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Sir,
Can photoreceptor loss also account for changes in pupil size following panretinal photocoagulation?

We have read with interest the paper entitled 'Changes in pupil size following panretinal retinal photocoagulation: conventional laser vs pattern scan laser (PASCAL)' by Yilmaz *et al*[1] This work reports an increase in pupil size under different illumination levels following conventional and PASCAL panretinal photocoagulation (PRP) in patients with proliferative diabetic retinopathy (PDR). The authors interpret these findings as a consequence of laser damage to the efferent pupillary pathway, notably the short posterior ciliary nerves. Although we agree with the authors' interpretation, we bring forth the hypothesis that PRP may also affect pupil size via damage to the afferent retinal photoreception.

Intrinsically photosensitive retinal ganglion cells (ipRGCs), located in the inner retina and expressing the photopigment melanopsin, are at the origin of the afferent pupillary pathway.[2] These atypical ganglionic cells integrate their intrinsic photosensitivity with inputs from traditional outer-retina photoreceptors, before projecting to subcortical regions driving pupillary constriction. PRP for PDR purposefully destroys a considerable fraction of peripheral rods and cones, but also directly damages the inner retina.[3] The extent of retinal damage generated by PRP is dependent upon the laser beam's diameter, power, and duration.[4] Even though the exact power of the used beams was not specified by the authors, it is conceivable that a light-intensity photocoagulation such as the one they have used, especially with conventional PRP, might have inflicted structural and functional damage not only to the photoreceptors, retinal pigment epithelium, and choroid, but also to the retinal nerve fiber layer and inner retina as well,[4,5] possibly altering the photoreceptive and integrative capabilities of ipRGCs and increasing pupil size under various conditions of illumination. Furthermore, it would be of great benefit if the authors could clarify whether the non-studied/untreated eye was also exposed to light during the direct pupillometric measurement and whether anisocoria was observed.

In conclusion, we suggest that damage sustained by the peripheral photoreceptors, especially in the inner retina, could partially account for changes in pupil size following PRP. Additional studies are required to establish whether inner-retina sparing, through adequate yet effective laser-treatment strategies, could reduce pupil dilation and consequently photophobia in PRP-treated patients.

Conflict of interest

The authors declare no conflict of interest.

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Sir,
Reply to 'Can photoreceptor loss also account for changes in pupil size following panretinal photocoagulation?'

We thank the authors for showing interest in our study[1] and for their valuable contributions.

In our study, we aimed to evaluate the possible changes in pupil size subsequent to panretinal laser photocoagulation (PRP) via Conventional laser and pattern scan laser (PASCAL). We found out that the pupil size increases (according to objective pupillary measurements) following PRP in patients with proliferative diabetic retinopathy (PDR).[1] Although we have not known the exact underline mechanism of pupillary size changes, we hypothesize that it may be secondary to damage to short posterior ciliary nerves, which transverse the suprachoroidal space. There are some minor studies in literature that supported our hypothesis.[2,3]

The authors pointed out to a good hypothesis that the damaged peripheral retinal photoreceptors following PRP may be a partially mechanism, which explains the increased pupil size after PRP.[4] Additional studies are required to find out the exact underline mechanism.

The authors also added that it would be of great benefit if we could clarify whether the untreated eye was also exposed to light during the direct pupillometric measurement and whether anisocoria was observed.[4] However, we do not have the pupillometry measurements of non-studied eyes.

Conflict of interest

The authors declare no conflict of interest.

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Sir,
Aflibercept in persistent neovascular AMD: comparison of different treatment strategies in switching therapy

The article by Ricci *et al*[1] carries several shortcomings that prevent the validation and extrapolation of their results and that can be specifically summarized as follows:

1. Except for the morphological findings of the pigment epithelium detachment (PED) and choroidal neovascularization (CNV) presented in details, there were no data on the other anatomical types of neovascular maculopathy including serous and/or hemorrhagic detachment of the neurosensory retina, retinal hard exudates, subretinal and subretinal pigment epithelium fibrovascular proliferation, and disciform scar.

2. There were relevant baseline differences between the two groups. Thus, patients in the fixed regimen had greater best-corrected visual acuity (BCVA) score (68 *vs* 63 Early Treatment Diabetic Retinopathy Study (ETDRS) letters), significantly greater central retinal thickness (CRT 480 *vs* 346 μm), and higher time of CVN diagnosis (22 *vs* 18 months), than those in the pro re nata (PRN) regimen. Accordingly, a comparison between the two groups of patients seems questionable.

3. In the assessment of the final results of this study, we considered the current assertion that evaluation of the outcomes has to be guided by anatomical measure data with visual changes as a secondary guide.[2] Thus, patients in the PRN group lost a median of 3 ETDRS letters and the CRT decreased significantly to a median of 252 μm, a value considered within normal limits.[3] In contrast, patients in the fixed regimen gained a median of 3 ETDRS letters and the CRT significantly decreased to a median of 332 μm. Of note, this CRT value is more than the cutoff (315.2 μm) for the upper level of the normal CRT (270 ± 22.5 μm) plus 2 standard deviations.[3] We believe that the persistence of this high value of CRT in patients with fixed regimen highlights unresolved macular edema and indicates that the disease process is still active and progressive requiring further treatment with anti-angiogenic agents. The better efficacy of the PRN therapy against the fixed regimen was also substantiated by the greater proportions of the dry macula (58 *vs* 42%), the greater number of complete PED flattening (3 *vs* 1), and the smaller number of intravitreal injections (3.5 *vs* 7).

Altogether, we believe that the results of the PRN strategy in the present study have been better than those achieved in the fixed regimen in terms of visual improvements in switching therapy.

Conflict of interest

The authors declare no conflict of interest.

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The authors have full control of the primary data and they agree to allow the Eye Journal to review their data if requested.

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