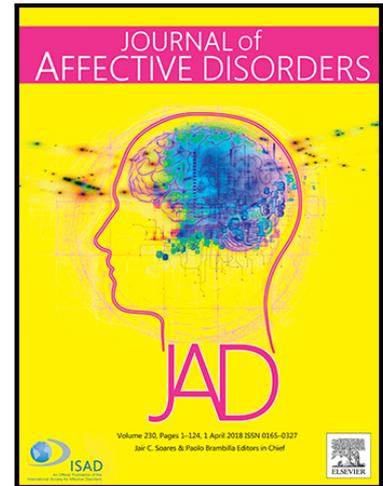# Accepted Manuscript

Methodological concerns on Retinal Thickness evaluation by Spectral Domain Optical Coherence Tomography in patients with Major Depressive Disorder

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Please cite this article as: Lorenzo Ferro Desideri MD , Fabio Barra MD , Mohamed Ihsen Skhiri MD , Simone Ferrero MD, PhD , Methodological concerns on Retinal Thickness evaluation by Spectral Domain Optical Coherence Tomography in patients with Major Depressive Disorder, *Journal of Affective Disorders* (2018), doi: 10.1016/j.jad.2018.05.048

Highlights

- Major depression is being investigated in relation with neurodegenerative processes occurring in different sites, such as retinal degeneration
- OCT has allowed us to improve our knowledge about retinal morpholology and anatomy, giving a thee-dimensional visualization of all the single retinal layers
- Many confounding factors may influence retinal volume and thickness; retinal diurnal variation has been described in literature
- When measuring retina by OCT an optical biometry examination should be performed in order to evaluate axial length
- Antidepressant drugs exerts important ocular side effects and therefore should be considered as important confounding factors

Title: Methodological concerns on Retinal Thickness evaluation by Spectral Domain Optical Coherence Tomography in patients with Major Depressive Disorder

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Abstract: The aim of this article is to underline the importance of all the possible confounding factors involved in the variation of retinal thickness. More in detail, antidepressant drugs represent an important confounding factor that should not be neglected when measuring retinal thickness by Spectral Domain Optical Coherence Tomography (SD-OCT) in patients with major depressive disorder

To the Editor,

We read with interest the article entitled "Retinal changes in patients with major depressive disorder – A controlled optical coherence tomography study" recently published by Schönfeldt-Lecuona et *al*. [1] in your journal.

In this study the authors analyzed the overall retinal thickness and five different retinal layers in patients with major depressive disorder by using Spectral- Domain- Optical Coherence Tomography (SD-OCT) and compared the results with age-matched healthy subjects. In this regard, the authors should be congratulated for having studied first, to the best of our knowledge, every retinal single layer in patients with majore depressive (MD) disorder and , nonetheless, for having reported a small but significant difference in total retinal thickness between the two eyes in the examined group, differently from the control group [1].

However, we would like to raise some methodological concerns from an ophthalmologic point of view. Firstly, the authors did not clarify if they performed the OCT examination at the same part of the day for both the patients with MD and healthy subjects; in this regard, it has been reported that retinal thickness can be subjected to small but statistically significant diurnal variations [2,3]. Thus, we deem that more precise information about the timing of the examination should have been provided, especially not neglecting the possible difference between the examined and the control group. Secondly, they did not specify if the complete ophthalmological examination, beside the slit lamp examination combined with indirect ophthalmoscopy, tonometry and refraction, included also optical biometry with the measurements of important ocular parameters such as axial length (AL) . In fact, extrapolated data from the Beijing Eye Study has shown in multivariate analysis that an increase in central foveal thickness was positively associated with a longer AL[4]. Moreover, another prospective study demonstrated not only the positive correlation between AL and total retinal thickness, but also with single retinal layers like the ganglion cell and inner plexiform layer complex (GCL+IPL), the inner nuclear layer (INL) and outer plexiform layer (OPL)[5] . Hence,

when measuring retinal thickness by SD-OCT, it should be suggested to perform an optical

biometry examination in order to rule out important confounding factors such as AL.

Thirdly, the authors did not report in the exclusion criteria the smoking status of the subjects.

However, Dervisigullari et *al*. revealed in smokers subjects the presence of a thinner retina nerve

fiber layer (RNFL) in comparison with age-matched non-smokers subjects [6]. Thus, we deem that

also a screening for smoking status should have been provided by the authors in order to adjust

another possible confounding factor.

Lastly, we think that the administration of antidepressant therapy in the examined group could have

altered the results in this study. In fact, it is well known that tricyclic antidepressants (TCAs) are

responsible for several ocular side effects due to their anticholinergic effect, including cycloplegia,

mydriasis and uveal tract disorders. Moreover, also a case of maculopathy induced by sertraline, a

selective serotonin reuptake inhibitor (SSRI) antidepressant drug, has been previously documented

in the literature [7]. In conclusion, given this evidence, it cannot be excluded that the results reported

by the authors could have been influenced by the administration of antidepressant drugs in the

examined group and therefore this could represent an important and not negligible limitation of the

study. In the near future, further studies should be carried out in order to better define the boundary

between the effect exerted by antidepressant drugs and by the depressive disorder itself on the eye

and in particular on retina.

Disclosure: All the authors have materially participated in the article and approved the final article

References

1.   Schonfeldt-Lecuona C, Schmidt A, Kregel T, et al. Retinal changes in patients with major depressive disorder - A controlled optical coherence tomography study. *Journal of affective disorders.* 2018;227:665-671.
2.   Ashraf H, Nowroozzadeh MH. Diurnal variation of retinal thickness in healthy subjects. *Optom Vis Sci.* 2014;91(6):615-623.
3.   Read SA, Collins MJ, Alonso-Caneiro D. Diurnal variation of retinal thickness with spectral domain OCT. *Optom Vis Sci.* 2012;89(5):611-619.
4.   Jonas JB, Xu L, Wei WB, et al. Retinal Thickness and Axial Length. *Invest Ophthalmol Vis Sci.* 2016;57(4):1791-1797.
5.   Szigeti A, Tatrai E, Varga BE, et al. The Effect of Axial Length on the Thickness of Intraretinal Layers of the Macula. *PLoS One.* 2015;10(11):e0142383.
6.   Dervisogullari MS, Totan Y, Tenlik A, Yuce A, Guler E. Effect of smoking on retina nerve fiber layer and ganglion cell-inner plexiform layer complex. *Cutaneous and ocular toxicology.* 2015;34(4):282-285.
7.   Richa S, Yazbek JC. Ocular adverse effects of common psychotropic agents: a review. *CNS drugs.* 2010;24(6):501-526.