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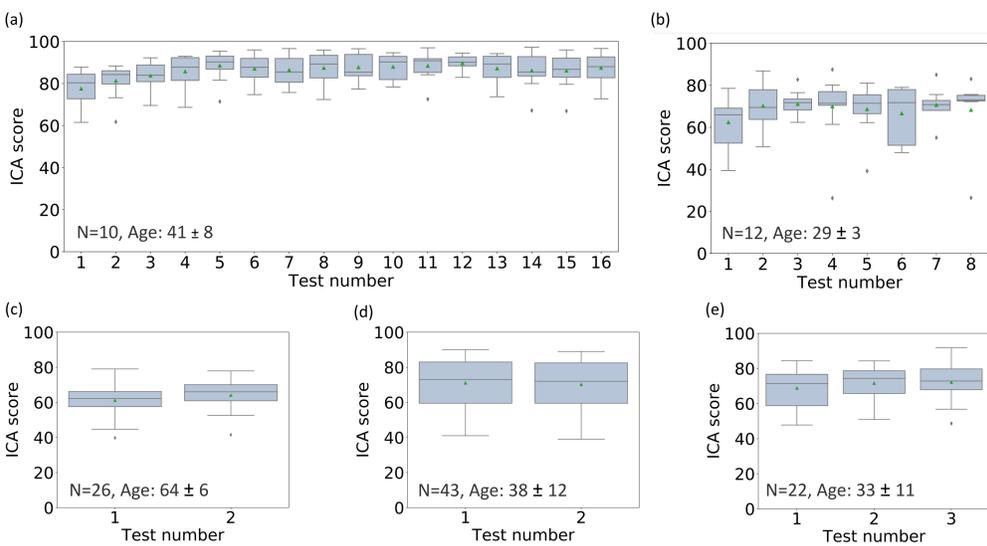
## Introduction

Neurodegenerative disorders, such as Alzheimer's Disease (AD), continue to present a major economic, social and healthcare burden. These diseases remain underdiagnosed or are diagnosed too late for meaningful interventions. The development of screening tests capable of detecting AD during early, preferably asymptomatic, stages has been a highly unmet need. Since such tests will be used for screening large populations of people, they should be non-invasive, inexpensive, and ideally independent of language, education, culture and practice.

## Methods

Taking advantage of new artificial intelligence (AI) and machine learning techniques, we have developed a 5-minute integrated cognitive assessment tool (ICA) that meets the above-mentioned criteria, and has the flexibility to learn from new data to improve its predictive power. The ICA is computerised, can be conducted without expert supervision, and is designed based on a rapid visual categorisation task, tracking participants' response-patterns to natural stimuli to detect small changes in their cognitive performance.

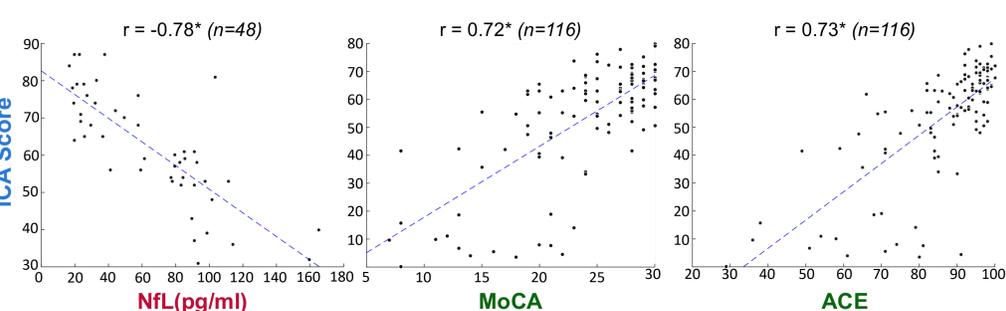
### ICA shows no significant learning bias



(a) 10 participants completed 16 tests on iPad and iPhone devices. ANOVA one way p-value=0.06 (b) 12 healthy participants took the ICA test every other day for over two weeks. From these 12 participants, 7 completed all sessions and the rest completed the test for at least the first three sessions. ANOVA one-way p-value=0.73 (c) A combination of 26 healthy/MCI/mild AD participants performed a test and subsequent retest. T-test p-value=0.06 (d) A combination of 43 healthy/MS participants performed a test and subsequent retest. T-test p-value=0.24 (e) 22 participants completed three tests on iPad and iPhone devices. ANOVA one-way p-value=0.54

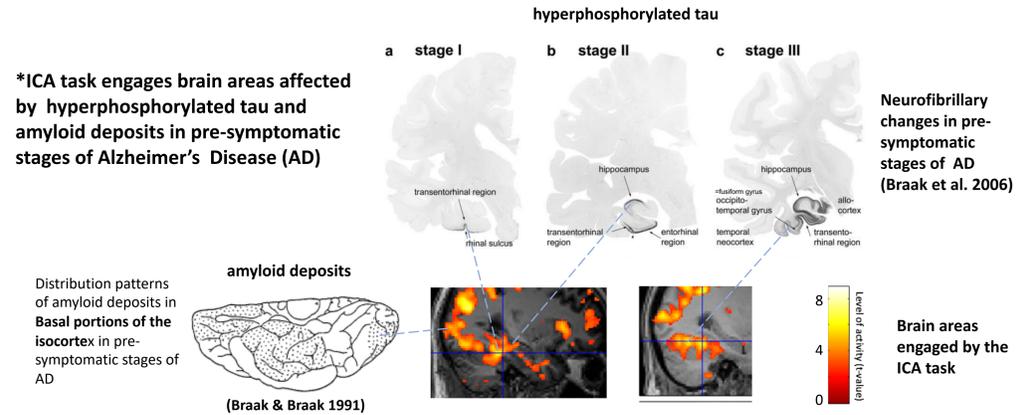
The ICA demonstrates no evidence of learning bias<sup>1</sup> (which affects standard cognitive assessments) for different demographics and platforms (Figure 1). Therefore the ICA test is suitable for frequent cognitive assessment or micro-monitoring of cognitive performance.

### ICA correlation with MoCA, ACE and plasma biomarker (NfL)



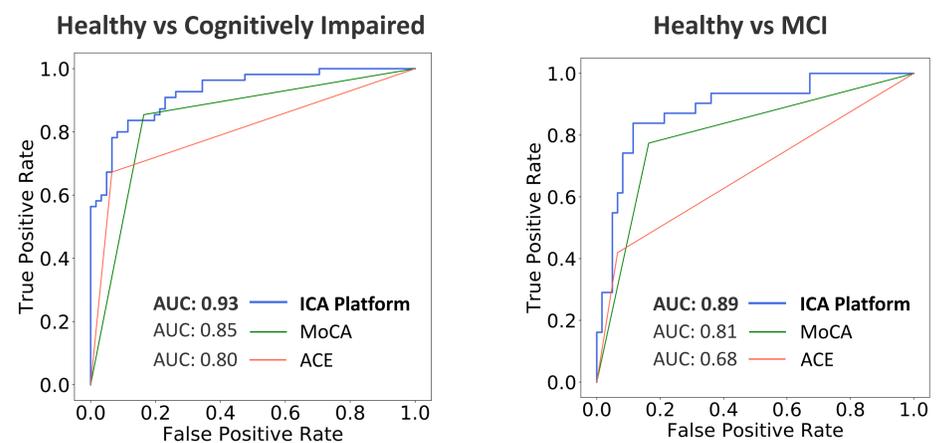
The ICA demonstrates convergent validity with MoCA and ACE and also shows a strong correlation with NfL and severity of cognitive impairment.

## Task-based fMRI



In a task-based fMRI investigation (30 participants), we find that the ICA task engages brain areas, such as transentorhinal, fusiform gyrus, inferior and middle temporal, that are anatomically identified among the earliest areas affected by tau-pathology and amyloid deposits in presymptomatic stages of AD, as shown by Braak and colleagues<sup>2,3</sup>, 1991 and 2006.

### ICA accuracy in detecting cognitive impairment



	Classification type	Number Subjects	Area under curve		
			ICA	MoCA	ACE
Mild AD / MCI / Healthy	Healthy vs Cognitively Impaired	116	0.93	0.85	0.8
	Healthy vs MCI	92	0.89	0.81	0.68
	Healthy vs mild AD	85	0.96	0.90	0.97
	MCI vs mild AD	55	0.91	0.74	0.82
MS / Healthy	Healthy vs Cognitively Impaired	152	0.97		
All subjects	Healthy vs Cognitively Impaired	268	0.93		

Summary of ICA Platform performance and comparison with MoCA and ACE

## Conclusions

- The ICA engages brain areas affected in early stages of AD, and shows high sensitivity in detecting cognitive impairment.
- The ICA is self administered and language independent, and as such the test can be used as an aid for early diagnosis of AD, ideally even in pre-symptomatic stages, and is appropriate for large-scale screening of cognitive impairment, and micro-monitoring of cognitive performance.
- The ICA has demonstrated to be free from a learning bias (i.e. practice effect).
- As an iPad test, the ICA has potential for integration with EHR and electronic medical record or research database integration.
- The above attributes yield significant clinical benefits in the day-to-day identification of MCI and AD in specialist clinical settings, in primary care and in remote cognitive monitoring.

## References

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