Digital Biomarker-based Diagnostic Score Predicts Cognitive Impairment and Amyloid Positivity in a Cohort with Subjective Cognitive Complaints and Mild Cognitive Impairment

M. Florencia Iulita*[1], Alberto Ferrari*[1], Adria Tort Merino[2], Gonzalo Sánchez-Benavides[3], Emmanuel Streel[1], Silvia Fallone[1],Carolina Minguillon[3], Mylea Charvat[1], Mircea Balasa[2] and Ioannis Tarnanas[1,4]; *Contributed equally

[1]Altoida Inc., Washington, DC 20003, USA; [2]Alzheimer's Unit and other cognitive disorders, Neurology Service, Hospital Clínic, IDIBAPS, Barcelona, Spain; [3]Barcelonaβeta Brain Research Center (BBRC), Pasqual Maragall Foundation, Barcelona, Spain; [4]Trinity College Dublin, Global Brain Health Institute – GHBI, Dublin, Ireland

BACKGROUND

- A significant proportion of individuals aged 65+ exhibiting mild cognitive impairment (MCI) remain underdiagnosed (1).
- People presenting with subjective cognitive decline (SCD), or MCI face a high risk of cognitive worsening over time (2).
- Digital biomarkers are gaining traction in neurology research for their capacity to enable early diagnoses and to streamline the patient's diagnostic journey to specialized care (3).

OBJECTIVE

- To assess the predictivity of Altoida DNS, a digital biomarker derived from a machine learning (ML) classification model, designed to identify cognitive impairment from normal cognition.
- To explore the agreement between Altoida DNS, MMSE (cut-off of 24), and amyloid positivity assessed via CSF biomarkers (Lumipulse instrument).

ALTOIDA DIGITAL BIOMARKER ASSESSMENT

- Altoida DNS is an investigational medical device based on ML that simulates conducting activities of daily living, providing an objective measure of cognition.
- 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.
- DNS-MCI is a ML model that can identify cognitive impairment with 82% accuracy (Pipeline Version v1.56.3; Feb2024).

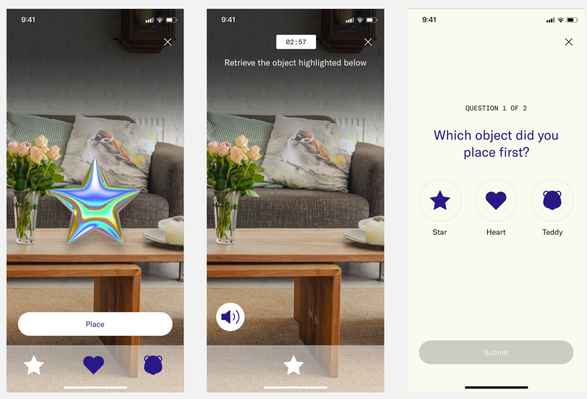

Figure 1. The Altoida Digital Biomarker Assessment evaluates multi-modal features, including micro-movements, speed, reaction times, or navigation trajectories, which are used to train specific machine-learning (ML) models.

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

A cohort of 246 adults, 62% cognitively normal (CN) and 38% with MCI were recruited at two clinical sites in Barcelona, Spain.

	CN (N=153)	MCI (N=93)	Total (N=246)	P-value
Center				
BBRC	143 (93.5%)	11 (11.8%)	154 (62.6%)	<0.001
Hospital Clinic	10 (6.5%)	82 (88.2%)	92 (37.4%)	
Sex				
female	90 (58.8%)	40 (43.0%)	130 (52.8%)	0.0228
male	63 (41.2%)	53 (57.0%)	116 (47.2%)	
Age				
Mean (SD)	66.8 (6.26)	70.3 (5.49)	68.1 (6.22)	<0.001
Median [Min, Max]	67.0 [55.0, 81.0]	71.0 [50.0, 80.0]	68.0 [50.0, 81.0]	
YearsOfEducation				
Mean (SD)	15.0 (3.54)	12.1 (5.09)	14.1 (4.28)	<0.001
Median [Min, Max]	15.0 [6.00, 20.0]	11.5 [3.00, 24.0]	15.0 [3.00, 24.0]	
DNS_class				
Below cutoff - (impaired)	4 (2.6%)	72 (77.4%)	76 (30.9%)	<0.001 ←
Above cutoff - (unimpaired)	149 (97.4%)	21 (22.6%)	170 (69.1%)	
MMSE				
Mean (SD)	28.6 (1.36)	25.4 (3.01)	27.7 (2.48)	<0.001 ←
Median [Min, Max]	29.0 [24.0, 30.0]	26.0 [16.0, 30.0]	28.0 [16.0, 30.0]	
Ab_pos				
Ab-	125 (81.7%)	35 (37.6%)	160 (65.0%)	<0.001
Ab+	28 (18.3%)	58 (62.4%)	86 (35.0%)	

Table 1. Participant demographics. Analysis with t-tests for quantitative variables and with chi-squared or Fisher's test for categorical variables, as appropriate. Ab = amyloid beta. BBRC = Barcelona Beta Brain Research Center. CN= cognitively normal. DNS = digital neuro signature. MCI= mild cognitive impairment. MMSE= Mini-Mental State Exam.

CONCORDANCE OF DNS, MMSE, AND AMYLOID POSITIVITY

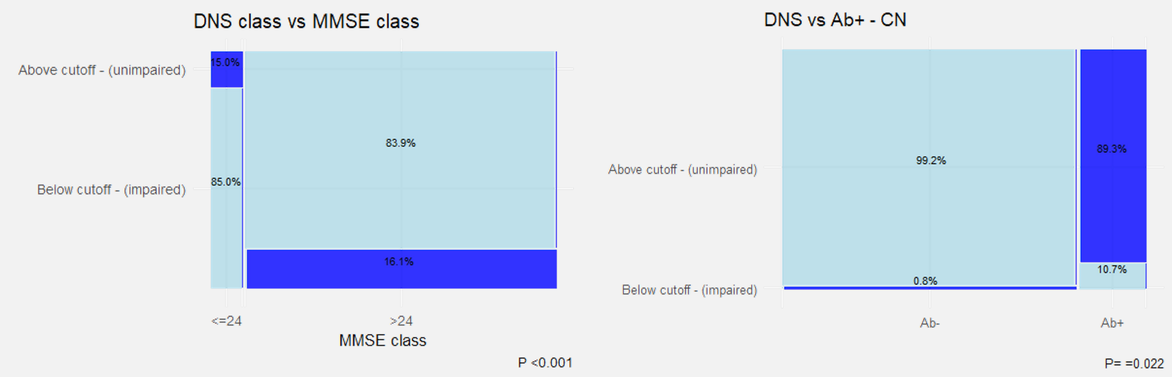

Figure 2. Comparison of DNS classification with the Mini-Mental State Examination (MMSE) cut-off of 24 in the whole cohort (left), as well as with amyloid status in the cognitively unimpaired subsample (right). There was significant agreement between DNS and MMSE (P<0.001), as well as with amyloid status within the cognitively unimpaired group. In the latter, the proportion of individuals with a DNS below the cut-off was significantly higher in those who were Aβ+ (P=0.022).

PREDICTIVITY OF ALTOIDA DNS-MCI ML MODEL

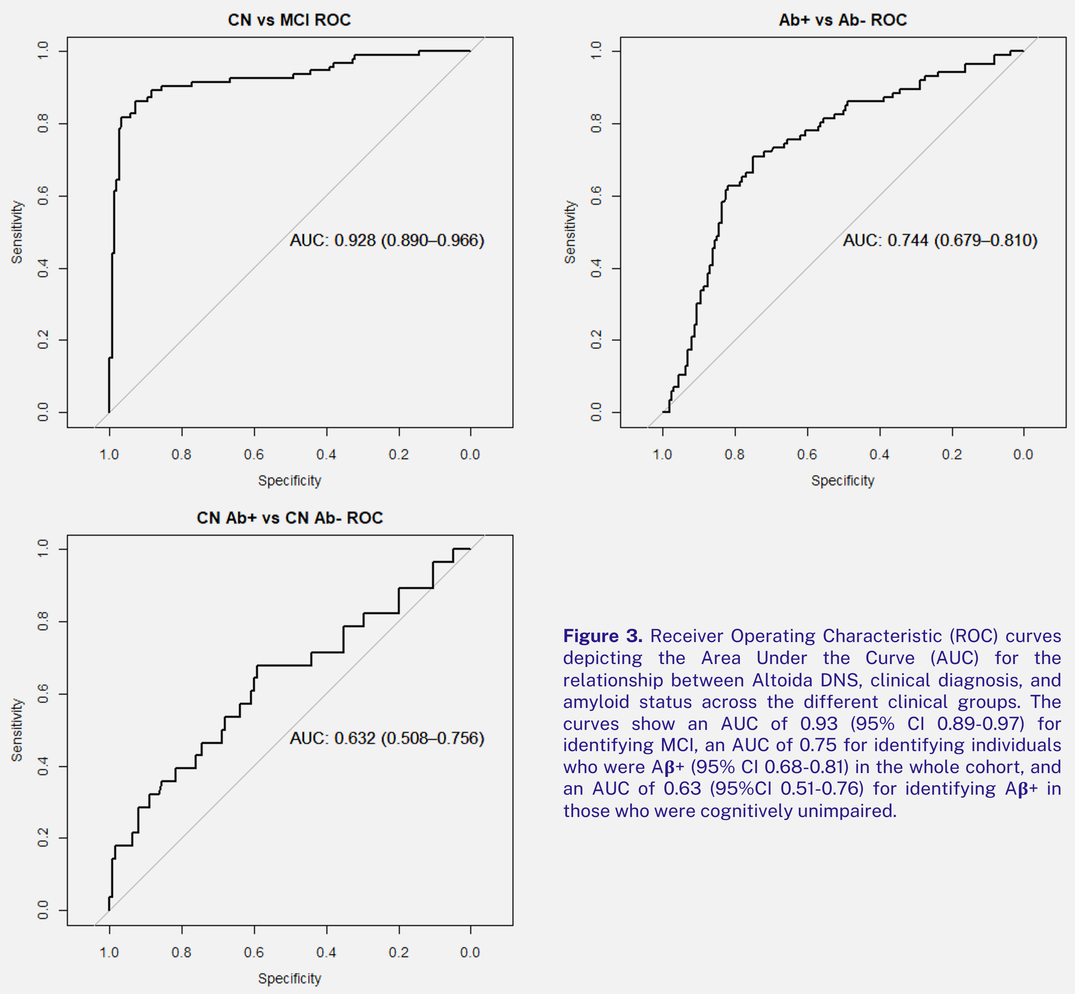

Figure 3. Receiver Operating Characteristic (ROC) curves depicting the Area Under the Curve (AUC) for the relationship between Altoida DNS, clinical diagnosis, and amyloid status across the different clinical groups. The curves show an AUC of 0.93 (95% CI 0.89-0.97) for identifying MCI, an AUC of 0.75 for identifying individuals who were Aβ+ (95% CI 0.68-0.81) in the whole cohort, and an AUC of 0.63 (95%CI 0.51-0.76) for identifying Aβ+ in those who were cognitively unimpaired.

CONCLUSIONS

- Altoida DNS shows promise in identifying cognitive impairment and amyloid positivity across the early cognitive spectrum of Alzheimer's Disease (AD).
- The concordance between DNS, MMSE-based classification, and amyloid status supports its potential as a complementary diagnostic tool for the early identification of MCI and prodromal AD.

This project received funding from the Alzheimer's Drug Discovery Foundation (GDADB-201906-2018897). BBRC's β-AARC cohort received funding from the Alzheimer's Drug Discovery Foundation and Barcelona's City Council (under agreement #22S09630). Mircea Balasa acknowledges support from Carlos III Health Institute (PI19/00198) and the European Union.

REFERENCES

1. Mattke S *et al.*, Alzheimers Res Ther 2023 Jul 22;15(1):128
2. Mitchell AJ, *et al*. Acta Psychiatr Scand 2014 Dec;130(6)
3. Öhman *et al.* 2021; Alzheimers Dement (Amst)

CONTACT INFORMATION

M. Florencia Iulita, PhD
Head of Medical Strategy and Operations
Altoida Inc.
florencia.iulita@altoida.com