The eye as a biomarker for Alzheimer's disease: oculomotor behaviours yield a novel digital biomarker for preclinical risk detection

Eye movements as a biomarker for AD risk detection

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Background: They eyes seem to hold a key to unveil early manifestations of Alzheimer's disease (AD) pathology beyond retinal analysis. We have recently confirmed that eye-tracking (ET) metrics recorded during performance on memory tasks can identify early and subtle changes in individuals at risk of or with AD dementia [1, 2]. There is a need for more robust and automatic classification methods that can provide affordable digital biomarker solutions for the preclinical detection of AD. This was the aim of this study.

Methods: A sample of 16 asymptomatic carriers (AC) of the mutation E280A-PSEN1 from the widely investigated cohort of Antioquia, Colombia[3], and 55 healthy controls (HC) entered the study. Both groups were assessed with the novel Visual Short-Term Memory Binding Task (VSTMBT)[4] coupled with an ET device. The VSTMBT assesses the ability to temporarily hold bicoloured objects whose colours had to be remembered either as individual features (baseline) or integrated within unified representations (binding). Oculomotor behaviours (i.e., fixations, saccades, pupillometry) recorded using ET were subjected to Artificial Intelligence technology. This relied on Machine Learning classification using Lasso and Elastic-Net Regularized Generalized Linear Models ("glmnet").

Results: AC and HC could not be distinguished based on traditional neuropsychological assessment (e.g., MMSE: HC = 29.7(0.4), AC = 29.5(0.8), p= 0.09). ML accuracy for classifying subjects into correct groups (HC and AC) was 98%. For a cut-off of 0.72, 55 out of 55 HC and 14 out of 16 AC were correctly classified (see Fig 1).

Conclusion: Relative to behavioural measures (i.e., percentage correct recognition) drawn from the VSTMBT, AI-powered technology can significantly enhance the detection of at risk individuals. By better characterising abnormal oculomotor behaviours, phenotypic features of the preclinical stages of AD can be unveiled [5]. The facts that such a phenotypic expression characterised the majority of AC warrants further investigation in populations who hold less-well known risk for AD.

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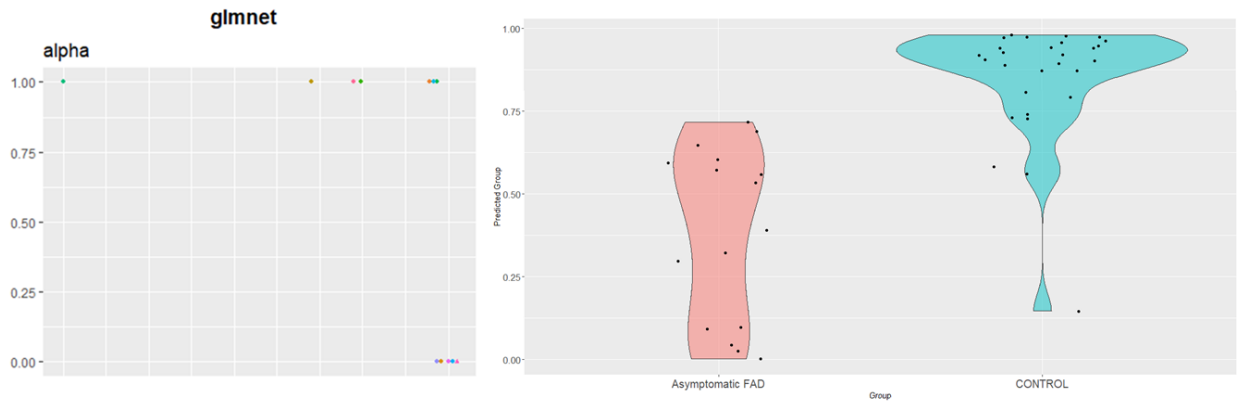

Figure 1. Outputs from the Machine Learning classification using Lasso and Elastic-Net Regularized Generalized Linear Models ("glmnet").

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