Correspondence

Re: Evidence of Müller Glial Dysfunction in Patients with Aquaporin-4 Immunoglobulin G–Positive Neuromyelitis Optica Spectrum Disorder

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To the Editor,

The study by You *et al.* reports intriguing retinal functional and structural findings in patients with aquaporin4-IgG positive (AQP4+) neuromyelitis optica spectrum disorder (NMOSD) compared with patients with multiple sclerosis (MS) and healthy subjects,[1] highlighting the potential insights into neurological disorders that can be generated from a study of retinal structure and function. Employing multiple approaches (*in vivo* retinal imaging and electrophysiological testing, and post-mortem immunohistochemistry), they describe significant differences that could be consistent with alterations in Muller cells. It would be helpful to know the ethnicity of the different groups (NMOSD, MS and control subjects). As the authors state, NMOSD is less common in Caucasians, and so it is possible there were ethnic differences between the groups. This is of relevance as both optical coherence tomography (OCT) and electroretinogram (ERG) parameters have been shown to vary with ethnicity: studies have found that people of African origin have thinner foveal thickness measurements on OCT;[2,3] also, ERG amplitudes (including the scotopic dim-flash b-wave) have been reported to be lower in brown-eyed Asians compared with blue-eyed Caucasian subjects.[4] If patients of African origin were over-represented in the NMOSD group (particularly the AQP4+ve patients) relative to the other groups, this might contribute to the findings of foveal thinning and b-wave reduction, representing a potential confounding factor.

In their Figure 1, they highlight the difference in the scotopic b-wave. In panel C of that figure, they show averaged photopic responses and point out that no change was found. This is correct in regard to the conventionally measured components (a-wave and b-wave); the two waveforms appear very close up to approximately 48 ms. After this time point, the averaged waveform from the control subjects appears to remain more negative compared with the AQP+ve trace, which returns to baseline and then falls again. The control trace does not reach the baseline, and has a second trough at around 70 ms that is not so clearly discernible in the AQP+ve trace. This negative trough forms

part of the photopic negative response, which is understood to arise from retinal ganglion cells (and is diminished in glaucoma and other diseases affecting retinal ganglion cells).[5] It would be useful to explore possible differences between the two groups at this time point. Can impairment of retinal ganglion cell function be detected in AQP4+ve patients by alterations in the late photopic ERG? This portion of the waveform can be affected by blink artefacts, and so caution would be needed to check that traces used to derive the average are reliable at these time points; such artefacts can distort the average considerably. The above potential confounding effects of ethnic differences (if present) might pertain here also.

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