#5 Multi-country evaluation of the Altoida Digital Neuromarker Platform: Advancing the Detection of Mild Cognitive Impairment (MCI) and Alzheimer's Disease with AR and ML-based Digital Biomarkers

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BACKGROUND

- Traditional cognitive assessments are not fit to detect the earliest signs of Alzheimer's disease due to their subjectivity, bias, and lengthy administration.
- Individuals with subjective cognitive decline (SCD) or mild cognitive impairment (MCI) face a high risk of cognitive worsening over time.
- Digital biomarkers, derived from assessments that engage the brain in daily living-like exercises, have the potential to enable early, accurate, and accessible diagnoses.

OBJECTIVES

- To evaluate the diagnostic accuracy of a machine-learning (ML)-based digital cognitive assessment (Altoida NeuroMarker Platform) to identify MCI.
- To evaluate the concordance between the Altoida Platform, the clinical classification and the Mini Mental State Examination (MMSE) cutoff of 25.
- To explore group differences in digital biomarkers captured by the augmented reality tasks in the Altoida Platform in individuals classified by amyloid status.

ALTOIDA NEUROMARKER PLATFORM

- The Altoida NeuroMarker platform is an investigational medical device that evalues cognitive and functional abilities by simulating iADL-like activities.
- The Altoida NeuroMarker platform evaluates multimodal features, which are used by specific ML classification models trained with validated data (clinical diagnosis, neuropsychological tests, etc.) obtained from clinical cohorts.
- The MCI NeuroMarker is a binary model that labels a patient's assessment results with either an MCI or no MCI classification.

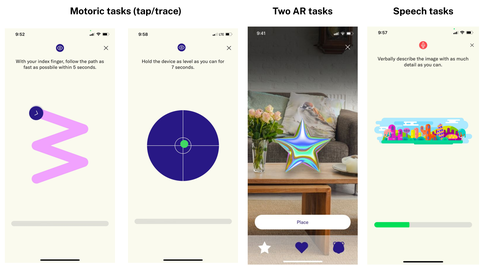

Figure 1. Screenshots from the Augmented Reality (AR) tasks of the Altoida Cognitive Assessment. The Altoida Cognitive Assessment is conducted on iOS tablets and lasts approximately between 10 and 15 minutes (data shown here was conducted at clinical sites on iPad Pro 11" devices). The Altoida Cognitive Assessment consists of motoric, speech and augmented reality tasks (see screenshots). In the AR tasks the participant is instructed to place 3 virtual objects in the room and retrieve them.

STUDY POPULATION

Diagnostic performance was tested across six (6) clinical cohorts comprising 390 individuals (469 Altoida Cognitive Assessments) in 13 countries (Greece, The Netherlands, Spain, UK, Romania, Germany, Portugal, Switzerland, Italy, Sweden, Norway, Slovenia and Brazil). The clinical cohorts consisted of cognitively unimpaired individuals as well as those with MCI. Their diagnosis was obtained through clinical evaluation and assessment with a standard neuropsychological battery.

We explored additional analyses on a subset cohort (n=116, number of assessments = 116) recruited at the Barcelonaβeta Brain Research Center (BBRC; Spain), diagnosed with Subjective Cognitive Decline (n = 106) and Mild Cognitive Impairments (n = 10).

Participant's characteristics by clinical group

	SCD (N=106)	MCI (N=10)	Total (N=116)	P-value
Sex				
female	64 (60.4%)	4 (40.0%)	68 (58.6%)	0.315
male	42 (39.6%)	6 (60.0%)	48 (41.4%)	
Age (years)				
Mean (SD)	65.8 (6.23)	70.6 (4.17)	66.3 (6.22)	0.00595
Median [Min, Max]	66.0 [55.0, 80.0]	70.5 [63.0, 76.0]	67.0 [55.0, 80.0]	
Education level				
College or University degree	57 (53.8%)	3 (30.0%)	60 (51.7%)	0.00264
High School diploma	35 (33.0%)	1 (10.0%)	36 (31.0%)	
No High School	14 (13.2%)	6 (60.0%)	20 (17.2%)	
MMSE				
Mean (SD)	28.6 (1.36)	27.4 (1.35)	28.5 (1.39)	0.0237
Median [Min, Max]	29.0 [24.0, 30.0]	28.0 [24.0, 29.0]	29.0 [24.0, 30.0]	
Amyloid status				
Aβ-	85 (80.2%)	5 (50.0%)	90 (77.6%)	0.0437
Aβ+	21 (19.8%)	5 (50.0%)	26 (22.4%)	

Table 1. Between-group demographic differences in continuous variables. The variables were tested with Student's t-test. Differences in proportions were tested with chi-squared or Fisher's test, as appropriate. Aβ = amyloid beta. SCD = subjective cognitive decline. MCI= mild cognitive impairment. MMSE= Mini-Mental State Exam. SD = standard deviation. No difference was found between groups in biological sex. Significant differences were found in age, educational level, and MMSE results.

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DIAGNOSTIC PERFORMANCE

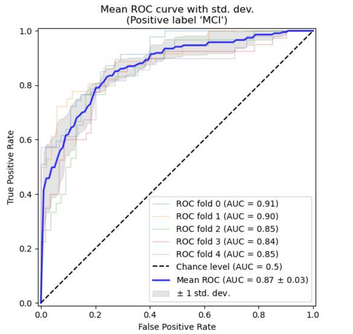

Figure 2. Receiver Operating Characteristic (ROC) curves depicting the Area Under the Curve (AUC) for the identification of MCI in the multi-country cohort (n = 390: 162 MCI, 228 CN; assessments = 469). The Altoida's NeuroMarker Platform differentiated individuals with MCI from those without MCI with an AUC of 0.87 ± 0.03.

CONCORDANCE OF THE MCI NEUROMARKER CLASSIFICATION

	"Negative clinical" - SCD (N=106)	"Positive clinical" - MCI (N=10)	Total (N=116)
MCI NeuroMarker Classification			
"Negative Altoida" – Cognitively unimpaired	101 (95.3%)	6 (60.0%)	107 (92.2%)
"Positive Altoida" - Cognitively impaired	5 (4.7%)	4 (40.0%)	9 (7.8%)

Table 2. Confusion matrix showing the concordance between the classification of the MCI NeuroMarker and the clinical diagnosis in the BBRC subset. SCD = negative for MCI, MCI = positive for MCI. 95.3% of the participants were classified correctly as Cognitively Unimpaired (Negative).

	MMSE>25 (N=111)	MMSE<=25 (N=5)	Total (N=116)
MCI NeuroMarker Classification			
"Negative Altoida" – Cognitively unimpaired	105 (94.6%)	2 (40.0%)	107 (92.2%)
"Positive Altoida" - Cognitively impaired	6 (5.4%)	3 (60.0%)	9 (7.8%)

Table 3. Confusion matrix showing the concordance between the classification of the MCI NeuroMarker and the MMSE by a threshold of 25 in the BBRC subset. MMSE = Mini-Mental State Examination. 94.6% of the participants were classified correctly as Cognitively Unimpaired (Negative) compared to those who scored above 25 or more on the MMSE.

	Aβ- (N=85)	Aβ+ (N=21)	Total (N=106)
MCI NeuroMarker Class			
"Negative Altoida" – Cognitively unimpaired	84 (98.8%)	17 (81.0%)	101 (95.3%)
"Positive Altoida" - Cognitively impaired	1 (1.2%)	4 (19.0%)	5 (4.7%)

Table 4. Confusion matrix showing the concordance between the classification of the MCI NeuroMarker and the the amyloid status in the BBRC subset. Aβ- = amyloid negative; Aβ+ = amyloid positive. 98.8% of the participants were classified correctly as Cognitively Unimpaired (Negative) compared to participants with a negative amyloid determination

LEVERAGING DIGITAL BIOMARKERS FROM AUGMENTED REALITY TASKS TO COMPARE CLINICAL GROUPS AND AMYLOID STATUS

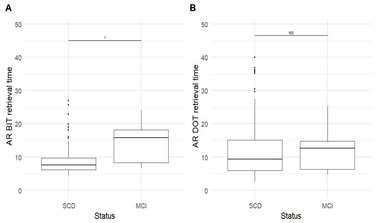

Figure 3. Boxplots indicating the time to retrieve the objects on the (A) Back in Time (BIT) and (B) Day Out Task (DOT) in SCD and MCI participants from the BBRC subset. SCD participants showed significantly lower retrieval times than the MCI participants on the BIT AR task (A), but not on the DOT task (B). *p<0.05 (gamma regression with Wald's test on the coefficients adjusted for age and education)

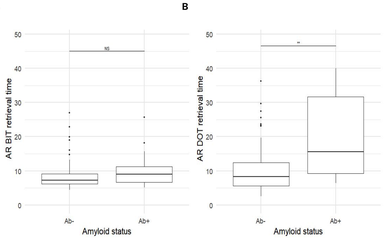

Figure 4. Boxplots indicating the time to retrieve the objects on the (A) Back in Time (BIT) and (B) Day Out Task (DOT) in Aβ- and Aβ+ participants from the BBRC subset. Aβ- participants showed significantly lower times to retrieve the objects on the DOT task, but not on the BIT task. **p<0.01 (gamma regression with Wald's test on the coefficients adjusted for age and education)

CONCLUSIONS

- The MCI NeuroMarker holds strong potential to identify MCI with a simple, tablet-based multimodal assessment lasting under 15 minutes.
- The MCI NeuroMarker classification aligns with the stratification of clinical diagnosis and well-established cognitive screening tools (MMSE).
- Digital biomarkers from tasks simulating activities of daily living could be leveraged to identify incipient signs of amyloid pathology.