Glaucoma

Retinal vein pulsation predicts increasing optic disc excavation

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Spontaneous retinal vein pulsation in glaucoma

Several factors are associated with glaucoma progression, most notably elevated intraocular pressure (IOP), age, stage of the disease and presence of optic disc haemorrhages.¹⁻⁴ In this issue of the *British Journal of Ophthalmology*, Balaratnasingam *et al*⁵ (see page 441) describe a new factor associated with glaucoma progression—that is, the ophthalmodynamometric force (ODF) necessary to induce central or hemiretinal vein pulsation. In their study, baseline ODF, measured in subjects with glaucoma or suspects of having glaucoma, predicted increased optic disc excavation determined by masked assessment of optic disc stereophotography (average of 82 months of follow-up). The same group of investigators have previously shown that approximately 50% of patients with glaucoma have spontaneous venous pulsation (SVP), compared to 98% of age-matched normal controls,⁶ which was confirmed in other cohorts.⁷⁻⁸ Moreover, a strong inverse correlation was observed between the ODF and the mean deviation of the visual field. In cases where different ODF was required to induce pulsation of the two hemi-veins, there was a strong association between differences in the ODF measured in the two veins and differences in the corresponding hemifield mean sensitivities.⁶⁻⁷ These findings suggest that determining the presence of SVP and measuring ODF in cases without SVP might be clinically relevant in glaucoma and certainly deserves further research.

Despite some controversy regarding the aetiology of SVP, it is generally believed that it is caused by the oscillation of IOP during the cardiac cycle at a level significantly higher than the pressure in the retrolaminar portion of the central retinal vein.⁹⁻¹¹ Several factors are known to influence the venous pulsation pressure (VPP), which is the minimum IOP necessary to induce venous pulsation, consequently, the presence of SVP. Increased cerebrospinal fluid (CSF) pressure and increased systemic blood pressure cause an increase in VPP.⁷⁻⁹⁻¹⁰ This is observed clinically by the common absence of SVP

in patients with elevated CSF pressure. Additionally, evidence from modelling experiments suggest that the increased arterial resistance before the venous system reduces VPP, and the increased venous resistance increases VPP.⁹

A very intriguing question is why does VPP increase in individuals with glaucoma? It is unlikely that CSF pressure increases in individuals with glaucoma. Systemic hypertension is weakly associated with glaucoma,¹²⁻¹³ but previous studies have shown that the venous pulsation findings in subjects with glaucoma are independent of blood pressure.⁷ Several studies have shown that arterial resistance is increased in glaucoma, probably early in the course of the disease, which would cause a reduction and not an increase in VPP.¹⁴⁻¹⁵ Therefore, the most likely explanation for an increased VPP in subjects with glaucoma is an increase in central retinal vein resistance as it exits the eye. This increased resistance could certainly help explain the higher risk of central and hemiretinal vein occlusions observed in subjects with glaucoma.¹⁶⁻¹⁷ It could also help explain another common vascular phenomenon observed in subjects with glaucoma, namely the occurrence of optic disc haemorrhages.¹⁻² The aetiology of optic disc haemorrhages is still controversial,¹⁸ but increased venous resistance could certainly contribute to its occurrence. It would be interesting to compare the ODF in individuals with and without optic disc haemorrhages, but unfortunately the study of Balaratnasingam *et al* was not adequately powered for that analysis.

It is not difficult to imagine why central retinal vein resistance would be increased in glaucoma, when we consider the significant changes that occur at the level of the optic nerve head and, particularly, at the lamina cribrosa as glaucomatous cupping develops.¹⁹⁻²¹ The posterior displacement of the lamina cribrosa associated with nasalisation of the vessels in the optic disc can cause disturbances in blood flow in the central retinal vein, ultimately leading to increased resistance. The fact that this higher venous resistance, in the

form of a higher ODF, predicts increased excavation is, however, very intriguing. This group of investigators have shown that ODF is strongly correlated with visual field mean deviation, and, therefore, could be considered as an epiphenomenon of more advanced stages of the disease.⁷ The fact, however, that ODF predicts increased excavation after adjustment for visual field mean deviation, and for other variables such as age and IOP, suggests that increased VPP might be in fact an independent factor contributing to glaucoma progression.

In the study of Balaratnasingam *et al*, subjects with glaucoma and suspects of having glaucoma were grouped together. It would be interesting if the authors had reported on the predictive value of ODF in these two groups separately. Since, in their original studies, 75% of glaucoma suspect individuals have SVP, and an arbitrary ODF value of zero was utilised in these subjects, it is expected a low predictive value of ODF in this group due to this truncated effect. Ophthalmodynamometry is a relatively cumbersome technique that is unlikely to be readily incorporated into clinical practice for glaucoma. Determining the presence of SVP, however, is much simpler and can easily be performed during routine examination of optic discs. Balaratnasingam *et al* showed that increased excavation was two times more frequent in patients without SVP than in those with SVP (28% vs 14%, respectively) and, therefore, the mere determination of presence of SVP can be clinically helpful. Here, again, it would be useful to know the predictive value of the absence of SVP for increasing excavation in the two groups of patients, separately. It would be particularly useful to know the proportion of conversion that occurred in the 25% of suspects of glaucoma, who did not have SVP at baseline.

The study of Balaratnasingam *et al* certainly generates several interesting hypothesis on the role of altered venous resistance in glaucoma and should lead to further studies in this otherwise relatively neglected side of the vascular blood supply in glaucoma. Meanwhile, based on the data presented, clinicians should be encouraged to observe the presence of SVP in their patients, which could indicate a lower risk for glaucomatous progression. For those patients without SVP, measurement of ODF, although technically more complicated, might be a valuable clinical tool.

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All in the timing

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Bryan J Winn

mfVEP as a measure of perimetry

In this issue of the *BJO*, the paper by Semela *et al*¹ (see page 445) reports on the characteristics of the multifocal visual evoked potential (mfVEP) in six cases of compressive optic neuropathy (CON) secondary to optic nerve meningiomas. The mfVEP can be thought of as an objective measure of perimetry. With the display used by Semela's group, the 60 sectors tested comprise about the same area of visual field as the Humphrey 24–2 standard automated perimetry (SAP) test. Unlike SAP, the mfVEP does not require the subject to consciously register and respond to stimuli but rather is generated by the electrical potentials evoked by the individual pattern-reversal stimuli at the primary visual cortex.² The amplitudes of mfVEPs have been shown to correlate well with SAP in several optic neuropathies including ischaemic optic neuropathy (ION) and glaucoma.^{2–8} It is not surprising that the mfVEP amplitudes in optic nerve meningiomas follow suit. This is in agreement with work by Danesh-Meyer *et al*⁹ using the AccuMap system of mfVEP, demonstrating good amplitude correlation with SAP in CON due to pituitary lesions.

However, unlike the mfVEPs seen in ION and glaucoma, Semela *et al* demonstrate that CON mfVEPs have significant latency delays.^{10–11} This is consistent with conventional VEP studies showing prolonged latencies in compressive neuropathies including those caused by chiasmal gliomas, orbital tumours and thyroid orbitopathy.^{12–17} Prolongations in latency have been attributed to disruptions of the saltatory conduction along the myelinated portion of ganglion cell axons and are the hallmark of demyelinating entities such as optic neuritis.^{7–18} Both mechanical and vascular mechanisms for CON have been proposed, and an experimental model of compressive peripheral neuropathy induced by a pneumatic tourniquet demonstrating anatomical disruption of the nodes of Ranvier and subsequent demyelination supports Semela *et al*'s findings.^{17–19}

Semela *et al* found that the latency delays occurred topographically at the interface between normal and abnormal regions of the visual field and could be seen in areas of visual field that test normal on SAP, as is shown in their cases 1 and 4. Delays may not be seen inside the scotoma

owing to the fact that the mfVEP amplitudes are typically so diminished in areas of significant field loss that information on timing in these sectors is lost. However, the delays seen outside the areas of field loss are perhaps more interesting. Do these delays represent early signs of compressive optic nerve dysfunction? Although potentially interesting, this is clinically irrelevant in cases of optic nerve meningiomas as most of the cases are diagnosed only after presenting with visual loss. However, if true, it could prove a useful method for diagnosing early compressive neuropathy in thyroid orbitopathy and pituitary adenomas.

Unlike ION and glaucoma, which typically are not associated with any recovery of visual field, CONs frequently will improve when the compression is relieved. What happens to the latency changes after surgery or radiation? Are the latency changes somehow linked to the ability of nerves for recovery? Studies documenting visual outcomes after either surgical or radiation decompression of CONs show that 40–47% improved, 33–40% remain stable and about 20% worsen.^{20–21} Does the presence or absence of latency delays correlate with prognosis? It would be interesting to see how the mfVEPs and SAPs of Semela *et al*'s six cases change after intervention.

Semela *et al* suggest monitoring changes in amplitude for evidence of progression or recovery of CON. This is good for modest visual field defects. We know, though, that mfVEP amplitudes can be completely wiped out when Humphrey visual field thresholds drop below –6 dB.²² Theoretically, a recovery from –20 to –10 dB in a localised area