Sir,

Central retinal artery occlusion and cerebral stroke

Aspects of the review by Varma and colleagues[1] conspire to amplify the confusion that surrounds central retinal artery occlusion (CRAO). First, they report that a foveal cherry-red spot is present in 90% of eyes examined within 1 week of CRAO onset, whereas only 58% show concomitant macular opacification. Surely these 'classic' CRAO signs must co-exist?

Second, Varma and colleagues discuss 'transient' CRAO, a small subgroup of eyes in the Iowa CRAO classification characterised by CRA reopening by the time of initial presentation and fluorescein angiography.[2,3] They state that 'transient' CRAO is 'analogous to a transient ischaemic attack affecting the eye' since 'restoration of blood flow … results in symptom resolution'.[1] This is not the case. The Iowa classification dispenses with terminological convention by labelling events as 'transient' even though complete reversal of symptoms and signs is precluded by a duration of ischaemic anoxia exceeding 4 h (inner retina's maximum survival time).[4] They also state that 'transient' CRAO presents 'greatly varied fundus findings'.[1] This is not the case. If the duration of 'transient' CRAO exceeds 4 h, the 'classic' signs will persist for at least a week. Alternative presentations in the form of 'scattered patches of retinal opacity'[2,3] usually signify 'partial', not 'transient', CRAO.[5]

Third, Varma and colleagues believe 'only a rare subgroup of individuals have viable tissue' in the inner retina by 24 h from CRAO onset.[1] This is not the case. Although the survival time of anoxic tissue in the posterior pole has been exceeded, this 'core' of infarction will be surrounded by a zone of critically hypoxic but viable tissue (the 'ischaemic penumbra'), just as in cerebral stroke. Unlike penumbral cerebral cortex, however, penumbral retina can persist indefinitely.[5] Reperfusion of this tissue explains the recovery of the ERG b-wave after CRA unclamping following 4 h of CRAO.[4] It can also account for the visual improvement frequently attributed to 'natural history' in patients,[1–3] provided neural connectivity is maintained between reoxygenated penumbra and optic nerve. However, if the CRA does not reopen and cilioretinal collaterals are not formed, the enduring penumbral state of the tissue will stimulate intraocular neovascularisation (developing in 15–20% of CRAO eyes).[5]

Conflict of interest

The author declares no conflict of interest.

References

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Sir,

Reply: 'Central retinal artery occlusion and cerebral stroke'

We are grateful to Dr McLeod[1] for the interest that he has shown in our paper.[2] Rather, then there being a conspiracy to increase the confusion within central retinal artery occlusion (CRAO), our study demonstrates that the disease is incompletely understood. In particular, we disagree with Dr McLeod that the retinal penumbra lasts for more than 24 h. Retinal and cerebrovascular ischaemia share a number of common pathophysiological features and is reflected by the recent extended definition of stroke involving retinal as well as cerebral ischaemia.[3]

In vitro experiments show that when neuronal cells are deprived of oxygen, that within 5 s, there is evidence of neuronal dysfunction. Within 10 s, cell death occurs. The elegant experiment of Astrup *et al*[4] demonstrated that the penumbra is a function of collateral perfusion and that if there was no resolution of the occlusion, then eventually the penumbra would fail, and infarction would be permanent.

In cerebral stroke using perfusion imaging, various groups have demonstrated that the ischaemic penumbra may persist beyond 24 h. However, randomised controlled trials of reperfusion therapy in acute stroke have demonstrated on that in the majority of individuals, the ischaemic penumbra only extends out to 4.5 h and at maximum, 6 h.[5,6]

The misperceptions that the retinal penumbra persists for 24 h, initially backed up by observational data, led to the design of two randomised controlled trials that recruited individual with central retinal artery occlusion of beyond 6 h. The EAGLE study recruited subjects up to 19 h of symptom onset,[7] while our group conducted a randomised controlled trial of intravenous tPA given to individuals within 24 h of symptom onset.[8] Both of these randomised controlled trials were negative studies, however, a signal was seen in individuals who receive tPA within 6 h of symptom onset.[8] This mirrors the retinal tolerance time demonstrated in Hayreh's animal experiments of 4 h.[9]