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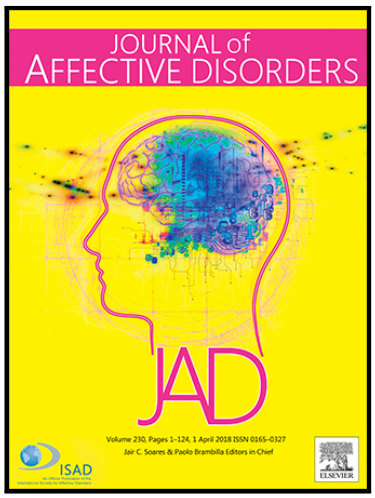

Methodological concerns on Retinal Thickness evaluation by Spectral Domain Optical Coherence Tomography in patients with Major Depressive Disorder

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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

Keywords: major depression; OCT; retina; confounding factors; antidepressant drugs

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.

Keywords: Major Depression; OCT; retina

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