Agreement between Altoida's Digital Biomarker Platform and Standard Neuropsychological Tests in Individuals with Subjective Memory Complaints

P-234

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BACKGROUND

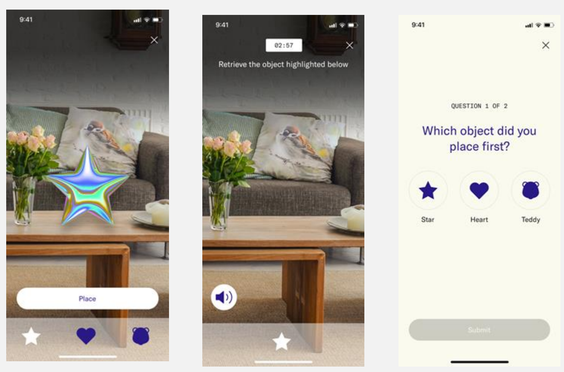
- The limited access to early diagnosis of Alzheimer's disease (AD) poses a significant bottleneck to accessing therapy (1).
- People presenting with subjective cognitive decline (SCD), or mild cognitive impairment (MCI) face a high risk of cognitive worsening over time (2).
- Digital biomarkers are gaining traction for their potential to enable early diagnosis and streamline the patient's dx journey to specialized care (3).

OBJECTIVES OF THE STUDY

1. To examine the effectiveness of a digital cognitive assessment (Altoida MCI NeuroMarker) in identifying cognitive impairment as established by a clinical evaluation and in conjunction with MMSE.
2. To evaluate the concordance of this digital assessment with a standard cognitive testing battery.
3. To leverage the digital biomarkers captured by the Altoida platform to explore differences beyond machine-learning (ML)-based classification associated with amyloid deposition.

ALTOIDA MCI NEUROMARKER PLATFORM

- The Altoida MCI NeuroMarker platform is an investigational medical device that simulates conducting activities of daily living, providing an ML-based classification of MCI.
- The assessment evaluates cognitive and functional impairment based on motor and augmented reality tasks, such as tapping and tracing shapes, as well as placing and locating virtual objects.
- The Altoida MCI NeuroMarker platform can identify objective cognitive impairment with 82% accuracy (Pipeline Version v1.56.3).



The Altoida NeuroMarker platform evaluates multi-modal features, including micro-movements, speed, reaction times, or navigation trajectories, which are used to train specific machine-learning (ML) models.

ML models are trained with data derived from clinical cohorts (ground truth).

The Altoida test can be conducted on a smart device (iOS tablet) and lasts approximately 10-15 minutes.

For this study, the assessment was conducted in the clinic on iPad Pro 11'' devices.

PARTICIPANT RECRUITMENT

The study sample was from a single-center, longitudinal cohort (n=116), established at the BarcelonaBeta Brain Research Center (Spain).

	SCD (N=106)	MCI (N=10)	Total (N=116)
Sex			
Female	64 (60.4%)	4 (40.0%)	68 (58.6%)
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)
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%)
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)
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%)
Aβ+	21 (19.8%)	5 (50.0%)	26 (22.4%)

Table 1. Between-group demographic differences in continuous 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.

AGREEMENT BETWEEN ALTOIDA, CLINICAL ASSESSMENT, AMYLOID STATUS AND A STANDARD NPS COGNITIVE BATTERY

Table 2	"Negative clinical" - SCD (N=106)	"Positive clinical" - MCI (N=10)	Total (N=116)
MCI NeuroMarker Class			
"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 3	MMSE>25 (N=111)	MMSE<=25 (N=5)	Total (N=116)
MCI NeuroMarker Class			
"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 4	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%)

Tables 2-4. Confusion matrices displaying the concordance between Altoida's NeuroMarker classification with the clinical assessment (Table 2), the Mini-Mental State Examination (MMSE) cut-off of 25 (Table 3), as well as with amyloid status in the cognitively unimpaired subsample (Table 4).

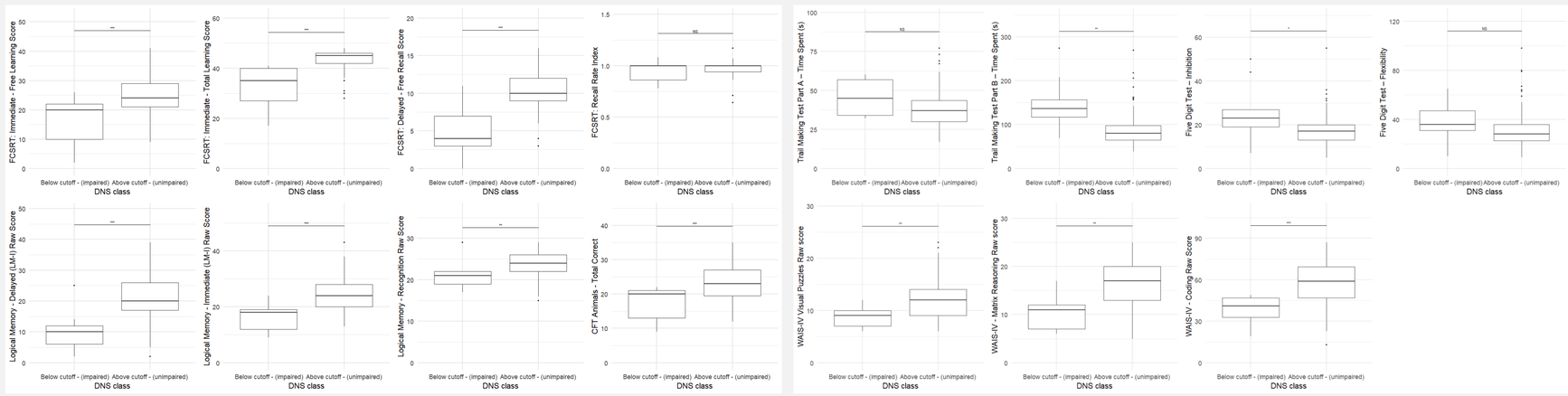


Figure 1. Comparison of cognitive scores from a standard neuropsychological assessment battery and the clinical classification determined with the Altoida NeuroMarker platform. The NPS battery was comprised of the Free Cued Selective Reminding Test (FCSRT), Trail Making Test (TMT), semantic fluency, WAIS-IV subtests (Coding, Visual Puzzles, Matrix Reasoning), and WMS-IV Logical Memory. Comparisons were evaluated with linear regression. Individuals identified by Altoida as cognitively impaired had poorer scores in the FCSRT ($p<0.0001$), TMT-B ($p<0.01$), category fluency (animals) ($p<0.001$), logical memory ($p<0.01$) and in the WAIS-IV visual puzzles ($p<0.01$), matrix reasoning ($p<0.01$) and coding scores ($p<0.001$), as well as in the Inhibition ($p<0.05$) but not in the Flexibility domain ($p>0.05$) of the Five Digit Test.

Dx PERFORMANCE IN MCI & SCD

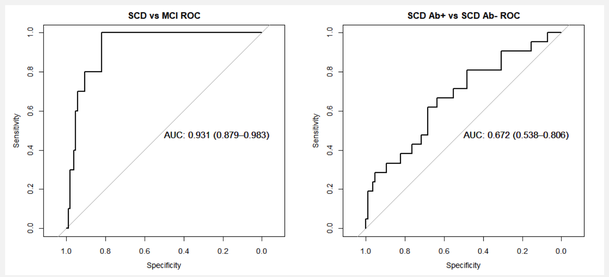


Figure 2. Receiver Operating Characteristic (ROC) curves depicting the Area Under the Curve (AUC) for the identification of MCI in the whole sample and of amyloid-positive individuals in the SCD group.

EXPLORING BEYOND ML-BASED CLASSIFICATION

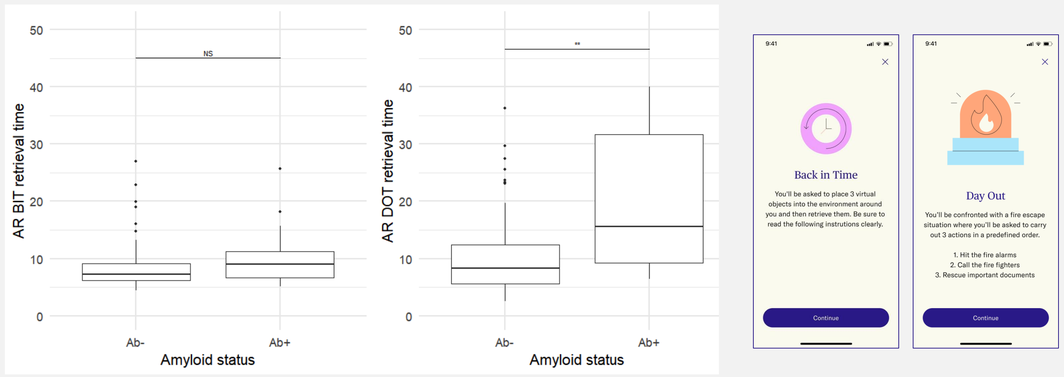


Figure 3. Altoida's augmented reality (AR) Day Out Task (DOT) revealed differences between cognitively unimpaired individuals with underlying amyloid pathology (Aβ+) and those without (Aβ-). There were no differences in object retrieval time in the cued AR exercise Back in Time (BIT). Comparisons were evaluated with gamma regression with log-link function.

CONCLUSIONS

- The alignment between Altoida, clinical evaluation, & the neuropsychological assessment battery supports its convergent validity.
- Altoida shows potential in distinguishing early cognitive impairment associated with Aβ deposition.

REFERENCES

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CONTACT INFORMATION

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