

Supplementary Material

Association of Tooth Loss with Alzheimer's Disease Tau Pathologies Assessed by Positron Emission Tomography

Supplementary Table 1. Summary of all correlation coefficients and *p*-values in the manuscript

	HCs		AD	
	Remaining teeth	BGI index	Remaining teeth	BGI index
Demographic data				
Age	-0.476* (0.039)	0.201 (0.409)	-0.283 (0.181)	-0.053 (0.807)
Years of schooling, y	0.372 (0.117)	-0.067 (0.785)	-0.089 (0.680)	0.177 (0.408)
Onset, y	N/A	N/A	-0.220 (0.301)	0.370 (0.075)
MMSE	0.159 (0.516)	0.061 (0.803)	0.107 (0.619)	0.011 (0.958)
FAB	-0.318 (0.185)	-0.095 (0.698)	0.214 (0.316)	0.174 (0.415)
CDR	N/A	N/A	-0.063 (0.771)	0.061 (0.776)
¹⁸F-PM-PBB3 PET SUVR				
Locus coeruleus	0.375 (0.113)	N/A	-0.479* (0.018)	N/A
Middle frontal gyrus	-0.169 (0.489)	N/A	-0.394 (0.057)	N/A
Hippocampus	-0.116 (0.634)	N/A	0.009 (0.968)	N/A

Spearman's rank correlation test. Values are listed as Spearman's rank correlation coefficient (*p*-value). * *p* < 0.05

AD, Alzheimer's disease; BGI, biofilm–gingival interface; CDR, Clinical Dementia Rating; FAB, frontal assessment battery; HCs, healthy controls; MMSE, Mini-Mental State Examination; N/A, not applicable; SUVR, standard uptake value ratio.

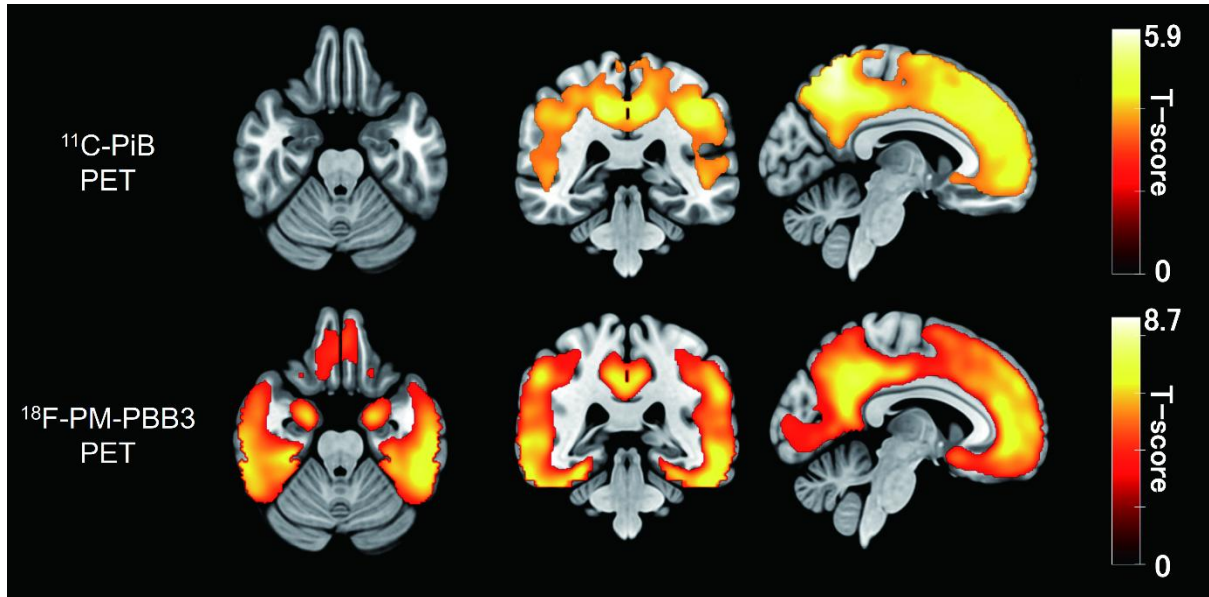
Supplementary Table 2. Brain areas showing negative correlations of tau deposits with the number of remaining teeth in the AD group

Hemi-sphere	Anatomical region	cluster-level			peak-level		MNI coordinates		
		<i>p</i> (uncorrected)	<i>p</i> (FWE)	T	<i>p</i> (uncorrected)	<i>p</i> (FWE)	x	y	z
R	Middle frontal gyrus	0.242	0.991	3.726	0.001	0.866	28.5	60	21
-	Locus coeruleus	0.176	0.967	3.511	0.001	0.939	0	-40.5	-22.5
L	Middle frontal gyrus	0.782	0.079	3.130	0.003	0.992	-27	60	18

Only the location with the highest peak value is listed in each of the three clusters. The anatomical location was identified using the AAL atlas. For the brainstem, because numerous nuclei were detected within this cluster, we have described an arbitrary brainstem nuclei. The anatomical location of the entire cluster was determined through visual inspection in conjunction with an overlay of the WFU PickAtlas template.

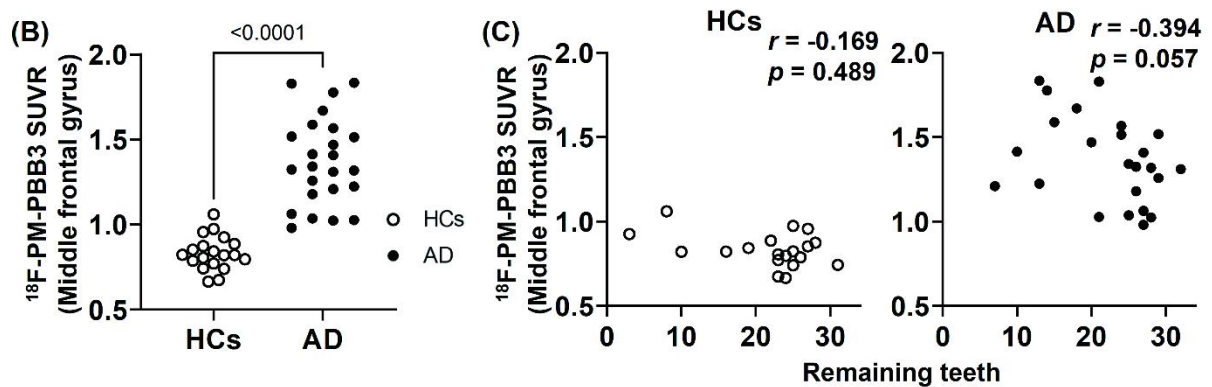
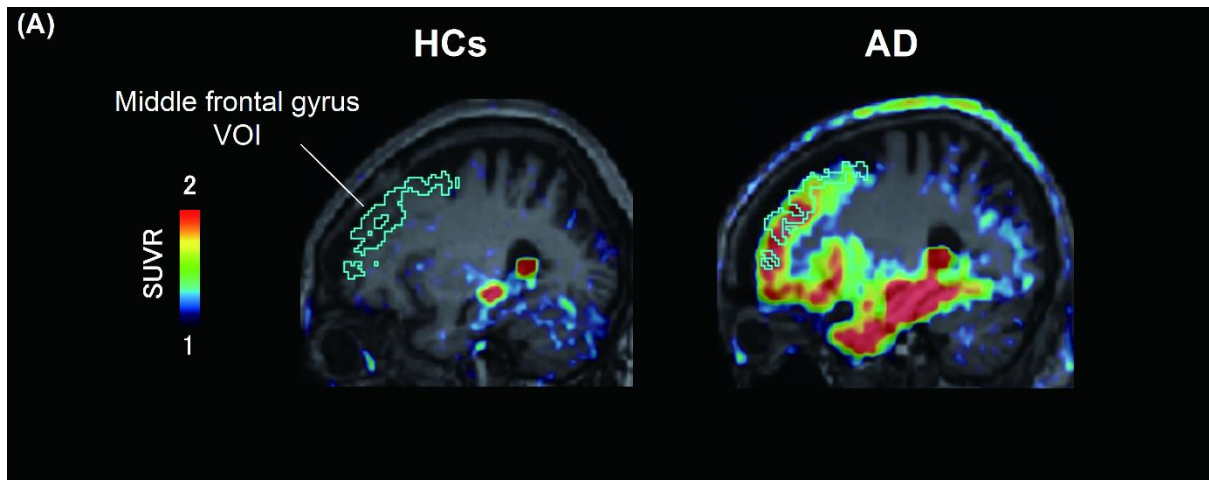
The statistical significance threshold was set as $p < 0.05$ (uncorrected, > 3069 voxels). Anatomical regions were detected by an AAL atlas.

FWE, family-wise error; L, left; MNI, Montreal Neurological Institute; R, right.



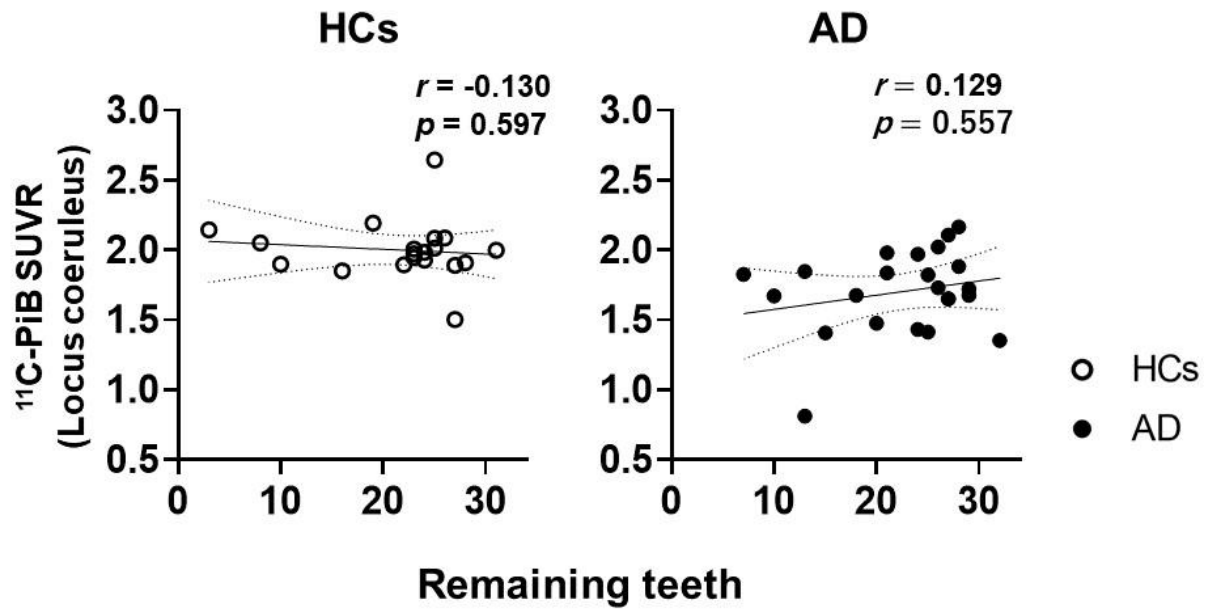
Supplementary Figure 1. A β and tau deposition in the AD group compared with the HC group.

Whole brain and group analysis illustrated A β and tau PET signal increase in the AD group compared with the HC group ($p < 0.05$, family-wise error corrected at cluster level). T-score maps were expressed in MNI space. AD, Alzheimer's disease; HC, healthy control; MNI, Montreal Neurological Institute; PET, positron emission tomography.



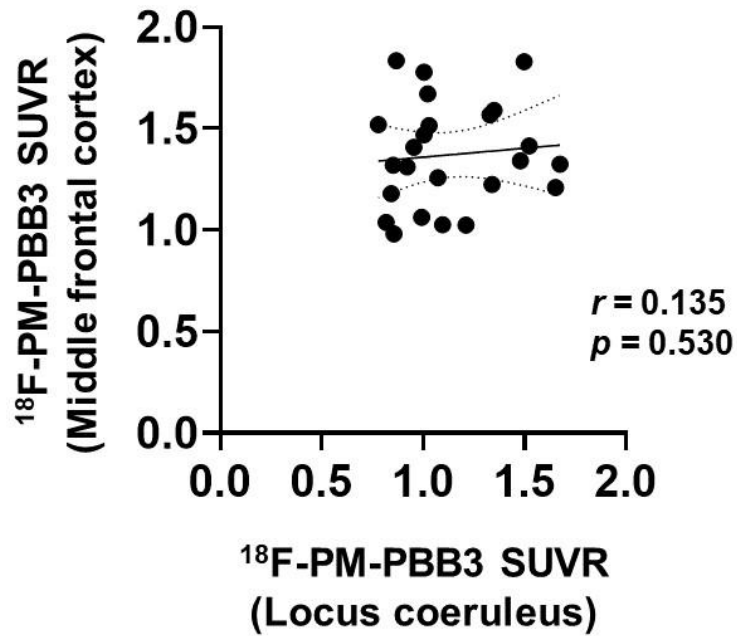
Supplementary Figure 2. Number of remaining teeth and correlation with tau lesions in the frontal cortex.

From the frontal lobe clusters identified in the whole-brain analysis, the automated anatomical labeling atlas was utilized to determine the anatomical location of the region, with the middle frontal gyrus selected as the region of interest (MFG-VOI). A) MFG-VOI on sagittal slices of spatially normalized and fused MRI and PET images of HCs and AD. B) Group comparison of tau PET SUVR values in MFG-VOI between HCs and AD groups. The p value was estimated by Mann-Whitney U-test. Open and filled circles indicate HCs and AD-spectrum patients, respectively. C) Correlations of tau PET SUVR values in MFG-VOI and the number of remaining teeth in HC and AD groups; r and p values were assessed by Spearman's rank correlation test. AD, Alzheimer's disease; HCs, healthy controls; MFG, middle frontal gyrus; PET, positron emission tomography; SUVR, standard uptake value ratio; VOI, volume of interest.



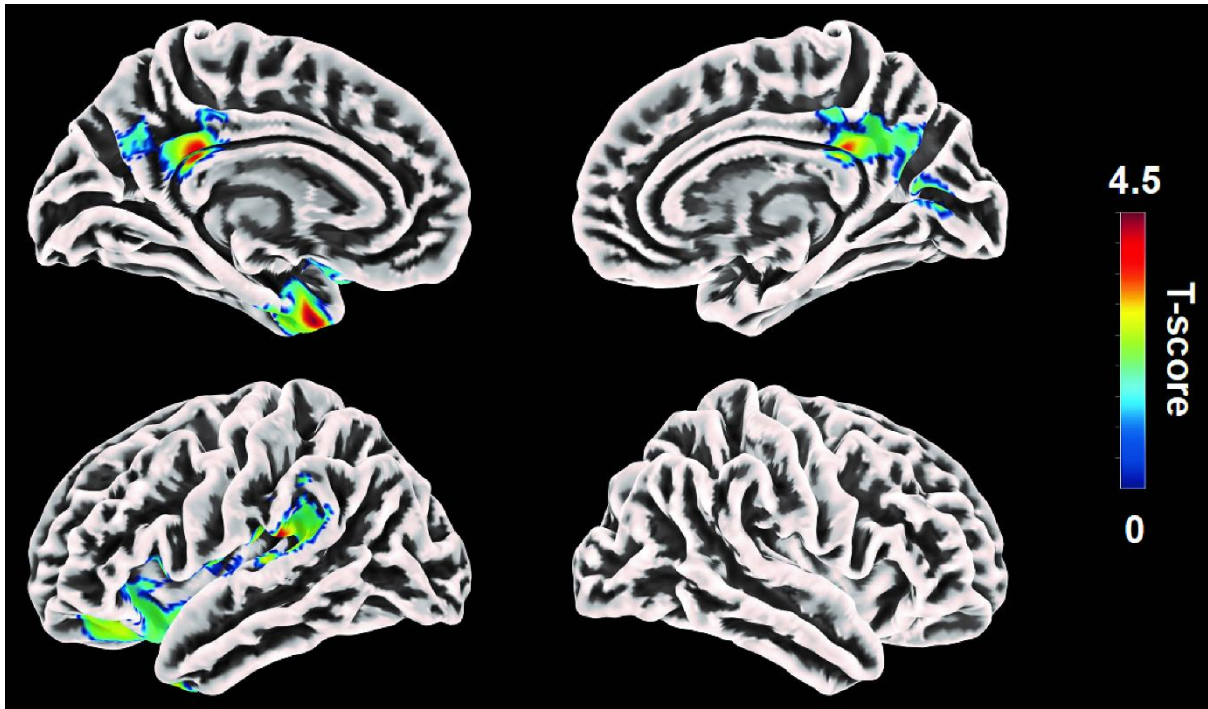
Supplementary Figure 3. Correlations of A β PET tracer binding in LC-VOI and the number of remaining teeth.

Correlations of A β PET tracer binding in LC-VOI and the number of remaining teeth in HCs and AD groups; r and p values were estimated by Spearman's rank correlation coefficient. Open and filled circles indicate HC and AD groups, respectively. AD, Alzheimer's disease; A β , amyloid β ; HC, healthy control; LC, locus coeruleus; PET, positron emission tomography; SUVR, standard uptake value ratio; VOI, volume of interest.



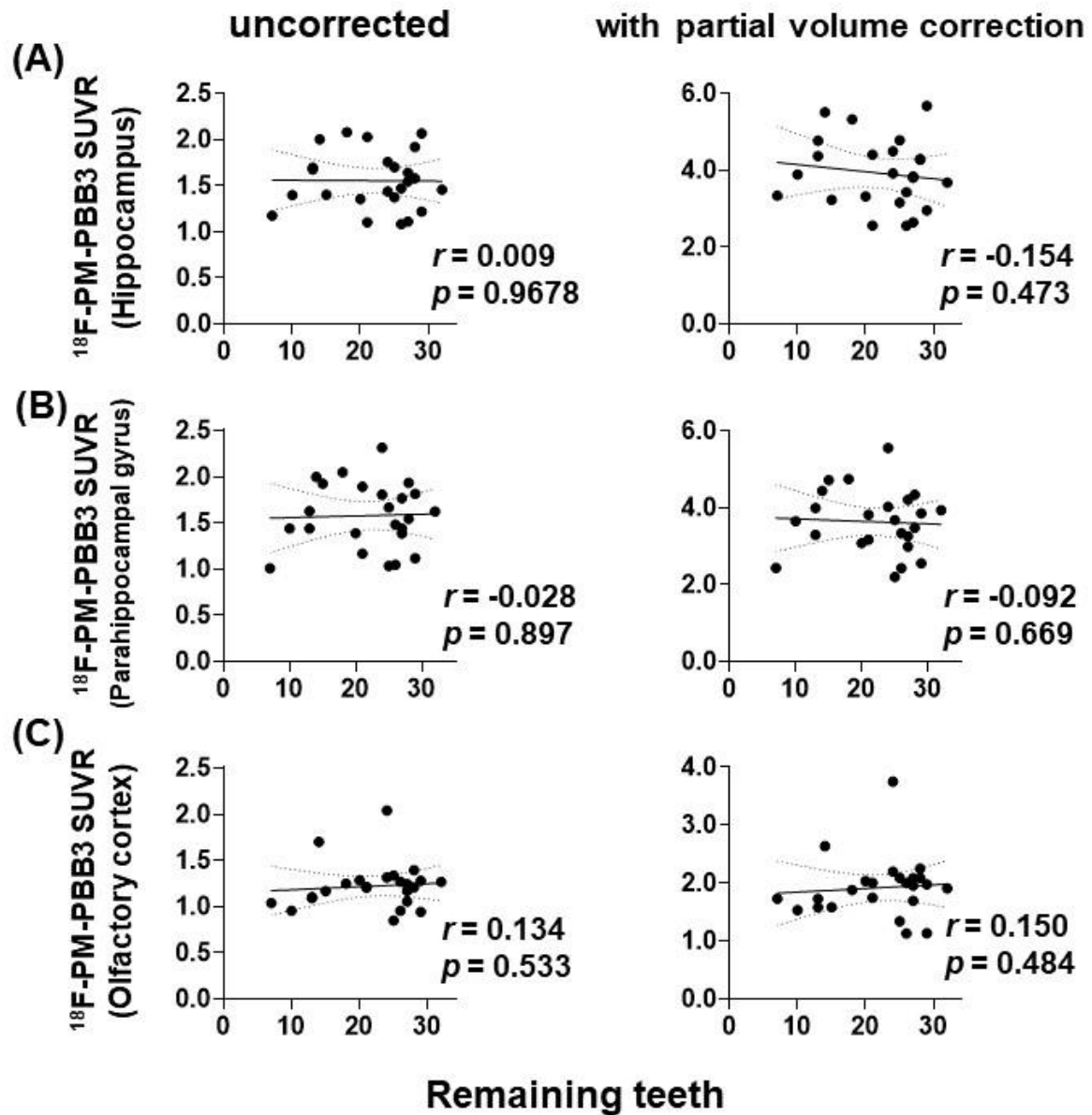
Supplementary Figure 4. Correlations of tau PET tracer binding in LC-VOI and MFG-VOI in AD.

r and p values were estimated by Spearman's rank correlation coefficient. AD, Alzheimer's disease; LC, locus coeruleus; MFG, middle frontal gyrus; PET, positron emission tomography; SUVR, standard uptake value ratio; VOI, volume of interest.

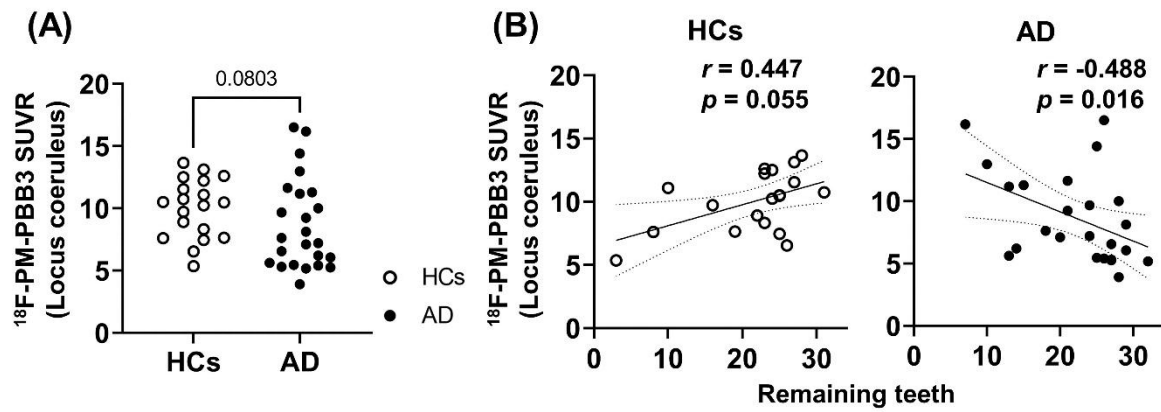


Supplementary Figure 5. Correlations of gray matter atrophy and number of remaining teeth in AD-spectrum patients.

Gray matter atrophy was evaluated using voxel-based morphometry, standardized by the DARTEL algorithm in SPM12, based on MRI images. Regions with significant correlations indicated a gray matter atrophy with a decrease in the number of remaining teeth (uncorrected, $p < 0.05$). The cluster size threshold was set to the expected voxel of each analysis. Results were expressed in the MNI coordinate space. DARTEL, Diffeomorphic Anatomical Registration Through Exponentiated Lie Algebra; SPM12, Statistical Parametric Mapping software; MRI, magnetic resonance imaging; AD, Alzheimer's disease; MNI, Montreal Neurological Institute.



Supplementary Figure 6. Correlations of tau PET tracer binding in (A) hippocampus, (B) parahippocampal gyrus and (C) olfactory cortex VOI with and without partial volume correction, and the number of remaining teeth in AD groups; r and p values were estimated by Spearman's rank correlation coefficient. AD, Alzheimer's disease; PET, positron emission tomography; SUVR, standard uptake value ratio; VOI, volume of interest.



Supplementary Figure 7. Correlations of tau PET tracer binding in LC-VOI with partial volume correction and number of remaining teeth.

A) Group comparison of tau PET tracer binding in LC-VOI with partial volume correction between HC and AD groups. The p value was estimated by the Mann-Whitney U-test. B) Correlations of tau PET tracer binding in LC-VOI with partial volume correction and the number of remaining teeth in HC and AD groups; r and p values were estimated by Spearman's rank correlation coefficient. Open and filled circles indicate HC and AD groups, respectively. AD, Alzheimer's disease; HC, healthy control; LC, locus coeruleus; PET, positron emission tomography; SUVR, standard uptake value ratio; VOI, volume of interest.