Fixational eye movements as biomarkers for pre-symptomatic AMD

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Résumé

Age-related Macular Degeneration (AMD) is the main cause of vision loss in developed countries. Atrophic or dry AMD starts with the accumulation of extracellular deposits, called drusen, in-between the Bruch's membrane and the RPE, and it accounts for about 90% of the cases. It has become a major public health concern as no effective treatment currently exists. It is however possible to engage in risk mitigation strategies, including lifestyle modifications and the use of food supplements, to slow down drusen accumulation and geographic atrophies growth. However patients often receive a diagnosis only upon the emergence of clinical indications, often at a stage too advanced for effective implementation of these preventive strategies. A presymptomatic detection of dry-AMD would also allow for the testing of novel clinical therapies being developed.
In this study we tested the hypothesis of a relationship between subtle structural retinal anomalies and fixational eye movements characteristics by examining healthy young and older controls, and participants with foveal drusen but no scotoma or atrophy yet. Importantly, this presymptomatic condition is not necessarily meant to degenerate into geographic atrophy, and it rather reflects a higher risk for dry-AMD onset with respect to normal eye senescence. Hence, this study aimed at revealing anatomo-functional biomarkers of dry-AMD onset, thus paving the way for the implementation of preventive approaches.

In order to record fixational eye movements, we set forth a novel method to imaging and tracking the foveal region with high speed, high resolution, and no distortion, while simultaneously projecting stimuli on the retina for psychophysical testing. This was made possible by the use of the PARIS Adaptive Optics Flood-Illumination Ophthalmoscope (AO-FIO) developed by ONERA. This AO-FIO allowed micro eye movements to be tracked with one of the highest possible precisions and no motion artifacts. Foveal drusen were identified and visualized by applying the recently developed gaze-dependent AO-FIO protocol described by Rossi et al., which provides a higher drusen detection accuracy as compared to standard OCT methods. We were able to precisely measure drusen positions and sizes of each participant, and compare them to fixational eye movements data in order to analyze how fixation was impacted by small foveal drusen.

The primary finding of this study is that participants with foveal drusen exhibit significantly larger microsaccade amplitudes and fixation instability (measured by ISOA) as compared to healthy controls. Strikingly, drusen eccentricity with respect to the center of the fovea

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appears to be the main determinant factor for larger microsaccades and ISOAs. Indeed, we found that the more central the drusen were, the more unstable the fixation was; the further from the center of the fovea the drusen were, the more the participants tended to behave like controls, with minimal to no changes in fixation stability. Microsaccade amplitude started increasing exponentially when drusen were within 0.8◦ to 1◦ with respect to the center of the fovea. Considering the size of the drusen and the fixation target, we hypothesize that the inflexion point would correspond to the size of the foveola.

In conclusion, this study suggests a direct link between foveal drusen and FEM, providing a potential functional biomarker to detect dry-AMD at a presymptomatic stage.

Mots-Clés: fixation, fixational eye movements, FEM, drusen, AMD, eye tracking, AOFIO, retinal imaging