

We write to remind readers to consider this potential association between the use of SSRIs and increased risk of hemorrhage, especially during the consent process for lacrimal surgery.

### Conflict of interest

The authors declare no conflict of interest.

### References

- 1 Yamamoto T, Abe K, Kuyama Y. Selective serotonin reuptake inhibitor and gastrointestinal hemorrhage. *Nihon Rinsho* 2013; 71(4): 751–756.
- 2 Hackam DG, Mrkobrada M. Selective serotonin reuptake inhibitors and brain hemorrhage: a meta-analysis. *Neurology* 2012; 79(18): 1862–1865.
- 3 de Abajo FJ. Effects of selective serotonin reuptake inhibitors on platelet function: mechanisms, clinical outcomes and implications for use in elderly patients. *Drugs Aging* 2011; 28(5): 345–367.
- 4 Muluk V, Macpherson DS. Perioperative medication management. In Basow D ed. *UpToDate*. UpToDate: Waltham, MA, 2013. <http://www.uptodate.com/contents/perioperative-medication-management> (accessed 11 April 2014).
- 5 Auerbach AD, Vittinghoff E, Maselli J, Pekow PS, Young JQ, Lindenauer PK. Perioperative use of selective serotonin reuptake inhibitors and risks for adverse outcomes of surgery. *JAMA Intern Med* 2013; 173(12): 1075–1081.

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Sir,

### Concerning central retinal artery occlusion (CRAO) and cerebral stroke

I read with interest the correspondence on central retinal artery occlusion (CRAO) and cerebral stroke regarding Varma *et al*'s article 'A review of central retinal artery occlusion: clinical presentation and management'.<sup>1</sup> In a paper published in this journal in 1992 we looked at the relationship between central retinal artery and ocular neovascularisation in eight patients.<sup>2</sup>

We agree with McLeod<sup>3</sup> that penumbral retinal tissue viability can persist as half of our patients did not fall into the carotid occlusive disease group. This concurs with Kottow and Hendrickson,<sup>4</sup> who found anterior

**Table 1** A classification of the proposed mechanisms relating central retinal artery occlusion (CRAO) to ocular neovascularisation (NVN)

1. Chronic ocular ischaemia alone leading to ocular NVN	→ Rubeotic glaucoma <sup>a</sup>
Low CRA perfusion pressure	↓
2. Chronic ocular ischaemia + coincidental CRAO	→ CRAO
	→ Ocular NVN
3. Double embolism: CRAO + PCAO	→ Ocular NVN
4. CRAO alone	→ Ocular NVN

Abbreviation: PCAO, posterior ciliary artery occlusion.

<sup>a</sup>Rubeotic glaucoma is usually characterised by a low intraocular pressure.

segment neovascularisation following CRAO, as well as Brown,<sup>5</sup> who reported a case of neovascularisation following CRAO due to presumed single mitral valve embolus in the absence of carotid disease.

Varma *et al* also refer to preventing ocular neovascularisation following CRAO. The relationship between these two events is more complex than this paper implies, as we described in a table which I reproduce here for the sake of clarity (Table 1). As well as considering CRAO alone, it considers the concept of double embolism as reported by Wolter<sup>6</sup> as well as CRAO in a setting of chronic ocular ischaemia due to carotid occlusive disease.<sup>7,8</sup>

We do, however, strongly agree with Varma *et al* that such patients should be reviewed at regular intervals for at least 3 months following the diagnosis of CRAO.

### Conflict of interest

The author declares no conflict of interest.

### References

- 1 Varma DD, Cugati S, Lee AW, Chen CS. A review of central retinal artery occlusion: clinical presentation and management. *Eye* 2013; 27: 688–697.
- 2 Jacobs NA, Trew DR. Occlusion of the central retinal artery and ocular neovascularization: an indirect association? *Eye* 1992; 6: 599–602.
- 3 McLeod D. Letter to the editor: partial central retinal artery occlusion offers a unique insight into the ischemic penumbra. *Clin Ophthalmol* 2012; 6: 9–22.
- 4 Kottow M, Hendrickson P. Iris angiographic findings in retinal arterial occlusions. *Can J Ophthalmol* 1974; 9: 435–443.
- 5 Brown GC. Isolated central retinal artery obstruction in association with ocular neovascularization. *Am J Ophthalmol* 1983; 96: 10–11.
- 6 Wolter JR. Double embolism of the central retinal artery followed by secondary haemorrhagic glaucoma. *Am J Ophthalmol* 1972; 73: 652–657.
- 7 Sturrock GD, Mueller HR. Chronic ocular ischaemia. *Br J Ophthalmol* 1984; 68: 716–723.
- 8 Jacobs NA, Ridgway AEA. Syndrome of ischaemic ocular inflammation; six cases and review. *Br J Ophthalmol* 1985; 69: 681–687.

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Sir,

**Reply: 'A review of central retinal artery occlusion:  
clinical presentation and management'**

We thank Dr Jacobs<sup>1</sup> for drawing attention to the work showing 'persistence' of retinal tissue viability post central retinal artery occlusion (CRAO)<sup>2–4</sup> and to the studies by Kottow and Hendrickson<sup>5</sup> and Brown<sup>6</sup> demonstrating retinal viability post CRAO as a result of ocular neovascularisation.

The pioneering studies by Hayreh *et al*<sup>7</sup> in monkeys with direct occlusion showed that if the degree of central retinal artery occlusion can be reversed before 97 min, then there is retinal tissue viability, as evidenced by normalisation of the electroretinogram. However, the degree of electroretinogram recovery declines thereafter. The issue of the true retinal tolerance time where there is no viable return of function is still not known. A CRAO resembles an ischaemic cerebral vascular event since 'time is tissue'. Therefore, we respectfully disagree that there is persistence of retinal tissue viability.

Neovascularisation is a process of unregulated and misguided growth of new vessels in the eye.<sup>8</sup> Many variables affect neovascularisation, including the extent of ischaemia. Thus, the time to ocular neovascularisation onset ranges from 2 weeks to 4 months post CRAO.<sup>8</sup> Ocular neovascularisation is principally due to chronic retinal ischaemia and multiple mediators. Vascular endothelial growth factor (VEGF) is highly implicated in its pathogenesis.<sup>8</sup>

Neovascularisation in the eye is a maladaptive process occurring in ischaemic penumbral retinal tissue from events such as CRAO or ischaemic diabetic retinopathy, when there is insufficient blood supply to the retina. Neovascularisation results in an increased tendency to bleed, resulting in vitreous haemorrhage. If neovascularisation of the iris and angle occurs, this can result in neovascular glaucoma (NVG) with acute rise in intraocular pressure causing congestion and pain.

We showed a clear empirical correlation between thromboembolic CRAO and ocular neovascularisation.<sup>8</sup> The overall rate of neovascularisation in our cohort was

18.2%, consistent with most other studies. In the majority of neovascularisation cases there were no clinical features of ocular ischaemia and no association with a haemodynamically significant stenosis of the carotid artery. Given the association between neovascularisation and CRAO, it is prudent to review all patients with acute CRAO at regular intervals as early as 2 weeks and up to 4 months post CRAO.

### Conflict of interest

The authors declare no conflict of interest.

### References

- 1 Jacobs N. Concerning central retinal artery occlusion (CRAO) and cerebral stroke. *Eye* 2014; **28**: 1269–1270.
- 2 Varma DD, Cugati S, Lee AW, Chen CS. A review of central retinal artery occlusion: clinical presentation and management. *Eye* 2013; **27**: 688–697.
- 3 Jacobs NA, Trew DR. Occlusion of the central retinal artery and ocular neovascularization: an indirect association? *Eye* 1992; **6**: 599–602.
- 4 McLeod D. Letter to the editor: partial central retinal artery occlusion offers a unique insight into the ischemic penumbra. *Clin Ophthalmol* 2012; **6**: 9–22.
- 5 Kottow M, Hendrickson P. Iris angiographic findings in retinal arterial occlusions. *Can J Ophthalmol* 1974; **9**: 435–443.
- 6 Brown GC. Isolated central retinal artery obstruction in association with ocular neovascularization. *Am J Ophthalmol* 1983; **96**: 10–11.
- 7 Hayreh SS, Zimmerman MB, Kimura A, Sanon A. Central retinal artery occlusion. Retinal survival time. *Exp Eye Res* 2004; **78**: 723–736.
- 8 Rudkin AK, Lee AW, Chen CS. Ocular neovascularization following central retinal artery occlusion: prevalence and timing of onset. *Eur J Ophthalmol* 2010; **20**: 1042–1046.

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