Journal of
Alzheimer's Disease & Parkinsonism
ISSN: 2161-0460

Research Article Open Access

Do Neuropsychological Profiles Differ between Amyloid PET Positive and Negative Amnestic MCI Subjects?

Keaton Sorenson[1], Marwan N Sabbagh[2,3]*, Matthew Johnson[3] and Tamiko Azuma[1]

[1]*Arizona State University, Tempe, Arizona, USA*
[2]*Cleveland Clinic Lou Ruvo Center for Brain Health, Las Vegas, NV, USA*
[3]*Barrow Neurological Institute, Phoenix, AZ, USA*

Abstract

Objective: This study compares Amyloid β (Aβ) PET positive and negative patients with their neuropsychological profiles. A definitive link exists between Aβ deposits and cognitive disorders such as MCI or Alzheimer's disease (AD), but imaging tests based on Aβ's clinical context might be unjustified and could be cost-prohibitive.

Background: Amnestic MCI is considered prodromal to AD/dementia in a majority of cases. Many studies have shown a positive correlation between Aβ PET positive individuals and their likelihood to progress to AD. Aβ deposits in the brain are not always a sign of AD or even MCI, and many elderly people live normal lives with elevated levels. The presence of Aβ in the brain should be carefully considered alongside other tests before making a clinical diagnosis of MCI or AD.

Methods: 130 subjects from Barrow Neurological Institute (Phoenix, AZ) were included in this study. Amyloid PET report data was pulled from Dignity Health St. Joseph's Hospital and Medical Center Outpatient Imaging. All data was anonymized and categorized into positive amyloid PET, negative amyloid PET, and clinical diagnosis based on neuropsychological profiles.

Results: The demographic data indicates that 38.5% of the 91 patients diagnosed as amnestic MCI were amyloid PET negative, and 61.5% were amyloid PET positive. Of the 39 patients diagnosed as Dementia or AD 15.4% were amyloid PET negative and 84.6% were amyloid PET positive. Correlational analysis between diagnosis and neuropsychological variables suggests that some variables correlate well, while others do not.

Conclusion: This study indicates that PET is still a clinical indicator of MCI or dementia/AD, but it has its exceptions. A small number of patients diagnosed as dementia/AD had a negative amyloid PET suggesting that beta amyloid plaques are not the only cause of the disease.

Keywords: Mild Cognitive Impairment (MCI); Amnestic MCI; Positron Emission Tomography (PET); Amyloid PET; Neuropsychological testing

Introduction

Alzheimer's disease (AD) is the most common type of dementia, a general term for memory loss and a change in other cognitive abilities which lead to an interference in daily life. Alzheimer's disease accounts for 60-80% of dementia cases. While it most commonly affects people over the age of 65, approximately 200,000 Americans under the age of 65 suffer from early-onset Alzheimer's disease. Alzheimer's disease is a progressive disease worsening over the course of years. The early stage symptoms begin with mild memory loss and usually a diagnosis of Mild Cognitive Impairment (MCI) [1]. Later stages of disease cause individuals to lose the ability to converse effectively and respond to their environment. Alzheimer's disease occurs in approximately 8.8% of the older US population (65+) and is the sixth leading cause of death in the US [2]. Once the symptoms of AD become noticeable, the average life span of the individual with the disease is approximately eight years, but survival can range from four to 20 years, depending on age and other health factors.

Recently, F-18 amyloid PET has been a widely recognized imaging technique for detecting dense amyloid plaques. Amyloid plaques are a common sign of pathology for AD. However, studies have shown that presence of amyloid plaques may not be the most accurate clinical indicator of AD progression and that each patient is unique. Previous studies have also shown patients with normal cognition can be positive on amyloid PET [3]. Studies utilizing *in-vivo* functional imaging to detect amyloid plaques (ante-mortem) correlate with the gold standard diagnosis, or post-mortem histopathological diagnosis on autopsy. One international open-label multicenter phase 3 studies identified a negative predictive value of F18 amyloid imaging of 96%, suggesting that imaging techniques for detecting amyloid could rule out the presence of underlying Alzheimer's pathology with 96% certainty for patients with or without a clinical diagnosis of Alzheimer's disease [4]. Of the 57 patients meeting the clinical diagnosis of AD who underwent B-amyloid imaging and autopsy, 13 patients were amyloid negative on imaging (ante-mortem) and at autopsy despite meeting the clinical criteria for a diagnosis of Alzheimer's disease. While 12 of the 13 patients had neurodegenerative changes other than those consistent with Alzheimer's disease detected on autopsy, one patient lacked neurodegenerative disease on histopathological diagnosis [4]. This finding suggests that there might be more specific clinical characteristics correlated with the presence of amyloid pathology and that *in-vivo* detection of these plaques with Beta amyloid imaging might reveal patterns of clinical performance on more sophisticated cognitive measurement tools

***Corresponding author:** Marwan N Sabbagh, MD, FAAN, Cleveland Clinic Lou Ruvo Center for Brain Health, 888 W Bonneville Ave, Las Vegas, NV 89106, USA, Tel: 702-483-6029; E-Mail: sabbagm@ccf.org

Received June 21, 2019; **Accepted** August 23, 2019; **Published** August 30, 2019

Citation: Sorenson K, Sabbagh MN, Johnson M, Azuma T (2019) Do Neuropsychological Profiles Differ between Amyloid PET Positive and Negative Amnestic MCI Subjects? J Alzheimers Dis Parkinsonism 9: 476.

(neuropsychological testing). Detection of cognitive deficits correlated with the presence of B-amyloid pathology may help identify individuals at an earlier stage of the disease (i.e., MCI), which could allow them to benefit from earlier treatment interventions aimed at slowing the progression of Alzheimer's disease [5].

This study was carried out to examine the neuropsychological profiles of patients who had amnestic MCI to ascertain differences between patients who were amyloid PET positive and amyloid PET negative. We hypothesized that amnestic MCI would be strongly associated with positive amyloid PET. It was also expected that both diagnosis of AD/dementia and amyloid PET positive results would be strongly associated with neuropsychological measures.

Methods

Subjects

130 patients from Barrow Neurological Institute were enrolled in this study. The records of the patients were reviewed to determine their suitability for this study. Written consent was not required per minimum risk protocol criteria. Specifically, there was no more than minimal risk to the patients enrolled, and the study did not adversely affect the rights and welfare of the subjects.

Archival records from 130 patients who sought treatment at an outpatient neurology center in the Southwest United States and underwent an amyloid PET scan as part of the Imaging Dementia -Evidence for Amyloid Scanning (IDEAS) study were reviewed. The minimal risk protocol was approved by the St Joseph's/DignityHealth/ Barrow Neurological Institute Institutional Review Board (IRB) prior to Records being reviewed. All study procedures were reviewed and approved by the Institutional Review Board at Barrow Neurological Institute, St. Joseph's Hospital and Medical Center, Phoenix, Arizona.

Prospectively evaluated patients with mild to moderate AD or mild cognitive impairment were assessed in the memory disorders clinic prior to being enrolled in IDEAS. All participants met inclusion and exclusion criteria for the IDEAs study. They were excluded from this sample if they did not meet the criteria for amyloid PET imaging through the IDEAs study (see below). The diagnosis of MCI was made based on the Petersen criteria [6]. We included MCI patients with MMSE scores up to 30 that had Significant Memory Concern (SMC) and a clinical diagnosis of MCI with sufficient cognitive impairment to warrant a diagnosis and further evaluation including amyloid PET. Exclusion criteria included evidence of vascular, traumatic, or inflammatory causes of a MCI evident by non-contrast Magnetic Resonance Imaging (MRI) and history of major systemic diseases that could possibly affect cognitive function including other dementias (e.g., Dementia with Lewy bodies, frontotemporal dementia, overt primary progressive aphasia, such as Progressive Non Fluent Aphasia or Semantic Dementia), Parkinson's disease dementia, vascular dementia), cardiopulmonary failure, hepatic or renal failure, diabetes mellitus, head injury, stroke, or other neurodegenerative disease. Additional variables gathered from the patient medical record includes age, sex, education level, clinical diagnosis (established by a behavioral neurologist), and any significant medical history. Inclusion criteria were based on patients of Barrow Neurological Institute that had undergone an amyloid PET scan at St. Joseph's Hospital and Medical Center and completed a neuropsychological evaluation within the last 24 months.

Amyloid PET procedure

Sixty-five minutes following the intravenous administration of the radiotracer F-18 florbetapir, positron emission tomography was performed of the patient's brain per standard protocol. Images were reconstructed and displayed in transverse, coronal and sagittal planes. Immediately prior to the PET scan, a non-contrast, non-diagnostic, CT scan was performed for anatomic/physiologic correlation and attenuation correction. Amyloid PET scans were reviewed by an expert radiologist and given a qualitative status of amyloid PET positive (+) or amyloid PET negative (-).

Neuropsychological reports

Neuropsychological assessments were not available for every patient in the sample. Fifty-eight neuropsychological assessment reports were included in the data analysis. Completed measures were not consistent across participants, which are reflected in the different sample sizes (N) across statistical tests.

Dementia rating scale: The Dementia Rating Scale is a widely used measure of global cognition based on five subtests that measure attention, initiation/perseveration, construction, conceptualization, and memory [7]. Severity ratings are based on the patient's current behavior relative to "normal" behavior.

WAIS – digits forward and backward and sequencing: The Wechsler Adult Intelligence Scale (WAIS) is an IQ test designed to measure intelligence and cognitive ability in adults [8]. The most recent version, WAIS-IV, was developed in 2008. Analyses focused on the digit span subtests. For forward digit span, the patient hears a sequence of numbers and recalls the sequence in the same order. For the backward digit span, the patient hears a sequence of numbers and recalls the sequence in reverse order. For digit span sequencing, the patient hears a sequence of numbers and recalls the numbers in ascending order. These tests measure simple working memory span and mental manipulation.

Trail making test: The trail making test is a neuropsychological test of visual attention and task switching [9]. In Part A, the patient is asked to sequentially connect 25 circled numbers or letters in a connect-the-dot manner. In Part B, the patient connects the circles, but must alternate between letters and numbers. Performance is measured by completion time and number of errors.

Wisconsin card sorting task: The Wisconsin card sorting task measures the cognitive flexibility and set-switching ability [9]. Participants are asked to sort 64 cards by a given rule: by color (red, blue, yellow, or green), form (crosses, circles, triangles, or stars), or number of figures (one, two, three, four). The participant is not explicitly told the rule but is given feedback on their accuracy. After eight consecutive correct answers, the rule is changed. Performance is measured by the number of cards correctly sorted and number of perseveration errors (errors showing that the patient has reverted back to a previous rule).

Phonemic (letter) verbal fluency: Phonemic (letter) verbal fluency is a measure of executive function and lexical access. In the test, the patient is given one minute to provide words that start with a specific letter. Scores are based on the number of unique words produced.

Semantic (category) verbal fluency: Semantic (category) verbal fluency is an executive function measure and strategic lexical retrieval. In a semantic fluency test, the patient is given one minute to provide as many unique correct words as they can from a given category. Scores are based on number of unique words produced.

Boston naming test: The Boston Naming Test is a neuropsychological assessment tool used to measure confrontational word retrieval. During the test, the patient is shown 60 line-drawings of common objects one at

a time and asked to name them orally. These drawings range in difficulty from high frequency to low frequency objects.

Wechsler memory scale – logical memory I and II: The Wechsler Memory Scale test measures different memory functions and consists of seven subtests. The measures included in the analyses included Logical Memory I and II. In the Logical Memory I subtest, the patient is asked to immediately recall two short stories, which are presented orally by the neuropsychologist. This test assesses narrative memory under immediate, free recall conditions. In the logical memory II subtest, the patient is asked to retell both stories after a 20 minute delay. They are also asked questions about both stories. This test assesses longer-term recall of verbal information.

Brief Visuospatial Memory Test (BVMT) – Learning, delay, recognition: The BVMT is used to measure visuospatial learning and memory abilities [10]. In the most current revised version, the patient is shown a visual display of six figures arranged in a 2 × 3 matrix for three consecutive 10-second trials. Following each trial, the patient is asked to draw as many designs as accurately as they can and in the same locations. After a 25-minute delay, the patient is asked to recall the designs in the same locations. Immediately following the delayed recall, the patient is given a forced-recognition test. Scoring is based on accuracy of the drawings and the location of the figures.

Beck anxiety inventory: The Beck Anxiety Inventory includes 21 questions regarding anxiety symptoms, for example: numbness or tingling, feeling hot, unable to relax, terrified or afraid, fear of losing control, fear of dying, indigestion, etc. [11]. The patient rates each symptom on a severity scale from 0-3. A score between 0-21 is indicative of very low anxiety, a score between 22- 35 is indicative of moderate anxiety, and a score of 36 or more indicates extreme anxiety.

Data collection

Amyloid PET scan status and neuropsychological profiles were sourced retrospectively from patient charts in the Barrow Neurological Institute EHR. Amyloid PET scan reports from June 2016 to December 2017 were used. Any neuropsychological measures that were completed up to 24 months prior to the amyloid PET scan were included in the analyses. Variables used from the patient chart included: Age, Sex, Education Level, other significant medical history, Amyloid PET scan qualitative scores, and neuropsychological measures.

The Principal Investigator and Ancillary staff (research assistants and coordinators) have access to the data. Data is considered Protected Health Information (PHI) and is kept secured as long as is required per the Health Insurance Portability and Accountability Act of 1996 (HIPAA) for a minimum of three years. Data was kept on encrypted, password-protected Dignity Health networks. All data was collected from the appropriate EHR and de-identified by the study investigator (participant data were assigned identification numbers). No medical records were printed or kept in any study files.

Statistical considerations

Pearson correlational analyses were conducted to test for the relationships between diagnosis (MCI/Dementia), PET results, and neuropsychological measures. Two-tailed independent t-tests were used to test for group differences.

Results

The demographic data indicates that 38.5% of the 91 patients diagnosed as amnestic MCI were amyloid PET negative while 61.5% were amyloid PET positive. Of the 39 patients diagnosed as dementia or AD, 15.4% were amyloid PET negative and 84.6% were amyloid PET positive. Of the total 130 patients, 31.5% were amyloid PET negative and 68.5% were amyloid PET positive. A total of 59 females and 71 males were included in this study. For the negative PET group, 36.6% were female and 63.4% were male. For the positive PET group, 49.4% were female and 50.6% were male. For the negative PET group (N=41), the age range was 66-88 with a mean and standard deviation of 75.54 and 6.132 respectively. For the positive PET group (N=89), the age range was 65-91 with a mean and standard deviation of 76.72 and 6.468 respectively. Due to the lack of controls, a false positive rate could not be calculated (Table 1 and Table 2).

Correlational analyses were conducted on diagnosis and neuropsychological measures (Table 3). Significant correlations were observed between: diagnosis and dementia rating scale (DRS) r(24)=-

Diagnosis	Amyloid PET			Percentage	
	Negative	Positive	Total	Negative	Positive
MCI	35	56	91	38.50%	61.50%
Dementia	6	33	39	15.40%	84.60%
Total	41	89	130	31.50%	68.50%

Table 1: Frequency table

Parameters		Amyloid PET		Percentage		
		Negative	Positive	Negative	Positive	
Diagnosis	MCI	35	56	85.40%	62.90%	
	Dementia	6	33	14.60%	37.10%	
Sex	Female	15	44	36.60%	49.40%	
	Male	26	45	63.40%	50.60%	
		N	Min	Max	Mean	Std. dev.
Age	Neg PET	41	66	88	75.54	6.132
	Pos PET	89	65	91	76.72	6.468

Table 2: Demographic data

Variables	N	Pearson Correlation	Sig. (2-tailed)
Age	130	0.123	0.163
PET	130	.228*	0.009
DRS Total	24	-0.762	0
DRS SS	24	-0.706	0
WAIS-F	30	0.139	0.465
WAIS-B	30	0.148	0.434
WAIS-Seq	19	0.106	0.666
TrailsB Time	41	.397*	0.01
TrailsB Error	39	-0.014	0.933
WCST Cat.	33	-0.314	0.076
WCST Tot. Err.	34	0.123	0.488
WCST Pers. Err.	34	0.192	0.277
PhonFluency	30	-.383*	0.037
SemFluncy	29	-.369*	0.049
BNT	36	-0.312	0.064
WMS LM1	26	-0.165	0.421
WMS LM2	26	-0.003	0.988
WMS Recog	25	0.059	0.778
BVMT Learn	25	-0.073	0.728
BVMT Delay	25	-0.036	0.864
BVMT Recog	25	0.19	0.362
Beck Anxiety	22	0.09	0.691

Table 3: Correlation analyses -diagnosis with neuropsychological variables

0.762, diagnosis and TrailsB Test r(39)=0.397, diagnosis and phonetic fluency r(30)=-0.383, diagnosis and semantic fluency r(29)=-0.369, and diagnosis and the Boston Naming Test (BNT) r(36)=-0.312. Correlation analyses conducted on PET results and neuropsychological measures revealed only two significant correlations: PET results and the Boston Naming Test (BNT) r(36)=-0.316 and PET results and Semantic Fluency r(29)=-0.305. As expected, diagnosis was also significantly correlated with PET results, r(130)=0.228 (Table 4).

Group differences between PET positive and PET negative groups were tested for all neuropsychological measures (Table 5). The PET positive and PET negative groups had marginally different Boston Naming Test scores (t(34)=1.945, p=0.06) with PET positive individuals showing lower performance than PET negative individuals. Other tests that approach a marginal significance are the Wisconsin Card Sorting Task (WCST) (t(32)=1.599, p=0.120) and Semantic Fluency (t(27)=1.662, p=0.108). No other group differences were observed (Table 6).

Discussion

The results of this study demonstrate that an individual can be amnestic MCI and amyloid PET negative. 15.4% of the dementia/AD patients had a negative amyloid PET, suggesting that dense beta-amyloid deposits may not be the primary clinical marker for the disease. However, the difference in percent of MCI patients with a positive amyloid PET (61.5%) and dementia/AD patients with a positive amyloid PET (84.6%) does advocate the role of beta-amyloid deposits in the progression of dementia. In practice, a positive amyloid PET cannot be the only clinical marker for dementia/AD and therefor other tests must be used to ultimately make a diagnosis.

The neuropsychological tests that were significantly correlated with the diagnosis included the trail making test, phonetic fluency, semantic fluency, and the Boston Naming Test (BNT). Patients with dementia were expected to score lower than patients with MCI, but it is interesting that they did not score lower on all of the neuropsychological measures. The significant correlations were primarily observed for measures of higher-order cognition functions. For example, the Trail Making Test, phonetic fluency, and semantic fluency are all considered measures of executive function. This finding suggests that tests that rely on more complex cognitive processes may be more sensitive to the differences between MCI and dementia diagnosis. The significant correlation between diagnosis and PET results reflected that severity of the diagnosis increased with PET positivity. These results are to be expected as patients with severe dementia/AD are expected to have significant positive amyloid PET results. Amyloid plaques are also expected to exacerbate the decline of cognitive function [12]. PET results were not correlated with most neuropsychological tests, but were significantly correlated with Boston Naming Test scores and Semantic Fluency performance. This result

Variables	N	Pearson Correlation	Sig. (2-tailed)
Age	130	0.087	0.327
Diagnosis	130	0.228*	0.009
DRS Total	24	0.165	0.44
DRS SS	24	-0.035	0.871
WAIS-F	30	0.097	0.612
WAIS-B	30	0.093	0.626
WAIS-Seq	19	0.105	0.669
TrailsB Time	41	0.201	0.207
TrailsB Error	39	0.094	0.571
WCST Cat.	33	-0.112	0.536
WCST Tot. Err.	34	0.272	0.12
WCST Pers. Err.	34	0.191	0.28
PhonFluency	30	-0.175	0.355
SemFluncy	29	-0.305	0.108
BNT	36	-0.316	0.06
WMS LM1	26	-0.136	0.507
WMS LM2	26	0.188	0.357
WMS Recog	25	0.126	0.549
BVMT Learn	25	-0.115	0.584
BVMT Delay	25	0.042	0.841
BVMT Recog	25	-0.024	0.91
Beck Anxiety	22	0.311	0.16

Table 4: Correlation analyses -PET results with neuropsychological variables

Variables	Amyloid PET Negative Group	Amyloid PET Positive Group	Significance
DRS Total	123.7 (26.14)	129.36 (6.18)	t(22)=-0.786, p=0.440
	N=10	N=14	
DRS SS	7.70 (3.40)	7.50 (2.57)	t(22)=0.165, p=0.871
	N=10	N=14	
WAIS-F	7.69 (2.78)	8.18 (2.38)	t(28)=-0.514, p=0.612
	N=13	N=17	
WAIS-B	6.31 (3.07)	6.88 (3.24)	t(28)=-0.493, p=0.626
	N=13	N=17	
WAIS-Seq	7.20 (3.29)	7.89 (3.62)	t(17)=-0.434, p=0.669
	N=10	N=9	
TrailsB Time	123.53 (69.44)	151.82 (71.07)	t(39)=-1.285, p=0.207
	N=19	N=22	
TrailsB Error	0.44 (0.92)	0.62 (0.97)	t(37)=-0.572, p=0.571
	N=18	N=21	
WCST Cat.	1.93 (1.53)	1.61 (1.42)	t(31)=0.626, p=0.536
	N=15	N=18	
WCST Tot. Err.	25.25 (8.43)	30.89 (11.65)	t(32)=-1.599, p=0.120
	N=16	N=18	
WCST Pers. Err.	14.06 (5.45)	16.06 (5.13)	t(32)=-1.099, p=0.280
	N=16	N=18	
PhonFluency	34.15 (9.38)	31.24 (7.64)	t(28)=0.940, p=0.355
	N=13	N=17	
SemFluency	16.62 (4.57)	13.63 (5.01)	t(27)=1.662, p=0.108
	N=13	N=16	
BNT	52.56 (4.98)	46.65 (11.29)	t(34)=1.945, p=0.060
	N=16	N=20	
WMS LM1	9.00 (2.13)	8.43 (2.17)	t(24)=0.674, p=0.507
	N=12	N=14	
WMS LM2	6.33 (3.82)	7.64 (3.30)	t(24)=-0.939, p=0.357
	N=12	N=14	
WMS Recog	16.91 (3.30)	17.71 (3.27)	t(23)=-0.609, p=0.549
	N=11	N=14	
BVMT Learn	8.83 (3.83)	8.00 (3.67)	t(23)=0.555, p=0.584
	N=12	N=13	
BVMT Delay	2.67 (2.19)	2.85 (2.23)	t(23)=-0.203, p=0.841
	N=12	N=13	
BVMT Recog	5.50 (0.67)	5.46 (0.97)	t(23)=0.114, p=0.910
	N=12	N=13	
Beck Anxiety	5.11 (5.35)	10.62 (10.33)	t(20)=-1.461, p=0.160
	N=9	N=13	

Table 5: Statistical significance of neuropsychological assessments (MCI and Dementia).

Variables	PET Negative Group	PET Positive Group	Significance
DRS Total	134.25 (5.12)	130.38 (5.04)	t(19)=1.696, p=0.106
	N=8	N=13	
DRS SS	9.13 (1.81)	7.85 (2.30)	t(19)=1.333, p=0.198
	N=8	N=13	
WAIS-F	7.33 (2.57)	8.27 (2.52)	t(25)=-0.948, p=0.352
	N=12	N=15	
WAIS-B	6.17 (3.16)	6.73 (3.08)	t(25)=-0.470, p=0.643
	N=12	N=15	
WAIS-Seq	7.00 (3.43)	7.89 (3.62)	t(16)=-0.535, p=0.600
	N=9	N=9	
TrailsB Time	113.22 (54.49)	145.05 (66.33)	t(35)= -1.590, p=0.121
	N=18	N=19	
TrailsB Error	0.41 (0.94)	0.67 (1.03)	t(33)=-0.764, p=0.450
	N=17	N=18	
WCST Cat.	2.00 (1.53)	1.81 (1.38)	t(28)=0.349, p=0.730
	N=14	N=16	
WCST Tot. Err.	25.13 (8.71)	30.38 (12.28)	t(29)=-1.362, p=.184
	N=15	N=16	
WCST Pers. Err.	14.00 (5.63)	15.56 (5.19)	t(29)=-0.804, p=0.428
	N=15	N=16	
PhonFluency	35.08 (9.15)	32.33 (7.42)	t(25)=0.863, p=0.396
	N=12	N=15	
SemFluency	17.25 (4.14)	14.14 (5.10)	t(24)=1.687, p=0.105
	N=12	N=14	
BNT	52.80 (5.10)	47.94 (8.81)	t(31)=1.888, p=0.068
	N=15	N=18	
WMS LM1	9.09 (2.21)	8.54 (2.22)	t(22)=0.608, p =0.549
	N=11	N=13	
WMS LM2	6.45 (3.98)	7.54 (3.41)	t(22)=-0.719, p=0.480
	N=11	N=13	
WMS Recog	16.50 (3.17)	17.92 (3.30)	t(21)=-1.042,p=0.309
	N=10	N=13	
BVMT Learn	9.27 (3.69)	7.75 (3.72)	t(21)=0.984, p=0.336
	N=11	N=12	
BVMT Delay	2.82 (2.23)	2.75 (2.30)	t(21)=0.072, p=0.943
	N=11	N=12	
BVMT Recog	5.45 (0.69)	5.42 (1.00)	t(21)=0.105, p=0.917
	N=11	N=12	
Beck Anxiety	5.50 (5.58)	9.91 (9.66)	t(17)= -1.153, p=0.265
	N=8	N=11	

Table 6: Statistical significance of neuropsychological assessments (MCI Only)

was surprising. Significant correlations were expected for several of the neuropsychological measures given that a higher percent of PET positive patients were diagnosed as dementia/AD.

The standard deviations for each test are provided in the table of results. The standard deviation for the Dementia Rating Scale for PET negative (26.14) was significantly higher than the standard deviation for PET positive (6.18). These results are to be expected as many of the PET negative results included MCI patients while most of the PET positive were dementia/AD. A difference in standard deviations with the Boston Naming Test between PET negative and PET positive groups suggests that there is greater variability in performance of this test with the PET positive group than the PET negative group. The PET negative standard deviation was 4.98, and the PET positive standard deviation was 11.29. This variability could be attributed to the fact that some PET positive patients do not see a decline in mental function.

Conclusion

Based on all the results of this study, amyloid PET is still a clinical indicator that an individual might be MCI or dementia/AD, but it has its exceptions. A small number of patients diagnosed as dementia/AD had a negative amyloid PET, suggesting that beta amyloid plaques are not the only cause of the disease. Amyloid plaques appear to be a major factor in the progression of dementia or AD. However, the results from an amyloid PET cannot be directly related to a diagnosis.

Funding

The study was supported by NIH COBRE **5P20GM109025** and the Barrow Neurological Foundation and the Keep Memory Alive Foundation.

References

1. Powell J, Lendrum J, Huff R, Belden C, Sabbagh MN (2017) Early and Mild Phases of Primary Progressive Aphasia: A Case Series. Curr Aging Sci 10: 136-142.
2. Kemle K, Ackermann RJ (2018) Issues in Geriatric Care: Alzheimer's Disease. FP Essent 468: 26-34.
3. Patricio CM, Gabriela C, Julieta RM, Marcos FS, Federico N, et al. (2015) Concordance between 11C-PIB-PET and clinical diagnosis in a memory clinic. Am J Alzheimers Dis Other Demen 30: 599-606.
4. Sabri O, Sabbagh MN, Seibyl J, Barthel H, Akatsu H, et al. (2015) Florbetaben PET imaging to detect amyloid beta plaques in Alzheimers disease: Phase 3 study. Alzheimers & Dement 11: 964-974.
5. Doraiswamy PM, Sperling RA, Johnson K, Reiman EM, Wong TZ, et al. (2014) Florbetapir F 18 amyloid PET and 36-month cognitive decline: a prospective multicenter study. Mol Psychiatry 19: 1044-1051.
6. Petersen R, Caracciolo B, Brayne C, Gauthier S, Jelic V, et al. (2014) Mild cognitive impairment: A concept in evolution. J Intern Med 275: 214-228.
7. http://www.scirp.org/(S(351jmbntvnsjt1aadkposzje))/reference/ReferencesPapers.aspx?ReferenceID=204639
8. Wechsler D (2008) WAIS-IV technical and interpretive manual. Pearson.
9. https://doi.org/10.1080/09084280701280502
10. https://www.parinc.com/products/pkey/30
11. Beck AT, Epstein N, Brown G, Steer RA (1988) An inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psychol 56: 893.
12. Struble RG, Ala T, Patrylo PR, Brewer GJ, Yan XX (2010) Is brain amyloid production a cause or a result of dementia of the Alzheimer's type?. J Alzheimers Dis 22: 393-399.