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Selective cell death in glaucoma

EDITOR.—In his recent article J E Morgan raises various interesting medical points. However, I would like to draw attention to several facts that I believe were not completely addressed in this article. We had previously analysed the lateral geniculate nucleus from patients with glaucoma, as well as a control population. We identified a selective diminution of cell density in the magnocellular system of glaucomatous patients. In describing our data on lateral geniculate changes in human glaucoma, Morgan suggests, first, that our technique incorrectly assayed cells per unit area rather than accurately considering volume. This methodological comment points up the tremendous difficulty in properly designing a valid stereological study. Secondly, when one examines cell bodies, however, we were able to avoid this pitfall. Rather than counting the cell body per se, we only included cells in which the nucleolus could be detected. This allowed for an accurate assessment of density, given that microscopic thickness could easily be determined. The conservation of nucleolar size between magnocellular and parvocellular cells, as well as the relatively small size of the nucleolus compared with the overall thickness of the sections, minimised the technical errors he suggests. Since the microscopic section has a fixed thickness, our measurements are indeed per unit volume, and not per unit area. More importantly, Morgan suggests that we have not adequately considered the possibility that lateral geniculate cell density might actually go up in the face of ganglion cell loss. We should point out that the seminal point of our paper was that we saw a differential effect on magnocellular and parvocellular tissue. No matter how you slice it (pun intended) this difference suggests that glaucoma is doing different things to the magnocellular and parvocellular systems. The simplest interpretation (supported by the majority of papers cited by Morgan) would be that even if glaucoma causes some parvocellular loss (as is most certainly the case), earlier damage is done at the magnocellular level.

This brings me to a more significant comment. It is certainly possible we are wrong, and that some as yet undetermined flaw in our study (or those of other groups) has confounded the issue. But Morgan does not cite any referred work supporting the hypothesis that glaucoma does not first damage large retinal ganglion cells, while there are many publications supporting this hypothesis. We certainly recognise that these data contradict the fondly held hypothesis that glaucomatous damage is not preferential to the magnocellular system. I would be the last to suggest that this question is definitively answered, and that we know that glaucoma beyond all doubt damages larger cells and therefore the magnocellular system first. But the weight of published data does support this statement. Without any data as presented, the current answer to Morgan’s question—does selective cell damage in glaucoma occur—must be yes.

Nevertheless, we would like to reinforce one corollary of our work that was alluded to obliquely in our article. The anatomical and functional elegance of the magnocellular and parvocellular layering of the lateral geniculate nucleus has led to the seductive but unfortunately incorrect assumption that a similar simple distinction of magnocellular and parvocellular cells exist at the level of the retina. The retinal ganglion cell layer contains a plethora of cell types, and we have as yet only a limited knowledge of how these cell types function in the normal as well as the glaucomatous retina. Future psychophysical and histopathological studies will hopefully shed light on what is a most compelling question.

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Reply

EDITOR.—Dreyer discusses some important aspects of his work on the lateral geniculate nucleus in glaucoma.1 In my review I referred specifically to the volume of the geniculate laminae and not to the calculation of cell density. The finding of a differential effect on the density of geniculate cells in magnocellular and parvocellular laminae is interesting and is not what is at issue here. The point is that without reference to the lamina volume, density measurements cannot reflect the changes in the number of cells in a given population. A decrease in cell density certainly reflects cell loss (assuming that expansion of the geniculate laminae had not occurred). However, changes in cell density are the product of changes in the total cell population and laminar volume. In macaques, for example, the cell density is deafferented laminae can increase by as much as 53% but when the lamina volume is taken into account the estimated decrease in the cell population for that lamina is of the order of 22%.2 In the human, monocular enucleation results in marked geniculate cell loss3 but the change in cell density in the deafferented laminae is minimal because of laminar shrinkage. A similar process may explain why the parvocellular cell densities in Dreyer’s study did not change significantly even with the inclusion of subjects with extensive peripheral visual field damage. The differential effects of glaucoma on cell densities could reflect selectively greater cell death in the magnocellular laminae. However, caution must be exercised in drawing this conclusion without knowing the degree of laminar shrinkage.

The aim of the review was to emphasise alternative explanations of the published data and not to offer a definitive conclusion or to decide in favour of selective or non-selective mechanisms. I referred to one important paper that certainly raises questions about the role of selective cell death. Casson et al4 have described that defects occurred in both temporal modulation and blue yellow sensitivity at a similar stage in the disease, arguing against selective M or P pathway damage. Further work needs to be done to characterise the anatomical changes that occur early in


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SELECTIVE CELL DEATH IN GLAUCOMA

EDITOR.—Recently Peyman et al reported a fascinating study, demonstrating an analgesic effect of topically applied morphine formulation in patients with post-surgical corneal abrasions.1 Their results are in accordance with numerous clinical experiences within the past 10 years in different fields of acute and chronic pain therapy showing that a local application of opiates is useful in clinical practice. It might be of interest to Peyman and colleagues that the use of opiates as topical ophthalmic analgesics has been reported previously.

Remarkably, as seen from a communication of Keil,2 opthalmic surgeons obviously used opiates in this way more than 500 years ago. In the late 14th century the most important old German ophthalmic monograph was published. The author (probably named ‘meister Johannes’), of whom little is known, cited Arabic and Middle Ages authorities such as Arnold of Villanova. In this little book there are many prescriptions for ‘kräncke augen’ (sick eyes), including some – for example, corneal application of opium (popp) for surgery and pain relief. Therefore, the indisputable merit of Peyman et al’s paper is the rediscovery and scientific proving of an old medical technique.

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Reply

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