Simerdip Kaur takes a look at the latest ophthalmology-related news stories and asks which are based on facts and which are 'fake news'.

Headline: Can OCT predict Alzheimer's disease?

In 1986 Hinton et al. demonstrated evidence of optic nerve degeneration on post-mortem studies of patients with Alzheimer's disease (AD) in contrast to age-matched healthy non-demented controls. He found patients with AD to have a reduced number of axons with increased number of glial cells in their optic nerve [1]. Light microscopy on portions of the supero-temporal retina of these patients also showed loss of retinal ganglion cells (RGC) and thinned retinal nerve fibre layer (RNFL). Three years later in 1989, David Huang and Joel Schuman performed the first retinal imaging using the optical coherence tomography (OCT). The clinical prototype of the machine was built and trialled between 1993 and 1996 and the first commercially available OCT machine reached the market in 1996. Today every eye department in the country is home to at least one [2]. OCT technology was revolutionary in allowing 3D imaging and submillimetre resolution of ocular structures and in 2014 OCT-angiography (OCT-A) became commercially available, enabling clinicians to visualise retinal microvasculature non-invasively and in more detail than standard fluorescein angiogram (FA) [3].

The interest surrounding OCT and OCT-A with progressive neurodegenerative disease such as AD stems from the theoretical presumption of both the retina and brain structures sharing the same embryological and histological origin, thus assuming that the eye could be used as a biomarker for neurological disease [4]. Furthermore, identifying AD biomarkers is often an invasive process requiring cerebrospinal fluid (CSF) samples for total tau and amyloid proteins, in addition to imaging that is associated with radiation exposure for patients and so AD remains largely a post-mortem diagnosis. Thus the prospect of being able to detect it at preclinical stage would give patients the best chance at preserving their cognitive function for longer, hence improving the success of treatment.

Several findings have been reported in retinas of patients with AD. Bulut et al. observed on OCT-A imaging a significantly enlarged foveal avascular zone (FAZ), a thinner choroidal layer and lower vascular density of retinal vessels in all retinal zones [5]. They hypothesised that these changes were likely related to reduced angiogenesis from binding of vascular endothelial growth factor (VEGF) to amyloid-beta proteins forming plaques in vessel walls leading to vascular occlusion and decreased blood flow. In another cross-sectional study, Zhang et al. noted hypoperfusion of the inner retina in the macula region in patients with early AD. There was also a positive correlation between this and cognitive performance [6]. Both studies were made up of small sample sizes and single centre cross-sectional in design, hence whilst able to demonstrate correlation, they cannot imply causation.

Perhaps more convincingly, the Rotterdam and UK Biobank studies have demonstrated RNFL thickness association with cognitive function. In the former, a five year prospective population based longitudinal study of 3289 Dutch individuals revealed that a thinner RNFL at baseline was associated with an increased risk of developing AD, leading the authors to suggest that this parameter could be used as a preclinical biomarker for the disease [7]. In the latter, a cohort study of 32,038 participants from a community population without diabetes, ocular or neurological disease or visual loss between the ages of 49 and 60, similarly there was a significant association between thinner RNFL at baseline and worse cognitive function with a doubling in the likelihood of cognitive decline over three years [8]. Therefore, the authors believe that RNFL thickness can be utilised as a potential risk-stratification tool for predicting cognitive decline in pre-morbid healthy participants. Nevertheless, they acknowledge that it should not be used in isolation. There is also lack of data on the impact of any interventions for AD on the OCT findings discussed thus far. Additionally, it would be unethical to use RNFL thickness as a screening tool for AD in the absence of successful prevention or treatment strategies.

And so, what does the future hold for using the eye as a biomarker for AD? The AlzEye study led by Dr Pearse Keane is currently underway and will link over two million retinal images and OCT scans of around 250,000 patients that have attended Moorfields Eye Hospital over the last 10 years with each individual's medical history and diagnoses including cardiovascular and neurodegenerative health, as well as hospital admissions, accident and emergency attendances and outpatient clinic appointments [9]. The researchers predict approximately 5,000 cases of incident dementia will be identified and expect to develop prediction models for AD through the application of artificial intelligence on the dataset. This study is eagerly anticipated by the scientific community and clinicians alike, as it will without a doubt provide robust evidence and answers to many unsolved questions including the chicken and egg dilemma surrounding retinal OCT findings and AD.

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