A novel peripheral biomarker for Mild Cognitive Impairment and Alzheimer’s disease

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Background
Recent evidence suggests that oculomotor behaviours linked to cognitive performance can be a biomarker of Alzheimer’s disease (AD) (Fernandez et al., 2018). Short-Term Memory Binding (STMB) declines in patients with AD dementia and in those at risk of dementia. STMB relies on brain regions relevant to visual processing which are known to support oculomotor behaviours. A combined analysis of oculomotor responses during STMB can enhance the sensitivity of the assessment of patients at risk of AD such as those with Mild Cognitive Impairment (MCI). We investigated this hypothesis.

Methods
The sample comprised 42 controls (Age M=72±SD=6.7; education = 12 years) and 63 patients with MCI (Age 73±6.1; education = 12). The sample was recruited at the AXIS Neuroscience Centre, Bahía Blanca, Argentina. The mean score of MCI patients in the MMSE was 26.6 (SD = 2.2) vs. 29.7 (SD = 0.4) in controls. The mean score of MCI patients in the ACE-R was 78.3±10.8 vs. 93.2± 0.8 in controls. The mean score of MCI patients in the INECO’s Frontal Screen was 18.4±5.2 vs. 27.0±1.1 in controls. Yesavage’s Geriatric Depression Scale (GDS) in MCI was 8.5±2.8, cut-off point 9. Pfeffer functional activity in MCI was 6.1±1.5, cut-off 6. Hamilton’s Anxiety Scale in MCI was 16.3±3.5, cut-off 18. Patients and controls were assessed with the STMB test (Figure 1). Patients’ clinical status was reassessed one year after their enrolment in the study.

Results
Relative to controls, MCI patients displayed significantly shorter fixation durations at baseline (Figure 2). This was more pronounced during the encoding (t=−21.81) than during retrieval (t=−4.34), and during the BC condition (t=−16.98) than the UC condition (t=−13.82). MCI patients also displayed larger saccades. Again, these were more pronounced during the encoding (t=23.51) than during retrieval (t=−9.06), and during the BC condition (t=21.46) than the UC condition (t=−11.68).

At follow up, 28 patients with MCI had progressed to dementia. Retrospective analysis (Figure 3) revealed the pattern above described was more pronounced in MCI patients who latter developed dementia than in those who remained stable.

Discussion
Taken together, the results above suggest that eye-tracking measures combined with cognitive markers for AD (STMB) can (1) enrich the clinical phenotype of this type of dementia, (2) unveil novel features of AD dementia unknown to date, and (2) provide more sensitive tools which can detect and trace aspects of such phenotype in people at risk, thus helping to ascertain the presence of the prodromal stages of the disease.