision impairments in schizophrenia and the role of antipsychotic medication type. Schizophr Res. 2019; 204:162-70*
9. *Hébert M, Gagné AM, Paradis ME, Jomphe V, Roy MA, Mérette C et al.: Retinal response to light in young non-affected offspring at high genetic risk of neuropsychiatric brain disorders. Biol Psychiatry 2010; 67:270-4*
10. *Joe P, Ahmad M, Riley G, Weissman J, Smith RT, Malaspina D: A pilot study assessing retinal pathology in psychosis using optical coherence tomography: Choroidal and macular thickness. Psychiatry Res 2018; 263:158-61*
11. *Jurišić D, Ćavar I, Sesar A, Sesar I, Vukojević J, Ćurković M: New insights into schizophrenia: a look at the eye and related structures. Psychiatr Danub 2020; 32:60-69*
12. *Karlović D & Silić A: Psihopatologija. In Karlović, D, Peitl, V & Silić A (eds): Shizofrenije, 41-65. KBC Sestre Milosrdnice and Naklada Slap, Zagreb, 2019*
13. *Kolb H: Neurotransmitters in the Retina. in: Webvision: The Organization of the Retina and Visual System, Ed. Kolb H, Fernandez E, Nelson R. University of Utah Health Sciences Center, 2009*
14. *Kulhara P, Banerjee A, Dutt A: Early intervention in schizophrenia. Indian J Psychiatry 2008; 50:128-34*
15. *Lee WW, Tajunisah I, Sharmilla K, Peyman M, Subrayan V: Retinal nerve fiber layer structure abnormalities in schizophrenia and its relationship to disease state: evidence from optical coherence tomography. Invest Ophthalmol Vis Sci 2013; 54:7785-92*
16. *Maric NP, Andric Petrovic S, Rojnic-Kuzman M, Reicher-Rossler A: Implementation of early detection and intervention services for psychosis in Central and Eastern Europe: Current status. Early Intervention in Psychiatry 2019; 1-6*
17. *Radic K, Curkovic M, Bagaric D, Vilibic M, Tomic A, Zivkovic M: Ethical Approach to Prevention of Schizophrenia - Concepts and Challenges. Psychiatr Danub 2018; 30:35-40*
18. *Sago D & Babic G. Roots of Alexithymia. Archives of Psychiatry Research 2019; 55:71-84*
19. *Silverstein SM, Paterno D, Cherneski L, Green S: Optical coherence tomography indices of structural retinal pathology in schizophrenia. Psychol Med 2018; 48:2023-33*
20. *Silverstein SM, Rosen R: Schizophrenia and the eye. Schizophr Res Cogn 2015; 2:46–55*

Correspondence:
Prof Dalibor Karlović, MD, PhD
Department for Psychiatry, University Clinical Hospital Sestre milosrdnice
Vinogradska 29, 10 000 Zagreb, Croatia
E-mail: dalibor.karlovic@gmail.com