Letter to the editor:

Pupil area and photopigment spectral sensitivity are relevant to study of

migraine photophobia

Omar A. Mahroo PhD, FRCOphth

1. NIHR Biomedical Research Centre for Ophthalmology at Moorfields Eye Hospital

and the UCL Institute of Ophthalmology, 162 City Road, London EC1V 2PD

2. Department of Ophthalmology, King's College London, St Thomas' Hospital

Campus, Westminster Bridge Road, London SE1 7EH

3. Physiology, Development and Neuroscience, University of Cambridge, Downing

Street, Cambridge CB2 3EG

Correspondence at address (1) above.

Email: oarm2@cam.ac.uk

Noseda and colleagues report findings from a very informative multifaceted study aimed at exploring the effect of different light wavelengths in eliciting photophobia in patients with migraine, and probing the basis for any differential effect (Noseda et al., 2016). They found that green light exacerbated headache significantly less than white, blue, amber or red lights. They went on to show, using eletroretinography and visual evoked potentials in patients, that green light stimuli produce less activation of cone-driven pathways, discernible at the level of retinal responses. Their patients did not undergo pharmacological mydriasis to minimise discomfort, and this may be reasonable in that it more faithfully reproduces natural circumstances. However, pupil diameter affects retinal illuminance (which is calculated as the product of pupil area and luminance at the cornea). Differences in the amplitude, velocity and latency of pupil light responses occur with different wavelengths of light (Lobato-Rincon et al., 2014), and it is possible that the pupil areas, and therefore light reaching the retina differed in the different conditions. It would be helpful to know whether pupil diameters were similar during the different coloured light exposures, in which case the effect would relate directly to stimulation of cone pathways by the different wavelengths. If the pupil diameters differed significantly, then a more complex interaction of effects of light wavelengths on the pupil area (the afferent pathway of the pupil reflex is driven ultimately by photon absorption by rod and cone photopigments as well as melanopsin) and the resulting retinal stimulation would need to be considered. It is also possible that activation of the pupil light reflex itself might contribute to photophobia.

The authors were also able, using multi-unit recordings in rats, to identify thalamic neurons responding differently to different wavelengths (least responsive to green light). This is of interest and relevance, but inter-species differences bear consideration. As photopigment spectral sensitivities differ between human and rat (Jacobs et al., 2001), it is not clear that patterns of relative stimulation by different wavelengths will be identical. Thus some degree of caution is advisable before directly relating findings in rodents to the human visual system.

References

Jacobs GH, Fenwick JA, Williams GA. Cone-based vision of rats for ultraviolet and visible lights. *J Exp Biol.* 2001 Jul;204(Pt 14):2439-46.

Lobato-Rincón LL, Cabanillas-Campos Mdel C, Bonnin-Arias C, Chamorro-Gutiérrez E, Murciano-Cespedosa A, Sánchez-Ramos Roda C. Pupillary behavior in relation to wavelength and age. *Front Hum Neurosci.* 2014 Apr 22;8:221.

Noseda R, Bernstein CA, Nir RR, Lee AJ, Fulton AB, Bertisch SM, Hovaguimian A, Cestari DM, Saavedra-Walker R, Borsook D, Doran BL, Buettner C, Burstein R. Migraine photophobia originating in cone-driven retinal pathways. *Brain*. 2016 Jul;139(Pt 7):1971-86.