PRIMARY eyecare
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Dementia, eyes, and other related issues …

Every six minutes in Australia a person is diagnosed with dementia.

This is unlikely to be simply because they are Australian. Dementia in all its forms is emerging as a very significant health issue in many western countries where the baby-boomer generation is creating a population bubble in the over 65 age group. In Australia the government is taking notice and dementia has now been designated as the ninth National Health Priority Area in that country.

But dementia is not just a problem for the medical profession in providing care, assessments, and treatments; it can also be a problem for assessments of visual function and eye health. Many practising optometrists will have stories about older patients who give poor and invalid results to automated visual field testing, not because of eye problems but because of cognitive impairment preventing them attending to the visual stimuli and remembering to press the signal button.

Psychiatrist Dr Ruth Kippen, who specialises in the psychiatry of old age, is familiar with eye-care issues among her patients. Poor vision can exacerbate and aggravate behavioural problems in dementia, according to Dr Kippen, making them more confused, uncertain, and bewildered. Impaired vision also increases the risk of falls.

Another eye health issue for people with dementia could be cataract. Often a patient with early cataract can still have vision better than 6/12 and will still meet the New Zealand standard for Medical Fitness to Drive. With this level of vision the patient would not meet the priority weighting for publicly funded cataract surgery so it is normal to wait until the vision deteriorates further before referring to the public hospital. However, dementia specialists, such as Dr Kippen, suggest that cataracts be removed as soon as possible in patients with dementia while the patient still has the cognitive function to understand what is happening and is able to give informed consent.

Quite apart from surgery, it is important that GPs refer their dementia patients for dental and optometry treatment soon after diagnosis as those treatments become more difficult to deliver as the dementia progresses. Upper Hutt optometrist, Wilson Sue, notes that dementia patients can make mistakes with the Snellen chart because they forget the name of the letters. There is also the risk that as dementia progresses the patient may not be aware they have poor vision.

Poor vision can exacerbate and aggravate behavioural problems in dementia

Links between eye conditions and neurologic conditions

Scientists have discovered a link between cataracts and Alzheimer's that they hope will pave the way for new treatments for the brain disease.

Alzheimer's Disease

Researchers at Boston University Schools of Medicine, found evidence which indicates that dementia might originate outside of the brain and be connected to the body as a whole[1]. The link could mean an eye exam might provide an early indicator that someone has Alzheimer's.

Multiple lines of evidence suggest that specific subtypes of age-related cataract (ARC) and Alzheimer disease (AD) are related etiologically.

To identify shared genetic factors for ARC and AD, the researchers estimated co-heritability of quantitative measures of cataract subtypes with AD-related brain MRI traits among 1,249 members of the Framingham Eye Study who had a brain MRI scan approximately ten years after the eye exam for the original study.

In particular, cortical cataract was found to be co-heritable with future development of Alzheimer's Disease.

To further explore the influence of processes occurring in the eye and brain, the researchers tested for association between development of cortical cataract and performance on a set of cognitive tests including the Boston Naming Test (BNT), Immediate Recall (LMI) and Delayed Recall (LMD) portions of Logical Memory subtest of the Wechsler Memory Scale, and the Hooper Visual Organization Test (HVOT). Results showed a clear link between cortical cataract formation and poorer results on cognitive tests given to patients.

Immunohistopathological analysis of lens tissue obtained from two autopsy-confirmed Alzheimer subjects and two non-Alzheimer controls revealed elevated expression of δ-catenin in epithelial and cortical regions of lenses from Alzheimer subjects compared to controls. The findings suggest that genetic variation in delta catenin may underlie both cortical lens opacities in mid-life and subsequent cognitive changes that presage the development of AD.

The researchers suggest these discoveries mean that diagnosing Alzheimer's could be done earlier and also suggests new treatment targets for the debilitating disease. Onset of cortical cataract could be a trigger for referral for cognitive assessments and MR imaging of the brain.

General Brain Health

A new US study suggests that retinopathy could serve as a marker for brain health. The researchers found that women aged 65 and over with even a mild form of the retinopathy were more likely to have cognitive decline and related vascular changes in the brain.

The study, lead by Dr Mary Haan[2], professor of epidemiology and biostatistics at the University of California, San Francisco (UCSF), used data from two sub-investigations of the Women's Health Initiative Clinical Trial of Hormone Therapy; the WHI Memory Study and the WHI Site Examination study.

The paper published last year in Neurology, suggest that an eye exam which would note early signs of retinopathy could highlight this as a marker for cognitive changes linked to vascular disease. Referral would allow for earlier diagnostic tests and potentially treatments to reduce the progression of cognitive impairment to dementia.

Since retinopathy usually results from Type II diabetes or hypertension, an early diagnosis of retinopathy would also allow early intervention with medicine and/or lifestyle changes; to potentially reduce the progression to full onset hypertension.

The study analysed data on 511 women with an average age of 69 years at the start of a 10-year follow up during which the women underwent an annual cognition assessment that tested their short-term memory and thinking ability. They also had had an eye test in the fourth year of follow-up, and a brain scan in the eighth year.

Results showed that during the follow-up, 39 (7.6%) of the participants developed retinopathy, and on average, their scores on the cognition tests were worse than the women who did not develop the eye disease.

When they examined the brain scans, the researchers saw that the women with retinopathy had more damage in their brain blood vessels. Specifically, they had 47% more ischemic lesions or holes in the overall blood vessel structure, and 68% in the parietal lobe. Such lesions are thought to be caused by high blood pressure. They are typically seen with vascular disease and sometimes stroke.

Another feature that was more prominent in the brain scans of the women with retinopathy was more thickening of the white matter tracks that transmit signals in the brain. These thickenings are also thought to be due to high blood pressure.

Retinopathy was not linked to more brain atrophy, which is a hallmark of Alzheimer's disease, suggesting that retinopathy is probably not a marker for Alzheimer's disease.

In an editorial accompanying the publication of the research, Dr Rebecca F. Gottesman, Assistant Professor, Neurology at Johns Hopkins Intracerebral Haemorrhage Centre, wrote:

"This study highlights the potential importance of retinal evaluation in understanding the extent of cerebral microvascular disease that may be present in older adults. Retinopathy was significantly associated with cognitive scores and cerebral microvascular disease independent of the effect of hypertension and diabetes, suggesting that either it captures information beyond a simple binary yes/no diagnosis of hypertension and diabetes, or that perhaps preclinical disease is better captured with measures of retinopathy ..."

Glaucoma and the Brain

Glaucoma shares a number of features with degenerative brain diseases such as Alzheimer's, Parkinson's, and Lou Gehrig's disease[3]. In all of these diseases, age and family history are significant risk factors, and specific areas of the brain are damaged over time. In glaucoma, the only difference is that the "specific area of the brain" affected is the eye and optic nerve!

Because the retinal ganglion cell axon stretches from the retina through the optic nerve to the brain, its surrounding cells also become damaged by glaucoma. Within the retina, other cells, such as amacrine cells, degenerate and rewire their connections after retinal ganglion cells are lost. There are also changes in the brain within the lateral geniculate nucleus (the main brain target of optic nerve axons), and even the visual cortex.

Thus, in addition to treatments directed at lowering eye pressure, still the mainstay of glaucoma therapy, there may be opportunities to develop treatments directed at the retina and the brain. Some promising treatments that promote nerve health, called neurotrophic factors, could help at multiple places in the visual pathway. For example, neurotrophic factors such as ciliary neurotrophic factor (CNTF) may keep retinal ganglion cells from dying, they may increase axon regrowth down the optic nerve, and they may improve the support between the dying retinal ganglion cells and their surrounding cells in the retina and brain.

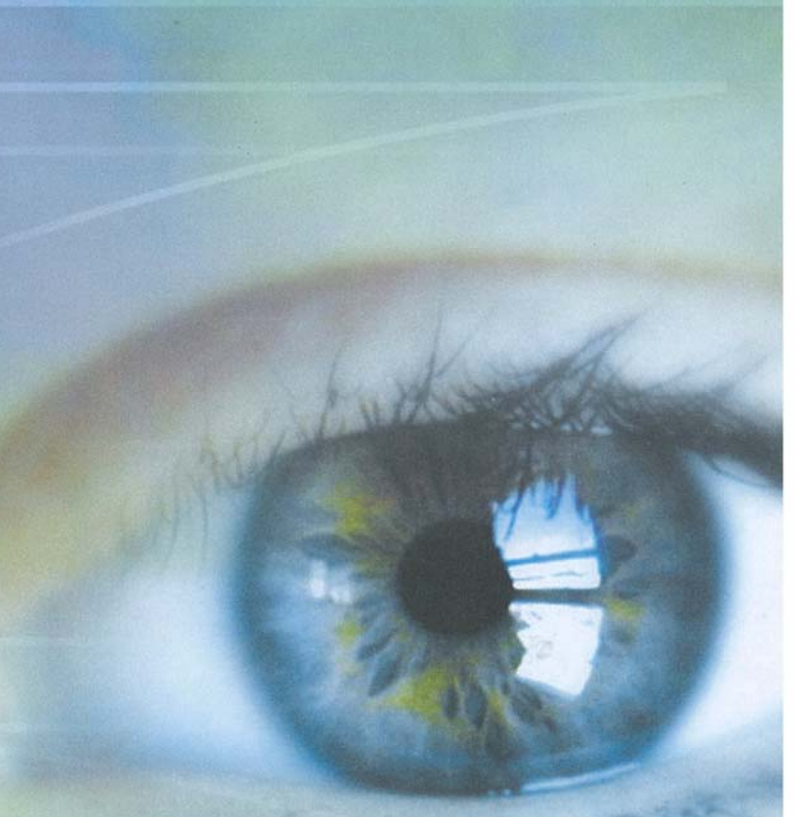
Retinal Nerve Fibre Layer and Diagnosis of Multiple Sclerosis

In an investigation of correlations between longitudinal changes in neuro-ophthalmologic measures and quality of life (QOL) and disability in patients with multiple sclerosis (MS), measures were taken using optical coherence tomography (OCT), visual evoked potentials (VEP), and visual field examination[4].

Fifty-four patients with relapsing-remitting MS took part in this study and completed the Multiple Sclerosis Quality of Life questionnaire (54 items) (MSQOL-54) and Expanded Disability Status Scale (EDSS) evaluation, as well as having a complete neuro-ophthalmologic examination including visual field testing and retinal nerve fibre layer (RNFL) measurements using OCT (Cirrus and Spectralis), and recording of visual evoked pootentials (VEP). All patients were re-evaluated at 12, 24, and 36 months. Logistical regression was performed to analyse which measures, if any, could predict their quality of life ratings.

Overall, RNFL thickness results at the baseline evaluation were significantly different from those at 3 years ($p \leq 0.05$), but there were no differences in functional measures (visual acuity, contrast sensitivity, colour vision, visual field, and VEP). Patients with progressive axonal loss as seen in RNFL results had a lower QOL and more functional disability.

Decreased thickness of the retinal nerve fibre layer (RNFL) is a classic finding on ophthalmoscopic examination of patients with MS and especially noted in those patients with a history of Optic Neuritis. The thickness of the RNFL can be measured by a non-invasive technique, optical coherence tomography (OCT).



Patients with xanthelasmata were found at increased risk of heart disease — regardless of cholesterol level.

More and more New Zealand optometrists are using OCT in their practices on a day to day basis making a review of OCT results to quantify axonal loss in the RNFL available to general practice as a promising tool to evaluate disease progression in MS and ON patients.

OCT measurements may also correlate with MRI measured brain atrophy and could provide an easily quantified and highly reproducible method in clinical trials to monitor the efficacy of both immune- and neuroprotective therapies. Potential correlations between OCT with other biomarkers that include low contrast vision, visual evoked potentials, colour vision and diffusion tensor imaging of the brain and advanced imaging of the optic nerve are promising new frontiers of research.

Plasma lipoprotein abnormalities and ischaemic heart disease

In the Lipids Research Clinics Program Prevalence Study, xanthelasma and corneal arcus were associated with increased levels of serum cholesterol and low density lipoprotein cholesterol (LDL-C), especially in young males[5]. People with either lesion had increased odds of having type IIa dyslipoproteinaemia. Adjusted odds ratios for ischaemic heart disease in participants with xanthelasma and corneal arcus were generally increased. The study concluded that the clinical findings of xanthelasma or corneal arcus, especially in young people, helped to identify those with plasma lipoprotein abnormalities.

Danish researchers also reported that the risk of having a heart attack, developing heart disease or dying over the next 10 years increased in people who had xanthelasma[6]. The older you are, the higher the risk.

Men ages 70 to 79 with the patches had a 53 percent increased risk of developing heart disease compared to a 41 percent risk for men without them. Women in their 70s had a 35 percent increased risk versus a 27 percent risk for women without the patches. The researchers found that patients with xanthelasmata did not necessarily have high cholesterol but—regardless of cholesterol level—were still at increased risk of heart disease. It has long been known that xanthelasmata are linked to raised cholesterol, but if the patient had normal cholesterol, no further action would have been taken. This suggests GPs need to consider CHD management of all patients with xanthelasmata, not just those with raised cholesterol levels.

References

1. Jun G, Moncaster JA, Koutras C, Seshadri S, Buros J, et al. (2012) δ -Catenin Is Genetically and Biologically Associated with Cortical Cataract and Future Alzheimer-Related Structural and Functional Brain Changes. PLoS ONE 7(9): e43728. doi:10.1371/journal.pone.0043728
2. Haan M, Espeland MA, Klein BE, Casanova R, Gaussoin SA, et al. (2012). Cognitive function and retinal and ischemic brain changes The Women's Health Initiative. Neurology 78(13): 942-949, doi: 10.1212/WNL.06013e31824d9655.
3. Article by Jeffrey L. Goldberg, MD, PhD**,** Associate Professor of Ophthalmology at the Bascom Palmer Eye Institute
4. Garcia-ME, Rodriguez-Mena D, Herrero R, Almarcegui C, Dolz I, Martin J, Ara JR, Larrosa JM, Polo V, Fernández J, Pablo LE. Neuro-ophthalmologic evaluation, quality of life, and functional disability in patients with MS. Neurology. 2013 May 24. [Epub ahead of print]
5. Segal P, Insull W Jr, Chambless LE, et al. The association of dyslipoproteinemia with corneal arcus and xanthelasma. The Lipid Research Clinics Program Prevalence Study. Circulation 1986;73:108–18.
6. Christoffersen M, Frikke-Schmidt R, Schnohr P, et al. Xanthelasmata, arcus corneae, and ischaemic vascular disease and death in general population: prospective cohort study. BMJ 2011; 343:d5497.