

Study	Study Population	Treatment/ intervention	Results	Validity /Conclusion																																																																																																																												
<p>Doraiswamy et al, 2012.</p> <p>Study type Prospective observational.</p> <p>Aim: To examine whether ¹⁸F-florbetapir- PET can predict subsequent cognitive decline in older at-risk subjects.</p> <p>Endpoints: Association between positive scan results and decline in memory and worsening of the disease.</p> <p>N of patients: N=151 (n=51 with mild cognitive impairment [MCI] n=31 with AD, and n= 69 cognitively normal controls [CN]).</p> <p>Blinding: Yes.</p> <p>Follow-up: 18 months in this report 97% complete for CN, 90% for MCI, and 87% for AD.</p>	<p>Inclusion criteria: 1. MCI group >50 years of age, with MMSE >24, CDR scale 0.5, and presenting for an initial evaluation, or were diagnosed with MCI within the previous year, 2. AD group: Individuals diagnosed clinically with AD and with MMSE ≤24. 3. Clinically normal healthy controls: ≥50 years of age, assessed clinically, CDR global of 0 and MMSE 29 or 30.</p> <p>Exclusion: Relevant neuropsychiatric disease, received amyloid investigational drugs, was unable to complete psychometric test, or had a contraindication to PET.</p> <p>Patient characteristics: There were differences between the groups in cognitive and functional variables; the AD group was slightly older, and there were no differences between the three groups in educational level, height, weight, gender, or race.</p>	<p>At screening all subjects underwent detailed history, physical and neurological exam, clinical interview, and laboratory evaluations. MRI at screening or within 6 months prior was performed to rule out significant CNS lesions. All participants underwent a 10-minute Florbetapir-PET imaging. The images we assessed visually by 3 nuclear medicine physicians using a semiquantitative score ranging from 0 (no amyloid to 4 (high level of cortical amyloid), and a binary qualitative scale (Aβ+ and Aβ-). The median rating served as the primary outcome.</p> <p>Subjects who completed the initial PET scan were eligible to participate in the follow-up. An interim assessment was made at 18 months, and a final will be performed at 36 months.</p>	<p>-Two of the three readers agreed with the majority in >96% of cases and the third reader agreed in 74% of cases (K statistics 0.58)</p> <p style="text-align: center;"><i>Baseline florbetapir amyloid positivity</i></p> <table border="1" data-bbox="892 422 1564 560"> <thead> <tr> <th></th> <th>Aβ positive n/N (%)</th> <th>Aβ negative n/N (%)</th> </tr> </thead> <tbody> <tr> <td>MCI</td> <td>19/51 (37%)</td> <td>32/51 (63%)</td> </tr> <tr> <td>AD</td> <td>21/31 (68%)</td> <td>10/31 (32%)</td> </tr> <tr> <td>CN</td> <td>10/69 (14%)</td> <td>59/69 (86%)</td> </tr> </tbody> </table> <p>P for difference between groups <0.0001 Aβ positive subjects tended to be older, and with worse cognitive performance at baseline.</p> <p style="text-align: center;"><i>Change from baseline to 18 months</i></p> <table border="1" data-bbox="861 649 1680 1372"> <thead> <tr> <th>Study groups</th> <th>Aβ positive</th> <th>Aβ negative</th> <th>P value</th> </tr> </thead> <tbody> <tr> <td colspan="4">Cognitively normal (CN)</td> </tr> <tr> <td>MMSE*</td> <td>-1.20</td> <td>-0.53</td> <td>0.100</td> </tr> <tr> <td>ADAS-Cog**</td> <td>2.02</td> <td>-0.13</td> <td>0.005</td> </tr> <tr> <td>CDR-SB***</td> <td>0.43</td> <td>0.09</td> <td>0.005</td> </tr> <tr> <td>Daily activities</td> <td>-0.91</td> <td>-0.41</td> <td>0.570</td> </tr> <tr> <td>Verbal fluency animals</td> <td>-0.78</td> <td>-0.35</td> <td>0.777</td> </tr> <tr> <td>Verbal fluency vegetables</td> <td>0.02</td> <td>0.00</td> <td>0.987</td> </tr> <tr> <td>WMS †delayed recall</td> <td>1.08</td> <td>0.88</td> <td>0.877</td> </tr> <tr> <td>WMS immediate recall</td> <td>-0.93</td> <td>0.95</td> <td>0.091</td> </tr> <tr> <td colspan="4">MCI group</td> </tr> <tr> <td>MMSE</td> <td>-2.54</td> <td>-0.20</td> <td>0.003</td> </tr> <tr> <td>ADAS-Cog</td> <td>3.84</td> <td>-0.61</td> <td>0.001</td> </tr> <tr> <td>CDR-SB</td> <td>1.18</td> <td>0.25</td> <td>0.020</td> </tr> <tr> <td>Daily activities</td> <td>-1.72</td> <td>-1.59</td> <td>0.937</td> </tr> <tr> <td>Verbal fluency animals</td> <td>-1.64</td> <td>0.56</td> <td>0.090</td> </tr> <tr> <td>Verbal fluency vegetables</td> <td>-1.97</td> <td>0.29</td> <td>0.025</td> </tr> <tr> <td>WMS delayed recall</td> <td>-1.99</td> <td>1.56</td> <td>0.012</td> </tr> <tr> <td>WMS immediate recall</td> <td>-2.35</td> <td>1.00</td> <td>0.005</td> </tr> <tr> <td colspan="4">Clinically diagnosed AD</td> </tr> <tr> <td>MMSE</td> <td>-2.10</td> <td>1.43</td> <td>0.089</td> </tr> <tr> <td>ADAS-Cog</td> <td>1.57</td> <td>4.86</td> <td>0.165</td> </tr> <tr> <td>CDR-SB</td> <td>1.99</td> <td>0.47</td> <td>0.176</td> </tr> <tr> <td>Daily activities</td> <td>-10.15</td> <td>-6.36</td> <td>0.539</td> </tr> <tr> <td>Verbal fluency animals</td> <td>-3.06</td> <td>0.27</td> <td>0.006</td> </tr> <tr> <td>Verbal fluency vegetables</td> <td>-1.23</td> <td>-0.11</td> <td>0.273</td> </tr> <tr> <td>WMS delayed recall</td> <td>0.04</td> <td>1.03</td> <td>0.399</td> </tr> <tr> <td>WMS immediate recall</td> <td>-0.61</td> <td>0.45</td> <td>0.493</td> </tr> </tbody> </table> <p>*Mini mental state examination, ** AD assessment scale-cognitive subscale *** Clinical dementia rating-sum of boxes †Wechsler memory scale</p> <p>Change in diagnosis after 18 months MCI group: 8 subjects progressed to AD (5/17 [29.4%] with Aβ+ and 3/29 [10.3%] with Aβ-(P=0.996) 7 subjects reverted to CN (5.9% for Aβ+ vs. 20%with Aβ-(p=0.177).</p>		Aβ positive n/N (%)	Aβ negative n/N (%)	MCI	19/51 (37%)	32/51 (63%)	AD	21/31 (68%)	10/31 (32%)	CN	10/69 (14%)	59/69 (86%)	Study groups	Aβ positive	Aβ negative	P value	Cognitively normal (CN)				MMSE*	-1.20	-0.53	0.100	ADAS-Cog**	2.02	-0.13	0.005	CDR-SB***	0.43	0.09	0.005	Daily activities	-0.91	-0.41	0.570	Verbal fluency animals	-0.78	-0.35	0.777	Verbal fluency vegetables	0.02	0.00	0.987	WMS †delayed recall	1.08	0.88	0.877	WMS immediate recall	-0.93	0.95	0.091	MCI group				MMSE	-2.54	-0.20	0.003	ADAS-Cog	3.84	-0.61	0.001	CDR-SB	1.18	0.25	0.020	Daily activities	-1.72	-1.59	0.937	Verbal fluency animals	-1.64	0.56	0.090	Verbal fluency vegetables	-1.97	0.29	0.025	WMS delayed recall	-1.99	1.56	0.012	WMS immediate recall	-2.35	1.00	0.005	Clinically diagnosed AD				MMSE	-2.10	1.43	0.089	ADAS-Cog	1.57	4.86	0.165	CDR-SB	1.99	0.47	0.176	Daily activities	-10.15	-6.36	0.539	Verbal fluency animals	-3.06	0.27	0.006	Verbal fluency vegetables	-1.23	-0.11	0.273	WMS delayed recall	0.04	1.03	0.399	WMS immediate recall	-0.61	0.45	0.493	<p>Advantages/ limitations: The study had the advantage of following three groups of patients prospectively. However, It was relatively small, the authors did not adjust for multiple comparisons, the follow-up duration was short for such a disease, and there was a low agreement between one versus the other two readers. The study was conducted in a research setting with three trained readers interpreting the images, which would not be the case in clinical practice.</p> <p>The authors of the study had financial ties, and /or were employed by Avid Radiopharmaceuticals.</p>
	Aβ positive n/N (%)	Aβ negative n/N (%)																																																																																																																														
MCI	19/51 (37%)	32/51 (63%)																																																																																																																														
AD	21/31 (68%)	10/31 (32%)																																																																																																																														
CN	10/69 (14%)	59/69 (86%)																																																																																																																														
Study groups	Aβ positive	Aβ negative	P value																																																																																																																													
Cognitively normal (CN)																																																																																																																																
MMSE*	-1.20	-0.53	0.100																																																																																																																													
ADAS-Cog**	2.02	-0.13	0.005																																																																																																																													
CDR-SB***	0.43	0.09	0.005																																																																																																																													
Daily activities	-0.91	-0.41	0.570																																																																																																																													
Verbal fluency animals	-0.78	-0.35	0.777																																																																																																																													
Verbal fluency vegetables	0.02	0.00	0.987																																																																																																																													
WMS †delayed recall	1.08	0.88	0.877																																																																																																																													
WMS immediate recall	-0.93	0.95	0.091																																																																																																																													
MCI group																																																																																																																																
MMSE	-2.54	-0.20	0.003																																																																																																																													
ADAS-Cog	3.84	-0.61	0.001																																																																																																																													
CDR-SB	1.18	0.25	0.020																																																																																																																													
Daily activities	-1.72	-1.59	0.937																																																																																																																													
Verbal fluency animals	-1.64	0.56	0.090																																																																																																																													
Verbal fluency vegetables	-1.97	0.29	0.025																																																																																																																													
WMS delayed recall	-1.99	1.56	0.012																																																																																																																													
WMS immediate recall	-2.35	1.00	0.005																																																																																																																													
Clinically diagnosed AD																																																																																																																																
MMSE	-2.10	1.43	0.089																																																																																																																													
ADAS-Cog	1.57	4.86	0.165																																																																																																																													
CDR-SB	1.99	0.47	0.176																																																																																																																													
Daily activities	-10.15	-6.36	0.539																																																																																																																													
Verbal fluency animals	-3.06	0.27	0.006																																																																																																																													
Verbal fluency vegetables	-1.23	-0.11	0.273																																																																																																																													
WMS delayed recall	0.04	1.03	0.399																																																																																																																													
WMS immediate recall	-0.61	0.45	0.493																																																																																																																													