**Figure 3** Left Goldmann Visual Field.

uninvestigated, family history and the observed phenotype makes the differential diagnoses of congenital abnormality related to choroidal inflammation, retinotoxic medication uses, infective, inflammatory, systemic metabolic or choroidal vasculopathy highly improbable.

Other causes of well-defined atrophy such as this occurs in choroideremia, gyrate atrophy, and bifocal choroidal atrophy. However, none of these are consistent with this case. In summary, we present a novel lobular chorioretinal dystrophy for discussion.

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Sir,
**Glutamate excitotoxicity in glaucoma: truth or fiction? By AJ Lotery**

Lotery's editorial (*Eye*, April 2005) seeks to use the findings of Kwon *et al* as a platform to put forward the view that the role of glutamate in glaucoma is fictional. The editorial is disappointing because it is based

on an article where the experimental model is ischaemia and not glaucoma, it does not point out the limitations of the study by Kwon *et al* and it focuses far too much on the work of one discredited scientist. Furthermore, it does not provide a balanced view of the subject matter.

The study by Kwon and collaborators was conducted on four elderly monkeys where the central retinal artery (CRAO) was occluded for 190 min. After a reperfusion time of 350 min, the animals were killed and the concentrations of different amino acids in the retina determined. Vitreous samples were collected for amino-acid analysis at three time points: before CRAO, 6 h into reperfusion, and after the animals were killed. The main findings of the study were firstly, that no statistically significant differences were apparent in the content of any of the amino acids when comparing control retinas and retinas that had been subjected to CRAO and secondly, that no differences occurred in the amino-acid content of the vitreous humour between eyes that had experienced CRAO and control eyes.

A number of problems occur when trying to determine the concentration of a particular amino acid in the vitreous humour. Any amino acid may not be evenly distributed in the vitreous humour and this must be considered when analysing samples of vitreous humour from different eyes. Thus analysing a small sample of the vitreous humour from any one eye will not give an indication of the absolute concentration in the whole of the vitreous humour. In addition, there is the possibility of contaminating the vitreous sample with blood when entering the globe. This would be particularly problematic when vitreous humour samples are taken a number of times from the same eye. It should also be emphasised that there are significant difficulties associated with currently available methodologies for the accurate quantitative analysis of amino acids in small samples of vitreous humour. Given these reservations, it is difficult to accept that even if the glutamate level in the whole of the vitreous humour in a glaucoma patient were to be elevated by 100% in absolute terms, any actual measurement would reliably show this to be the case. Kwon *et al* to their credit acknowledge some of these issues in their article, and indeed make the point (p 461) that a statistically significant result would only have been obtained in their study if any increase in the vitreous glutamate concentration had exceeded 4.6-fold.

Regardless of the accuracy of the measurements, and in contrast to the viewpoint expressed in the editorial, we do not consider that the inability to demonstrate an elevation of the glutamate concentration in the vitreous or retina following ischaemia in animal

models negates the possibility that glutamate plays a part in glaucoma. While it is correct that there is a lack of data that definitively proves a role for glutamate in *glaucoma*, a significant body of work has been accrued that does implicate glutamate in the cascade of injury to retinal neurons that follows *ischaemia*. For example, glutamate antagonists are known to offer protection against ischaemia-induced damage to the retina. The inability to detect an elevation of vitreal glutamate following retinal ischaemia does not refute the involvement of glutamate in ischaemia, rather it suggests that measurement of the gross level of glutamate is not a specific tool by which such a question can be answered.

Of similar importance is the recognition that ischaemia causes a *redistribution* of tissue glutamate, such that the extracellular level of the amino acid becomes elevated. There is no reason to assume that the *total* retinal content of glutamate *in situ* is altered after ischaemia. An elevated extracellular level of glutamate would be particularly dangerous to ganglion and amacrine cells, since these neurons express specific types of glutamate receptors that, when overactivated, cause excessive cellular depolarisation. Moreover, an elevated extracellular level of glutamate would cause oxidative stress to neurons generally. There is little doubt that glutamate at a certain extracellular level acts as a toxin to CNS neurons; however, whether such an elevated extracellular glutamate pool can eventually diffuse out of the retina and into the vitreous, or whether it is generally metabolised (glutamate is rapidly metabolised into products that include ammonia) and/or redistributed within the retina is unknown. Since glutamate does not cross the blood retinal barrier, it would appear likely that it does not simply diffuse out of the retina into the vitreous.

While it is correct to emphasise that interpretation of articles by a scientist who has been shown to falsify data needs to be viewed with caution, it is also necessary to consider findings from other scientists. A body of literature does exist to support the view that glutamate plays a part in the pathogenesis of glaucoma. Questions relating to the work of one scientist must not detract from these publications. It is our belief that glutamate and other toxins released from astrocytes play a part in the pathogenesis of glaucoma (see *British Journal of Ophthalmology* 2001; **85**: 1252–1259). If this proves correct, then the potential use of glutamate antagonists in the treatment of glaucoma cannot be ignored. In truth, it is questionable whether the precise role that glutamate plays in the pathogenesis of human glaucoma will ever be unequivocally demonstrated. Nevertheless, labelling the possibility as fiction is not only sensational but, unjustified. Ideas on the pathogenesis of almost every

known disease are hypothesis-driven, where many scientists have contributed a great deal in terms of thought and experimental data. It is important not to let one scientist's undoubtedly questionable data blind us in our attempts to understand more about glaucoma and so realise more appropriate therapies. If the trend is to encourage the argument that a role for glutamate in glaucoma is fictional, then it may not be to the benefit of future glaucoma patients.

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Sir,
## Charles Bonnet syndrome (visual hallucinations) following enucleation

We read with interest the excellent article by Drs Ross and Rahman, describing visual hallucinations in a patient following enucleation.[1] These hallucinations were characteristic of Charles Bonnet syndrome (CBS) and, interestingly, disappeared with eye closure. We would like to propose a possible pathophysiologic mechanism to explain this observation.

A visual acuity of 6/6 in the patient's other eye is not incompatible with the diagnosis of CBS, which has been described both in people with good visual acuity in the fellow eye[2,3] and in patients who have visual field defects and good central visual acuity in the affected eye.[2,4,5] Shiraishi *et al*[6] proposed that it is the dynamic reduction in visual acuity, rather than the actual visual acuity, that has a greater impact on CBS.[2,7]

This case is intriguing because the hallucinations ceased when the patient's eyes were closed, only to return when he opened his eyes. Although it is well known that eye closure may terminate hallucinations in patients with CBS, this is the first case in which it appears that transient reduction of light perception on closure of the *fellow* eye is associated with its cessation. The enucleated eye constantly has no light perception and lid closure will not have any additional effect. It is possible, as the authors suggest, that closing the eyes results in secondary normalization of sensory input, thus abolishing the abnormal independent impulses and resultant complex imagery.[1] Another possibility might be

that deafferentation induced changes in the cortical neurons, resulting in reorganization of the receptive field and increased sensitivity to sensory input.[8] Stimulation of these hypersensitive areas by normal sensory impulses (in this case from the left eye) may trigger visual hallucinations.[7,9,10] However, a minimum amount of sensory input is required in order to trigger the hallucinations. Therefore, when the patient closes both his eyes, normal input is abolished and the hallucinations cease, only to return when he opens his eyes. This theory would also explain why some hallucinations cease when patients eventually lose all light perception. This possibility is illustrated in another patient who experienced CBS following cortical resection for cortical dysplasia.[5] In this patient, the hallucinations diminished with eye closure, and varied in intensity with blinking, light intensity, and the sight of moving objects—factors that vary the intensity of the visual stimulation.

Regardless of the mechanism, we agree with the authors that it is important to recognize CBS and its possible occurrence following sudden loss of vision.

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