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Tau PET binding distinguishes patients with early-stage posterior cortical atrophy from amnesic Alzheimer disease dementia

Gregory S. Day, MD, MSc^{a,b,*}, Brian A. Gordon, PhD^{a,c,*}, Kelley Jackson, BA^c, Jon J. Christensen, BS^c, Maria Rosana Ponisio, MD^c, Yi Su, PhD^c, Beau M Ances, MD, PhD^{a,b,c}, Tammie L.S. Benzinger, MD, PhD^{a,c,d}, and John C. Morris, MD^{a,b}

^aThe Charles F and Joanne Knight Alzheimer Disease Research Center, Washington University School of Medicine, St. Louis, Missouri, United States of America

^bDepartment of Neurology, Washington University School of Medicine, St. Louis, Missouri, United States of America

^cMallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, Missouri, United States of America

^dDepartment of Neurological Surgery, Washington University School of Medicine, St. Louis, Missouri, United States of America

Abstract

Background—Flortaucipir (tau) PET binding distinguishes individuals with clinically well-established posterior cortical atrophy (PCA) due to Alzheimer disease (AD) from cognitively normal (CN) controls. However, it is not known whether tau PET binding patterns differentiate individuals with PCA from those with amnesic AD, particularly early in the symptomatic stages of disease.

Methods—Flortaucipir and florbetapir (β-amyloid) PET-imaging were performed in individuals with early-stage PCA (N=5), amnesic AD dementia (N=22), and CN controls (N=47). Average tau and β-amyloid deposition were quantified using standard uptake value ratios and compared at a voxel-wise level, controlling for age.

Results—PCA patients (median age-at-onset, 59 [51–61] years) were younger at symptom-onset than similarly-staged individuals with amnesic AD (75 [60–85] years) or CN controls (73 [61–90] years; $p=0.002$). Flortaucipir uptake was higher in individuals with early-stage symptomatic PCA versus those with early-stage amnesic AD or CN controls, and greatest in posterior regions. Regional elevations in florbetapir were observed in areas of greatest tau deposition in PCA patients.

Address for Correspondence: Gregory S. Day, Charles F. and Joanne Knight Alzheimer Disease Research Center, Washington University School of Medicine, 4488 Forest Park Avenue, Suite 160, St. Louis, MO 63108, gday@wustl.edu, Telephone: 314.286.2407, Fax: 314.286.1985.

*These authors contributed equally to this work

Conclusions and Relevance—Flortaucipir uptake distinguished individuals with PCA and amnesic AD dementia early in the symptomatic course. The posterior brain regions appear to be uniquely vulnerable to tau deposition in PCA, aligning with clinical deficits that define this disease subtype.

Keywords

posterior cortical atrophy; Alzheimer disease; visual variant; progressive posterior cortical dysfunction; tau imaging

Introduction

Individuals with posterior cortical atrophy (PCA; also known as progressive posterior cortical dysfunction for individuals with early-stage clinical features that may precede regional atrophy; or alternatively, visual variant Alzheimer disease [AD]), exhibit primary visual-spatial complaints that range from a loss of acuity to complex disruptions or misinterpretations of visual stimuli.^{1,2} Progressively disturbed visuo-perceptual and visuospatial processing commonly manifests as visual field defects, visual agnosia, and environmental disorientation, with or without additional elements of Balint or Gerstmann syndromes.¹⁻⁴ Visual deficits may appear in isolation, reflecting preferential involvement of posterior structures subserving visuo-perceptual and visuospatial processing, or posterior-predominant dysfunction may manifest as a component of a more generalized dementia syndrome.¹ Although clinicopathologic series establish AD pathology as the most common cause of PCA,^{1,2,5} other pathologies are also associated with this syndrome.^{1,2,6}

Until recently, our ability to visualize the distribution of AD neuropathologic change during life was limited to the indirect measurement of β -amyloid burden using PET ligands specific for the detection of fibrillary β -amyloid.^{7,8} Although some studies in patients with PCA report posterior predominant β -amyloid deposition,⁹⁻¹² regional specificity is not consistently seen when comparing individuals with PCA to those with more typical amnesic AD dementia,¹³⁻¹⁵ suggesting that β -amyloid imaging may predict the diagnosis of AD, but not the clinical phenotype. The recent advent of novel PET ligands has facilitated *in vivo* visualization of tau topographies in the brains of individuals with typical¹⁶⁻¹⁸ and atypical AD presentations.^{15,19} Qualitative analyses of flortaucipir (tau) PET imaging in individuals with PCA have demonstrated posterior-predominant uptake compared to cognitively normal (CN) controls,¹⁵ suggesting that tau deposition predicts neurodegeneration and neuronal dysfunction in PCA caused by AD.²⁰ However, it is unclear whether there are significant differences in flortaucipir binding in individuals with symptomatic PCA and amnesic AD dementia. We determined the density and distribution of flortaucipir binding in patients with very mild PCA and amnesic AD dementia (Clinical Dementia Rating [CDR] 0.5) to examine whether binding patterns would differentiate individuals in the earliest clinically-detectable stages of disease. We hypothesized that flortaucipir PET binding would distinguish patients with PCA and amnesic AD dementia, defining areas most vulnerable to tau deposition in PCA.

Methods

Standard Protocol Approvals, Registrations, and Patient Consents

Consecutive patients with PCA (N=5; CDR=0.5) were recruited from the university-affiliated Memory Diagnostic Center (MDC) outpatient clinic. Participants with amnesic AD dementia (CDR=0.5) and CN controls (CDR=0) were enrolled in longitudinal studies of memory and aging at the Knight Alzheimer Disease Research Center (ADRC). Twenty-two participants meeting criteria for amnesic AD dementia²¹ and 47 CN controls completed florbetapir (β -amyloid) and/or flortaucipir PET; findings were compared with those observed in the 5 PCA individuals. Patients and participants consented to study participation, including review of clinical records, and structural and PET neuroimaging. Study protocols were approved by the Washington University School of Medicine Human Subjects Committee, and registered with ClinicalTrials.gov (NCT02414282, NCT02414347).

Clinical assessment and Eligibility Criteria

Longitudinal symptoms and signs, and results of neuropsychological testing and investigations were obtained from MDC records or the Knight ADRC research database. All individuals were evaluated by experienced clinicians using a semi-structured interview with a knowledgeable collateral source and the symptomatic individual, and including a detailed neurological examination of the affected individual. A clinical diagnosis of dementia was considered at the conclusion of each assessment, integrating results from the clinical assessment and bedside measures of cognitive function (including the Mini-Mental Status Examination²²). Dementia was diagnosed according to National Institute on Aging-Alzheimer's Association diagnostic criteria,^{21,23} and staged using the global CDR.²⁴ The severity of cognitive impairment was indicated by the CDR Sum of Boxes (CDR-SB).²⁵ PCA was diagnosed in individuals fulfilling Tang-Wai clinical diagnostic criteria.² Briefly, these criteria require the insidious onset and gradual progression of visual symptoms, together with objective demonstration of visuospatial/visuoperceptual deficits (e.g., elements of Gerstmann or Balint syndrome, visual field defect, or prominent environmental disorientation) that result in substantial disability, and occur in the absence of primary ocular disease or an alternate cause of findings (e.g., stroke, tumor). Individuals with parkinsonism and/or asymmetric sensory/motor signs consistent with corticobasal degeneration were excluded.

Control participants were deemed "cognitively normal" by Knight ADRC clinicians (CDR 0). Recruitment of affected individuals was limited to those in the earliest symptomatic stage of disease (CDR 0.5), encompassing individuals with mild cognitive impairment due to AD and very mild AD dementia.^{21,23,26} The medical records of individuals diagnosed with PCA were reviewed for eligibility, and those meeting diagnostic criteria were invited to enroll. Participants were consecutively-accrued from 2014 to 2016, representing all eligible participants with available florbetapir or flortaucipir imaging data. Eligible participants with only one available imaging modality were enrolled in the interest of maximizing analytic power. All participants were selected on the basis of clinical diagnosis and dementia staging, without prior knowledge of AD biomarker results (cerebrospinal fluid or PET imaging measures of an AD pathophysiologic process). Thus, it is possible that affected cohorts

could include individuals with non-AD pathology, or that individuals with preclinical AD could be included as CN controls. The emphasis on assignment based on clinical presentation was selected to reflect clinical practice, where AD biomarkers are seldom known *a priori*.

Neuroimaging

T₁-weighted magnetic resonance images were acquired using a MPRAGE sequence with repetition time (TR)=2300 ms, echo time (TE) = 2.95 ms, flip angle (FA) = 9°, 176 slices, in plane resolution 240 × 256, slice thickness=1.2 mm acquired in sagittal orientation. Images underwent volumetric segmentation using FreeSurfer 5.3 (<http://freesurfer.net>) to identify a cerebellar region of interest used in the PET analyses.

All individuals with PCA, 20/22 (91%) of amnesic AD participants, and 42/47 (89%) of CN controls underwent β -amyloid PET imaging using florbetapir (¹⁸F-AV-45). Individuals received a bolus injection of between 7.7 and 11.5 mCi of florbetapir, and data from the 50–70 minute post-injection window were converted to standardized uptake value ratios (SUVRs), relative to cerebellar gray matter. All PCA patients, 11/22 (50%) amnesic AD participants, and all CN controls underwent tau PET imaging using flortaucipir (¹⁸F-AV-1451). Individuals received a bolus injection of between 7.2 and 10.9 mCi of flortaucipir. Data from the 80–100 minute post-injection window were converted to SUVRs using the whole cerebellum as a reference, in accordance with established techniques.^{16,17} For descriptive purposes PET data was analyzed using an ROI approach. Summary measures of florbetapir²⁷ and flortaucipir²⁸ are presented in Table 1.

Statistical analyses

Clinical data were analyzed using SPSS Statistics (IBM Corp., Version 24.0. Armonk, NY). Comparisons across all three cohorts (PCA, amnesic AD, CN controls) were performed using the non-parametric Kruskal-Wallis test. Continuous and categorical measures were compared using the Mann-Whitney U-test, and Fisher's exact test, respectively. Statistical significance was defined as $p < 0.05$, unless otherwise defined.

PET neuroimaging data were filtered with an 8mm Gaussian kernel and placed into a common anatomical space prior to analysis using a linear registration. Voxel-wise PET data was analyzed using nonparametric permutation testing implemented using Randomize,²⁹ part of the FSL software suite (<http://fsl.fmrib.ox.ac.uk>). Permutation techniques provide exact control of false positive rates and provide a more robust approach to analyzing PET or structural MRI data.^{30,31} The identification of significant clusters was performed using threshold-free cluster enhancement,³² also implemented using the FSL suite. Significance maps were corrected for multiple comparisons using a family-wise error rate of $p < 0.05$. Statistical models included age as a covariate.

Results

Table 1 details demographic and clinical features for individuals with PCA, amnesic AD dementia and CN controls. Individuals with PCA differed from those with amnesic AD dementia, with younger age at symptom onset ($p = 0.001$), and with visuospatial/perceptual

symptoms at presentation ($p<0.001$). There was a trend towards a greater proportion of females in the PCA group ($p=0.06$). Visuo-perceptual abnormalities ($p<0.001$), alexia ($p=0.003$) and apraxia ($p<0.001$) reliably distinguished PCA patients from those with amnesic AD dementia. Although individuals with PCA did not initially present with memory complaints, memory impairment developed in all PCA individuals by the clinical assessment nearest flortaucipir PET imaging. No differences were observed in dementia severity, as measured using the CDR-SB ($p=0.52$), performance on the Mini-Mental State Examination ($p=0.25$), or duration of symptomatic illness ($p=0.62$) at the time of flortaucipir PET imaging.

Mean florbetalpir and flortaucipir deposition for individuals with PCA, amnesic AD dementia, and CN controls are depicted in Figure 1. Mean β -amyloid SUVRs exceeded pre-defined thresholds for the diagnosis of a “positive” scan (mean SUVR 1.27 = consistent with AD¹⁷) in all patients with PCA and in 17/20 imaged patients with amnesic AD dementia. Significance maps comparing tracer uptake between groups are presented in Figure 2 (uptake within the right hemisphere is shown for ease of presentation; bilateral hemispheric data are presented in supplementary materials: eFigures 1–4). No laterality effects were noted. Florbetalpir uptake distinguished individuals with early-stage symptomatic PCA and amnesic AD dementia from CN controls (Figure 2a and 2b, left). Both symptomatic groups demonstrated elevated levels of β -amyloid in stereotypical AD regions, including the precuneus, posterior cingulate, temporal lobe, medial prefrontal cortex, and the bilateral parietal lobes. Unique to PCA patients, flortaucipir uptake was also increased in posterior areas (visual cortex), relative to controls. At the whole-brain level there were no significant differences in florbetalpir uptake in the PCA and amnesic AD dementia groups. However, when comparisons were limited to voxels with significant increases in flortaucipir binding, significantly greater florbetalpir uptake was noted in the visual cortices of individuals with PCA (Figure 2c, left).

Relative to CN controls, flortaucipir uptake in individuals with PCA and amnesic AD dementia was significantly elevated throughout the temporal lobe, temporal parietal junction, precuneus, posterior cingulate, lateral parietal regions, lateral occipital cortex, and prefrontal cortex (Figure 2a and 2b, right). When compared to individuals with amnesic AD dementia, flortaucipir uptake was consistently elevated within the primary and secondary visual areas, as well as bilateral parietal and supplementary motor cortices of individuals with PCA (Figure 2c, right). The topographical distribution of tau-PET binding was unchanged when controlling for mean cortical levels of β -amyloid PET deposition (eFigure 5). In addition, flortaucipir uptake in individuals with PCA was consistently demonstrated at or above levels observed in individuals with amnesic AD dementia within regions previously shown to reflect tau topographies relevant to amnesic AD¹⁶ (Figure 3), after controlling for age and mean cortical levels of β -amyloid PET deposition (Table 2).

Discussion

Tau-PET (flortaucipir) uptake within posterior brain regions, particularly the primary and secondary visual areas, distinguished individuals with early-stage symptomatic PCA and amnesic AD dementia. These findings build upon initial reports establishing preferential

tau-PET binding in the posterior cortical regions of small cohorts of patients with PCA versus CN controls,¹⁵ defining cardinal areas of increased tau deposition specific to patients with very mild dementia due to PCA. In addition, increased florbetapir binding was seen within posterior cortical regions that also demonstrated the greatest flortaucipir uptake, extending findings from other *in vivo* studies approximating β -amyloid deposition in individuals with PCA.^{9–12} The ability to differentiate individuals with varying phenotypes of AD using *in vivo* β -amyloid- and tau-PET imaging in this study, but not others,^{13–15} may reflect inclusion criteria emphasizing recruitment of patients with the earliest manifestations of symptomatic AD. Together, these findings suggest that posterior regions remain uniquely vulnerable to AD pathology, with tau deposition detectable early in the symptomatic course. By extension, preferential tau deposition within posterior regions may underlie the emergence of visuospatial/perceptual symptoms and signs that define the early stages of PCA due to AD.

Although flortaucipir uptake within posterior regions distinguished individuals with early symptomatic PCA from those with amnesic AD dementia in our series, it is important to note that tau deposition was not limited to these areas. On the contrary, comparable levels of flortaucipir binding were observed in individuals with PCA within brain areas commonly affected in amnesic AD. These findings suggest that the fundamental topographical distribution of tau pathology overlaps substantially in individuals with AD. Similar findings were observed when comparing regional β -amyloid topography: differences in florbetapir uptake were revealed only following post-hoc comparisons involving regions most susceptible to tau deposition. The intersection of neuropathology likely explains the overlapping patterns of cortical atrophy previously reported within the bilateral parietal, occipital, precuneus, posterior cingulate, posterior temporal and hippocampal regions of individuals with visual and amnesic AD.³³ Together, these findings support a common process governing the progression of AD neuropathologic change. It fits, therefore, that patient-specific factors may convey vulnerability to regional AD pathology, and by extension, disease phenotype. This suggestion is supported by the earlier age at symptom onset reported in individuals with PCA in this study and others,^{34,35} by a potential gender bias (with a higher proportion of female patients diagnosed with PCA),^{2,13,33,36–38} and by emerging reports identifying putative genetic associations in individuals with PCA.^{2,39,40}

Findings from this small cohort of individuals with symptomatic AD dementia add to the limited literature considering *in vivo* imaging of AD neuropathologic change, suggesting that regional differences in the deposition of both β -amyloid and tau predict posterior predominant dysfunction in PCA. Differences between regional β -amyloid deposition between this study and others,^{13–15} may reflect differences in study populations (this study favored recruitment of individuals with early-stage symptomatic AD), methodological differences owing to variations in PET-tracers (β -amyloid imaging was performed in other studies using [¹¹C] Pittsburgh compound B), or differences in the comparison populations. Although PCA and amnesic AD dementia cohorts were matched for dementia severity (emphasizing inclusion of individuals with very mild dementia, global CDR 0.5), CDR has been primarily validated in populations with amnesic AD. Thus, it remains possible that this measure may under-estimate disease severity in patients with atypical (i.e., visual) AD presentations. However, disparity in dementia severity is unlikely to fully account for

differences in β -amyloid and tau deposition observed in PCA patients, as regional differences in tau deposition persisted even after controlling for mean cortical levels of florbetapir (β -amyloid) PET uptake (eFigure 5)—a proxy imaging measure of disease severity. Finally, the possibility that β -amyloid and tau deposition (or tracer uptake) are fundamentally different in younger individuals cannot be excluded.¹⁵ Although statistical models controlled for age, such a finding could yet contribute to observed differences in flortaucipir uptake.

Our findings suggest that early tau deposition within primary and secondary visual areas corresponds to the emergence of visuoperceptual and visuospatial compromise in patients with PCA. Extending this logic, the gradual spread of tau pathology to signature AD regions (e.g., the precuneus, medial temporal lobes and frontal lobes) should predict the emergence of typical symptoms and signs of AD dementia. Tau deposition and propagation may be preceded by regional-specific β -amyloid deposition; alternatively, tau deposition may occur independent of this process. These hypotheses may be further evaluated through longitudinal PET imaging studies in greater numbers of PCA patients, with the potential to better understand both the mechanisms that give rise to the posterior-anterior gradient of neurofibrillary tangle pathology reported at the nadir of disease,^{2,6} and the factors that convey regional vulnerability to AD neuropathologic change.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix

Author Contributions

G.S. Day participated in study design and conduct, participant recruitment and care, acquisition and interpretation of clinical and imaging data, statistical analysis, and drafting, revision and finalization of the manuscript.

B.A. Gordon participated in acquisition and interpretation of imaging data, statistical analysis, and drafting, revision and finalization of the manuscript.

K. Jackson participated in study design and conduct, participant recruitment and care, acquisition of imaging data, and revision and finalization of the manuscript.

J. Christensen participated in interpretation of imaging data, and revision and finalization of the manuscript.

M.R. Ponisio participated in participant care, acquisition and interpretation of imaging data, and revision and finalization of the manuscript.

Y. Su participated in interpretation of imaging data and revision and finalization of the manuscript.

B.M. Ances participated in interpretation of imaging data and revision and finalization of the manuscript.

T.L.S. Benzinger participated in study design and conduct, participant care, acquisition and interpretation of imaging data, and revision and finalization of the manuscript.

J.C. Morris participated in study design and conduct, interpretation of clinical and imaging data, and revision and finalization of the manuscript. Dr. Morris had full access to all data and takes responsibility for the integrity of the data and the accuracy of the conclusions.

Conflict of Interest Disclosures

G.S. Day involved in clinical trials of anti-amyloid agents (sponsored by Eli Lilly), and holds stocks (>\$10,000) in ANI Pharmaceuticals (a generic pharmaceutical company).

B.A. Gordon is participating in a clinical trial examining the utility of the AV-1451 tracer sponsored by Eli Lilly/Avid Radiopharmaceuticals. Neither Dr. Gordon nor his family has direct equity interest in any pharmaceutical or biotechnology company.

K. Jackson has nothing to disclose. Neither K Jackson nor her family has direct equity interest in any pharmaceutical or biotechnology company.

J. Christensen is providing technical support for clinical trials of anti-dementia drugs sponsored by Lilly, Roche, and the DIAN-TU (Dominantly Inherited Alzheimer Network Trials Unit). Neither J Christensen nor his family has direct equity interest in any pharmaceutical or biotechnology company

M.R. Ponisio has nothing to disclose. Neither Dr. Ponsio nor her family has direct equity interest in any pharmaceutical or biotechnology company

Y. Su has nothing to disclose. Neither Dr. Su nor his family has direct equity interest in any pharmaceutical or biotechnology company

B.M. Ances has nothing to disclose. Neither Dr. Ances nor her family has direct equity interest in any pharmaceutical or biotechnology company

T.L.S. Benzinger has participated or is currently participating in clinical trials of anti-dementia drugs sponsored by: Lilly, Roche, DIAN-TU (Dominantly Inherited Alzheimer Network Trials Unit), and A4 (The Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease) trial. She receives research support from Eli Lilly/Avid Radiopharmaceuticals and is funded by NIH grants P50AG005681; P01AG003991; P01AG026276 and UF01AG032438. Neither Dr. Benzinger nor her family has direct equity interest in any pharmaceutical or biotechnology company.

JC Morris is currently participating in clinical trials of antidementia drugs (A4 trial: The Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease), funded by the National Institute on Aging, Eli Lilly and Company, and several philanthropic organizations. Dr. Morris has served as a consultant for Lilly USA. He is funded by NIH grants # P50AG005681; P01AG003991; P01AG026276 and UF01AG032438. Neither Dr. Morris nor his family owns stock or has equity interest (outside of mutual funds or other externally directed accounts) in any pharmaceutical or biotechnology company.

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Figure 1.

Depiction of *in vivo* β -amyloid and tau pathology in individuals with very mild dementia. Average maps of β -amyloid deposition measured with florbetapir (left) and tau deposition measured with flortaucipir (right) are shown for individuals with A) amnesic AD dementia; B) PCA; and, C) normal cognition. All comparisons control for differences in age. Values are standardized uptake value ratios (SUVRs).

Figure 2.

Significant elevations in β -amyloid and tau pathology between groups. Maps depicting significant elevations in β -amyloid (left) and tau PET deposition in individuals with A) amnestic AD dementia relative to cognitively normal controls; B) PCA relative to cognitively normal controls; and, C) PCA relative to amnestic AD dementia. The significant elevations in β -amyloid in individuals with PCA relative to those with amnestic AD dementia were only significant when restricting analyses to those voxels that showed significantly greater tau deposition. All comparisons control for differences in age.

Figure 3.

Scatter-plot showing inter-individual variation in flortaucipir SUVR within regions of interest. Greater flortaucipir binding was observed in the early-stage PCA patients in the extracted visual region of interest (ROI) identified in the voxel-wise analyses (Figure 2) compared to those with early-stage amnesic AD dementia and cognitively normal controls. Extracted values from Freesurfer ROIs for the inferior temporal ROI, inferior parietal ROI, and precuneus ROI are presented for comparison.

Table 1

Demographic and clinical details for study participants.

Participant Features	PCA (N=5)	Amnesic AD (N=22)	Controls (N=47)
<i>Demographics</i>			
Age-at-onset, median (range), y	59 (51–61) [†]	75 (60–85) [‡]	73 (61–90) [‡]
Female gender, No. (%)	5 (100)	11 (50)	21 (45)
Education, median (range), y	18 (12–18)	16 (10–20)	16 (12–20)
<i>Presenting Symptoms</i>			
Visual spatial/perceptual difficulties, No. (%)	5 (100) [†]	0	--
Alexia, No. (%)	3 (60) [†]	0	--
Word-finding difficulties, No. (%)	1 (20)	2 (9)	--
Memory loss, No. (%)	0 [†]	22 (100)	--
<i>Findings at clinical assessment closest to flortaucipir imaging</i>			
Visual field deficits, No. (%)	2 (40) [†]	0	--
Balint syndrome (partial/complete), No. (%)	5 (100) [†]	0	--
Gerstmann syndrome (partial/complete), No. (%)	5 (100) [†]	0	--
Apraxia, No. (%)	4 (80) [†]	0	--
Memory impairment, No. (%)	4 (80)	22 (100)	--
Mini-Mental State Examination, median (range)	25 (19–29) [*]	27 (14–30)	30 (27–30) ^{†‡}
Global CDR, median (range), y	0.5	0.5	0 ^{†‡}
CDR-SB, median (range), y	3.0 (0.5–4.0)	2.0 (1.0–4.0)	0 ^{†‡}
<i>PET neuroimaging, summary findings</i>			
Duration of symptomatic illness, median (range), y	3.4 (2.0–4.5)	3.6 (1.5–8.7)	--
Flortaucipir SUVR, mean (sd)	2.05 (.28) [†] (N=5)	1.43 (.25) [‡] (N=11)	1.11 (.10) ^{†‡} (N=47)
Florbetapir SUVR, mean (sd)	1.66 (.20) (N=5)	1.61 (.32) (N=20)	1.29 (.27) ^{†‡} (N=42)
Interval between florbetapir and flortaucipir imaging, median (range), days	9 (1–26) (N=5)	70 (7–310) (N=9)	145 (8–258) [‡] (N=42)
Interval between clinical assessment and flortaucipir imaging, median (range), y	0.7 (0.1–1.6) (N=5)	0.2 (0–0.5) (N=11)	0.4 (0–1.3) [†] (N=42)

[†] significantly different from participants with amnesic AD dementia;

[‡] significantly different from patients with PCA; significance defined as $p < 0.017$ ($p < 0.05$, Bonferroni corrected for multiple comparisons).

^{*} Mini-Mental State Examination data available from 4 patients with PCA; one patient was unable to complete testing due to the severity of visuospatial/spatial deficits. AD = Alzheimer disease; CDR = Clinical Dementia Rating; CDR-SB = Clinical Dementia Rating, Sum of Boxes; SUVR = standardized uptake value ratios.

Table 2

Comparisons of regional flortaucipir uptake between individuals with PCA and amnesic AD dementia.

Flortaucipir SUVR	PCA (N=5)	AD (N=11)	p value
Extracted Visual ROI, mean $\pm$ SE cortical SUVR [95% CI]	2.25 $\pm$ 0.12 [2.00–2.51]	1.16 $\pm$ 0.07 [1.01–1.30]	<.001
Inferior Temporal ROI, mean $\pm$ SE cortical SUVR [95% CI]	1.88 $\pm$ 0.22 [1.40–2.36]	1.74 $\pm$ 0.12 [1.47–2.01]	0.649
Inferior Parietal ROI, mean $\pm$ SE cortical SUVR [95% CI]	2.26 $\pm$ 0.24 [1.74–2.79]	1.63 $\pm$ 0.13 [1.33–1.92]	0.074
Precuneus ROI, mean $\pm$ SE cortical SUVR [95% CI]	2.04 $\pm$ 0.12 [1.78–2.30]	1.39 $\pm$ 0.07 [1.25–1.54]	0.002

All SUVR values corrected for age and mean cortical levels of β -amyloid PET deposition.

SUVR = standardized uptake value ratio; ROI = region of interest; SE = standard error