Brainstorm

ADMIRE: Alzheimer's Diagnosis via Multimodal Imaging of the Retina, towards novel diagnostic biomarkers

Poster number: 11
Poster presenter: Yasmin Dahdouh-Guebas

Aims, research questions and working hypothesis
This research aims to develop novel retinal biomarkers for Alzheimer's disease (AD). As an extension of the central nervous system, the retina manifests many of the characteristic pathological processes that occur in the AD brain and can be imaged at low-cost and non-invasively at high resolution. Therefore, it offers an opportunity for early AD detection and monitoring of disease progression. Emerging evidence also suggests that *in vivo* hyperspectral retinal imaging (HSRI) may serve as a biomarker for amyloid-β accumulation in the brain, although its specificity and pathological correlates remain unclear. This research aims to develop a multimodal retinal imaging approach for researchers and clinicians, integrating multiple potential biomarkers: amyloid-β deposition (via HSRI), neuro-retinal atrophy, and (micro)vascular alterations (using OCT, angio-OCT, and fundus imaging). Additionally, we aim to gather evidence on the specificity and molecular basis of the HSRI signal in both preclinical animal models and AD patients, and to establish whether common age-related eye diseases have HSRI signals that are distinct from those of AD. We hypothesise that multimodal retinal imaging is a sensitive and specific tool for AD screening, diagnosis and follow-up.

Means/methods implemented by the consortium
The BRAINSTORM consortium is the first of its kind to bring together leading clinicians and scientists with diverse expertise in AD in neuropathology, ophthalmology, imaging and artificial intelligence to validate multimodal retinal imaging biomarkers of AD. We implemented hardware, image acquisition protocols, and analysis algorithms to accurately measure early pathological processes within a (pre)clinical research framework. Preclinical studies in cell and animal models were used to establish a rationale for applying HSRI to detect retinal amyloid-β (Aβ) in human patients, by correlating the HSRI signature with established biomolecular quantifications of disease-associated proteins. Clinical studies were conducted in (i) adults at risk of developing AD, to validate the diagnostic and prognostic value of multimodal retinal imaging biomarkers and to evaluate the association between amyloid status and HSRI outcomes; and in (ii) volunteers with common age-related eye diseases, to establish whether these diseases have HSRI signals that are distinct from those of AD.

What are the outcomes of the project?
Outcomes of the project – already reached or anticipated by the end of the project – are: (i) to have evaluated retinal imaging biomarkers of AD, including HSRI, against CSF, neuroimaging, blood & neuropsychological biomarkers of AD in adults at risk of AD; (ii) to have established the specificity of these retinal imaging biomarkers of AD by imaging cognitively normal people with common age-related eye diseases; and (iii) to have established the pathological correlates of retinal imaging biomarkers of AD in preclinical models.

Significance and impact of the work on the field
This research seeks to revolutionize the clinical management of AD through improved detection at preclinical stages in a non-invasive, rapid and cost-effective manner. We address the need for novel, non-invasive and affordable biomarkers to identify individuals at risk of AD who require further neurological evaluation, to enable longitudinal monitoring of disease progression in these patients, and to support (pre)clinical research for more effective treatments. This approach leverages the retina, the most accessible part of the central nervous system, as a critical diagnostic tool.

Next steps and future challenges
The final phase of the project is dedicated to data processing and analysis of the data from the clinical studies that was collected thus far, and a correlation study of HSRI data and biomolecular analyses of post mortem retinal samples. At the same time, we plan to continue data collection via the streamlined approach set up during this project, to increase sample sizes. In follow-up research, we seek to evaluate whether this multimodal approach could be used for other proteinopathies such as Parkinson disease.