

Dissociating PET-determined Amyloid Positive Vs. Negative Memory Clinic Patients With Linus Digital Assessment Of Cognition (DAC)

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Introduction

- Alzheimer’s disease (AD) is characterized by extracellular amyloid- β (A β) plaques and intracellular hyperphosphorylated tau forming neurofibrillary tangles
- There is neuropathological heterogeneity among individuals with AD in clinical-pathologic studies
- Cognitive heterogeneity is also evident in neuropsychological test performance
- Executive dysfunction (vs. memory deficits) is increasingly linked to decline in instrumental activities of daily living (IADL)
- Interest is growing in the development and use of digital neuropsychological assessments, which offer increased precision, richer data acquisition, and reduced operator-related variability
- Linus Health platform allows assessment of multiple cognitive domains including memory, executive function, and language)

Objectives

- Compare neuropsychological performance on the Linus Digital Assessment of Cognition (DAC) between amyloid-positive and amyloid-negative groups determined by amyloid PET/CT
- Test the hypothesis that an amnestic memory profile on DAC will be associated with amyloid (+) PET/CT scan

Study Population

- 85 memory clinic patients from the Memory Assessment Program (MAP) at the New Jersey Institute for Successful Aging (NJISA) and outpatient referrals for suspected dementia
- Comprehensive outpatient assessment of neuro-cognitive and behavioral changes via MAP evaluation
- Neuropsychological testing and psychiatric evaluation
- Brain MRI with NeuroQuant™ volumetric measurements
- Blood/serum labs (CBC, CMP, TSH, B12, folate, lipids)
- Amyloid PET/CT performed using ¹⁸F-florbetaben (Neuraceq®)
- APOE genotyping (Labcorp Consumer Genetics, Burlington NC)

Neuropsychological Measures

- The Digital Assessment of Cognition (DAC):** Brief (~ 7 min), iPad-based battery assessing verbal episodic memory (6-word P(r)VLT), executive function (backward digit span), and language (category fluency by animal naming)
- Primary Outcomes (P(r)VLT):** Trials 1 and 2 immediate free recall, delayed free recall, delayed recognition ratio
- Process/error measures:** Semantic clustering and extra-list intrusion errors (scored per prior methods)
- Statistical analysis:** amyloid status (PET/CT (+) vs. (-)) as the dependent variable; DAC measures as independent variables (multiple and stepwise regression models)



Results

Table 1. Demographic and Clinical Information

	amyloid positive group	amyloid negative group	p
age	75.97 (4.88)	74.04 (5.47)	ns
education	14.83 (2.60)	15.15 (2.70)	ns
sex			
Brain Amyloid Plaque Load (BAPL)			
BAPL score 1	0	33	
BAPL score 2	24	0	
BAPL score 3	52	0	
APOE genotype			
$\epsilon 3/\epsilon 3$	30	4	
$\epsilon 4/\epsilon 4$	15	1	
$\epsilon 2/\epsilon 3$	4	2	
$\epsilon 3/\epsilon 4$	54	6	
indeterminate	2	0	
ns= not significant			

Table 2. Digital Assessment of Cognition (DAC)

	amyloid positive n= 67)	amyloid negative (n= 18)	significance	eta square
Memory Assessment				
P(r)VLT- immediate free recall trial 1	2.71 (1.34)	3.38 (1.33)	ns	n/a
P(r)VLT- immediate free recall trial 2	3.79 (1.37)	4.27 (1.17)	ns	n/a
P(r)VLT- delay free recall	0.89 (1.53)	2.66 (1.97)	p< 0.001	0.149
P(r)VLT- saving score (percent)	0.19 (0.32)	0.58 (0.39)	p< 0.001	0.171
P(r)VLT- recognition (percent)	0.68 (0.28)	0.90 (0.19)	p< 0.004	0.100
P(r)VLT- free recall cluster responses	0.80 (1.27)	1.50 (2.09)	ns	n/a
P(r)VLT- free recall extra-list intrusion errors	0.82 (1.42)	0.44 (0.78)	ns	n/a
P(r)VLT- delay recognition prototypic foils	1.14 (1.22)	0.22 (0.54)	p< 0.005	0.096
P(r)VLT- delay recognition generic foils	0.76 (0.90)	0.33 (0.84)	ns	n/a
P(r)VLT- all delay recognition foils	1.91 (1.68)	0.55 (1.14)	p< 0.004	0.101
Executive/ Language Assessment				
BDST- ANY order recall (percent)	87.90 (13.40)	91.85 (10.61)	ns	n/a
BDST- SERIAL order recall (percent)	57.11 (23.15)	59.99 (20.83)	ns	n/a
semantic ('animal') fluency output	13.10 (5.04)	14.50 (5.60)	ns	n/a

Discussion

- Both groups showed impaired verbal episodic memory (P(r)VLT), but with distinct impairment patterns
- No group difference in immediate recall although amyloid-positive group showed marked decline after delay
- Amyloid-negative group showed ~3x better retention (trial 2- delayed recall)
- Amyloid-positive profile suggests encoding deficit (amnestic pattern) due to impaired word recognition; amyloid-negative profile suggests retrieval deficit (word recognition preserved)
- Higher amyloid burden (BAPL) associated with lower trial 1 recall, more intrusion errors, and reduced semantic clustering

Conclusions

- Amyloid-negative group showed reduced DAC animal fluency and BDST with retrieval-based memory deficits, consistent with a dysexecutive, context-independent syndrome
- Underlying neuropathology of this dysexecutive profile remains unclear
- Amyloid-positive group showed P(r)VLT performance consistent with medial temporal dysfunction associated with excess amyloid deposition
- Lack of association between DAC executive measures and BAPL suggests dysexecutive deficits may reflect non-amyloid pathology (e.g., white matter changes, other proteinopathies, or mixed pathology)
- Results suggest multiple pathologic processes in amyloid positive patients, consistent with postmortem studies

References

