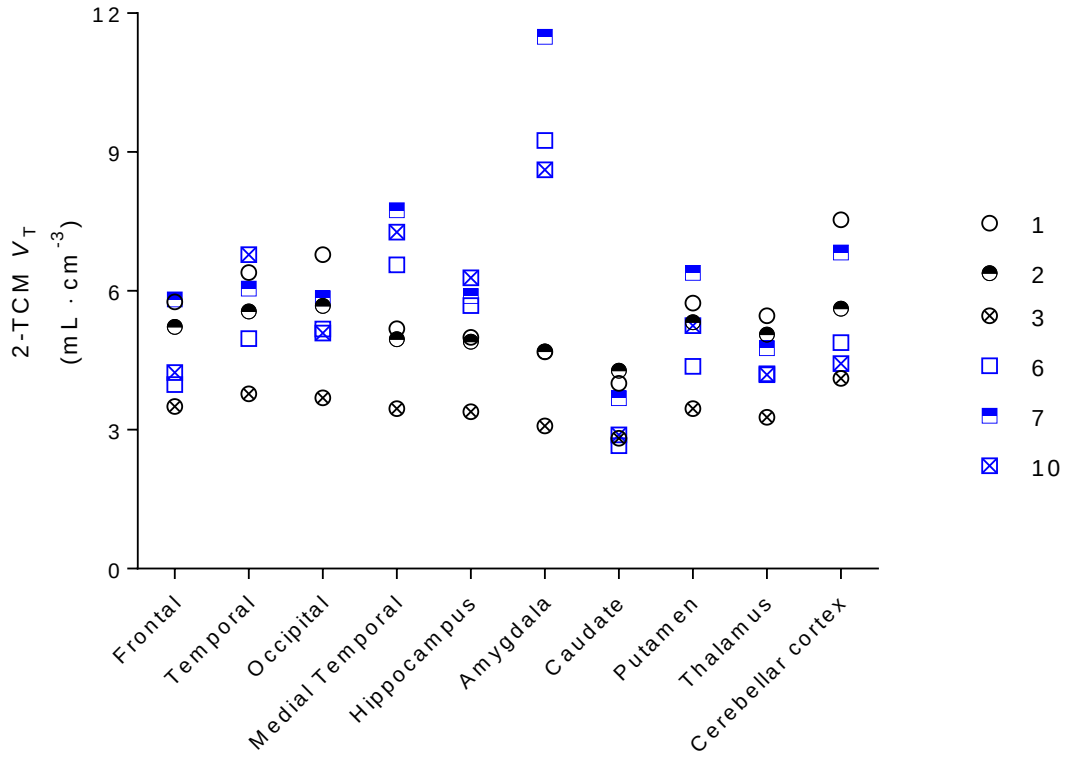
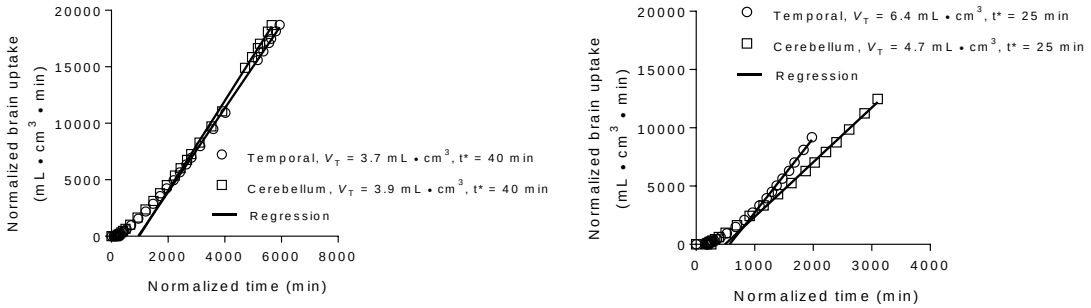
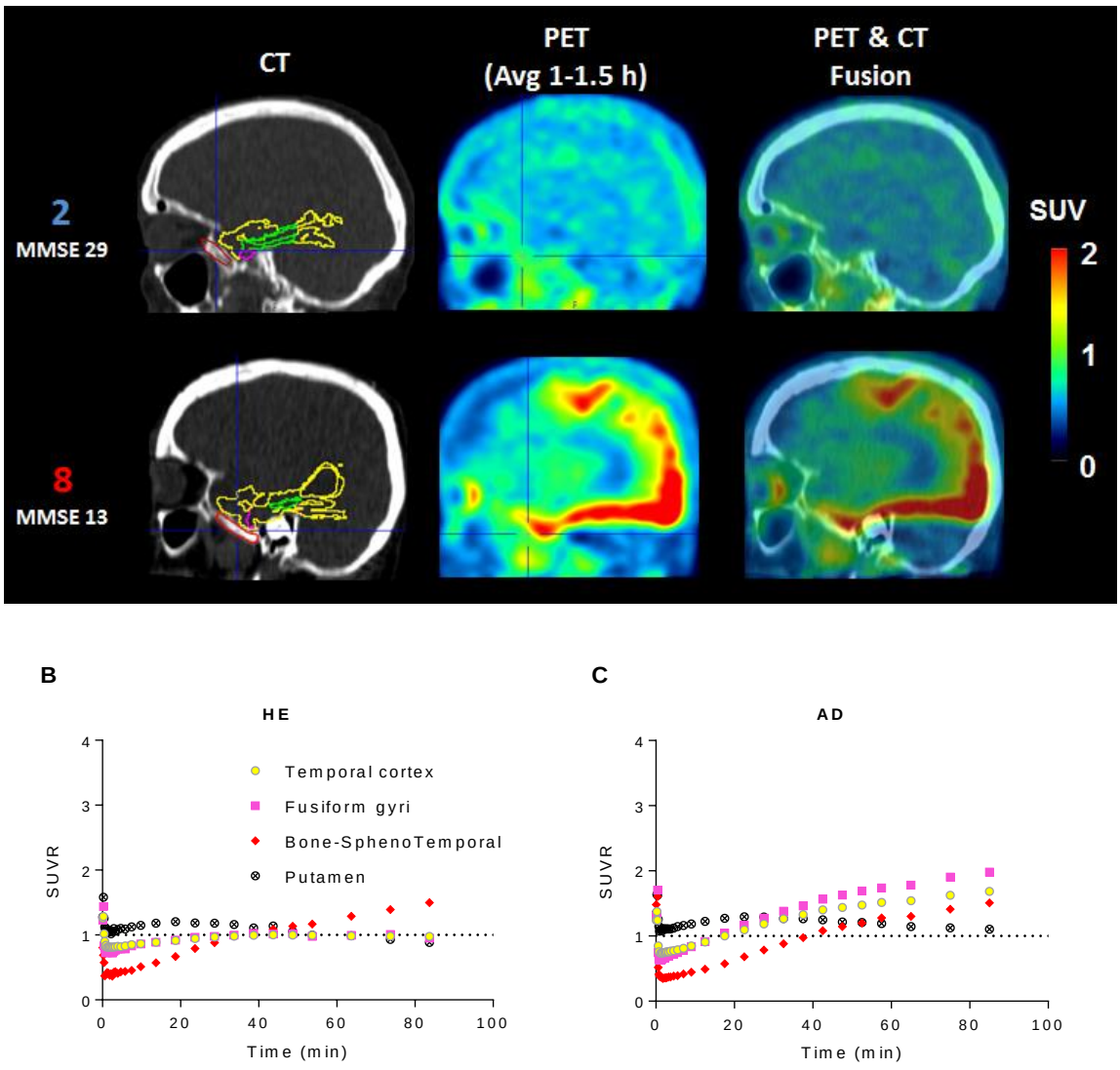


SUPPLEMENTAL FIGURE 1. Comparison of total V_T in various brain regions between cognitively HE subjects (1, 2, and 3) and AD subjects (6, 7, and 10) who received arterial sampling. V_T values were calculated using unconstrained 2-tissue compartmental model (2-TCM).



SUPPLEMENTAL FIGURE 2. Regional Logan plots (open symbols) and linear regressions (solid lines) derived from invasive Logan plot in a representative HE (Subject 3 – left plot) and AD (Subject 10 – right plot). Normalized time on x-axis is derived by the equation: $\int_0^T C_p(t)dt/C_t(T)$. Normalized brain uptake on y-axis is derived by the equation: $\int_0^T C_t(t)dt/C_t(T)$.



SUPPLEMENTAL FIGURE 3. Effect of bone uptake due to potential defluorination on brain cortical uptake. (A) Sagittal cross-sectional images (CT, PET, and PET and CT fusion) of a representative HE (2) subject and AD (8) subject showing atlas-derived regional VOI overlays (temporal cortex in yellow, fusiform gyri in pink, parahippocampal gyri in green) and manually drawn spheno-temporal bone VOIs (in red). PET images are averaged between 60-90 min and are color scaled as SUV between 0 and 2. (B) Regional (Brain cortices,

adjacent bone, and putamen) SUVR time course in HE subjects with cerebellar cortex as a reference. Curves represent a mean of 4 subjects. (C) Regional (Brain cortices, adjacent bone, putamen) SUVR time course in AD subjects with cerebellar cortex as reference. Curves represent a mean of 6 subjects.

SUPPLEMENTAL TABLE 1: CSF, Amyloid PET, and MRI characteristics in AD cohort

		CSF			Amyloid PET	MRI			
Subject ID	Clinical diagnosis	Aβ42 (>853 pg/mL)	Total tau (<400 pg/mL)	^{181}phosphotau (<65 pg/mL)	(SUVR <1.29)	MTA R	MTA L	ARWMC	GRE Hyperintensities
5	Dementia	439	163	29.4	N/A	2	2	3	8
6	Dementia	N/A	N/A	N/A	N/A	0	1	1	1
7	MCI	707	496	66	1.73	3	3	0	0
8	Dementia	409	1042	164	N/A	3	3	1	0
9	Dementia	N/A	N/A	N/A	N/A	2	3	0	0
10	MCI	782	1336	165	1.71	2	3	0	0

ARWMC = Age-related white matter change (based on reference *1*), CSF = Cerebrospinal fluid (cutoff criteria based on reference 2), GRE = Gradient recalled echo, MCI = Mild cognitive impairment, MTA R/L= Medial temporal lobe atrophy score (based on reference 3) right/left, N/A = not applicable, SUVR = Regional standard uptake value ratio. The values between brackets indicate the normal range. The amyloid PET was performed using ^{18}F-florbetaben.

SUPPLEMENTAL TABLE 2: Rate constants and total distribution volumes from two-tissue compartment model in HE subjects

	Two-tissue compartmental rate constants													
Brain region	**K_1 (mL • cm^{-3} • min^{-1})**		**k_2 (min^{-1})**		**k_3 (min^{-1})**		**k_4 (min^{-1})**		**Two-tissue V_T (mL • cm^{-3})**					
Temporal	0.326	(1.2%)	0.135	(2.1%)	0.012	(6.5%)	0.012	(8.4%)	5.2	±	1.3	(2.2%)		
Hippocampus	0.283	(1.5%)	0.115	(3%)	0.012	(11.3%)	0.017	(12.3%)	4.4	±	0.9	(2.2%)		
Amygdala	0.286	(2.5%)	0.108	(4.6%)	0.008	(18.2%)	0.013	(23.4%)	4.2	±	0.9	(4%)		
Caudate	0.274	(1.6%)	0.120	(3.1%)	0.012	(14.1%)	0.016	(12.1%)	3.7	±	0.8	(2%)		
Putamen	0.417	(1.3%)	0.124	(2.9%)	0.010	(17.2%)	0.023	(14%)	4.8	±	1.2	(1.4%)		
Cerebellar cortex	0.349	(1.2%)	0.143	(2%)	0.010	(6%)	0.010	(9.3%)	5.8	±	1.7	(2.8%)		

Rate constants are presented as median values and V_T values as mean ± SD from 3 subjects. For each brain region, median standard errors are listed in parentheses and are expressed as % of the variable itself.

SUPPLEMENTAL TABLE 3: Rate constants and total distribution volumes from two-tissue compartment model in AD subjects

	Two-tissue compartmental rate constants											
Brain region	**K_1 (mL • cm^{-3} • min^{-1})**		**k_2 (min^{-1})**		**k_3 (min^{-1})**		**k_4 (min^{-1})**		**Two-tissue V_T (mL • cm^{-3})**			
Temporal	0.336	(1.1%)	0.144	(2.2%)	0.022	(4.1%)	0.015	(5.2%)	5.9	±	0.9	(2%)
Hippocampus	0.267	(1.8%)	0.117	(4.5%)	0.033	(8.2%)	0.018	(8.4%)	6.0	±	0.3	(2.9%)
Amygdala	0.234	(2.3%)	0.103	(5.9%)	0.035	(9.1%)	0.011	(13.9%)	9.8	±	1.5	(6.6%)
Caudate	0.233	(2.5%)	0.141	(5.3%)	0.021	(13.2%)	0.023	(10.5%)	3.1	±	0.5	(2.1%)
Putamen	0.470	(1.2%)	0.145	(2.8%)	0.021	(9.2%)	0.034	(6.7%)	5.3	±	1.0	(1%)
Cerebellar cortex	0.335	(0.9%)	0.145	(1.7%)	0.017	(4.6%)	0.016	(6.4%)	5.4	±	1.3	(1.7%)

Rate constants are presented as median values and V_T values as mean ± SD from three subjects. For each brain region, median standard errors are listed in parentheses and are expressed as % of the variable itself.

SUPPLEMENTAL TABLE 4: SUVRs and DVRs from different models in HE subjects

Brain region	$SUVR_{60\text{-}90\ min}$	$DVR_{2\text{-}TCM}$	$DVR_{Logan\ Plot}$	$DVR_{LoganRefTissue}$
Temporal	0.98 ± 0.07	0.88 ± 0.08	0.92 ± 0.06	0.94 ± 0.04
Hippocampus	0.93 ± 0.10	0.76 ± 0.12	0.82 ± 0.09	0.91 ± 0.07
Amygdala	0.84 ± 0.11	0.70 ± 0.08	0.75 ± 0.09	0.84 ± 0.07
Caudate	0.79 ± 0.06	0.67 ± 0.10	0.70 ± 0.07	0.79 ± 0.04
Putamen	0.91 ± 0.04	0.84 ± 0.11	0.89 ± 0.06	1.01 ± 0.06

DVR_{2TCM} and $DVR_{Logan\ Plot}$ values are Mean ± SD from n = 3 HE subjects, whereas $SUVR_{60\text{-}90\ min}$ and $DVR_{LoganRefTissue}$ are from n = 4 HE subjects

SUPPLEMENTAL TABLE 5: SUVRs and DVRs from different models in AD subjects

Brain region	$SUVR_{60\text{-}90\ min}$	DVR_{2TCM}	$DVR_{Logan\ Plot}$	$DVR_{LoganRefTissue}$
Temporal	1.64 ± 0.72	1.12 ± 0.21	1.12 ± 0.22	1.39 ± 0.57
Hippocampus	1.37 ± 0.25	1.16 ± 0.05	1.20 ± 0.13	0.99 ± 0.50
Amygdala	1.67 ± 0.40	1.61 ± 0.14	1.73 ± 0.15	1.20 ± 0.60
Caudate	0.71 ± 0.16	0.62 ± 0.06	0.65 ± 0.08	0.68 ± 0.10
Putamen	1.15 ± 0.35	0.97 ± 0.12	1.03 ± 0.08	1.19 ± 0.20

DVR_{2TCM} and $DVR_{Logan\ Plot}$ values are Mean ± SD from n = 3 AD subjects, whereas $SUVR_{60\text{-}90\ min}$ and $DVR_{LoganRefTissue}$ are from n = 6 AD subjects

SUPPLEMENTAL TABLE 6: Correlations between SUVR and DVRs across subjects

	$SUVR_{60\text{-}90min}$ vs. $DVR_{2\text{-}TCM}$			$SUVR_{60\text{-}90min}$ vs. $DVR_{Logan\ Plot}$			$SUVR_{60\text{-}90min}$ vs. $DVR_{Logan\ Ref.Tissue}$		
Subject	**R^2**	**Slope**	**Intercept**	**R^2**	**Slope**	**Intercept**	**R^2**	**Slope**	**Intercept**
1	0.61	0.64	0.39	0.78	0.8	0.21	0.88	1.18	-0.17
2	0.54	0.80	0.29	0.65	1.01	0.06	0.5	1.02	0
3	0.77	0.99	0.05	0.78	0.86	0.17	0.63	1.07	-0.08
4	N/A	N/A	N/A	N/A	N/A	N/A	0.31	0.9	0.14
5	N/A	N/A	N/A	N/A	N/A	N/A	0.85	1.17	-0.01
6	0.94	1.14	-0.09	0.95	1.13	-0.12	0.83	1.47	-0.44
7	0.96	1.06	-0.09	0.94	1	0	0.79	1.36	-0.29
8	N/A	N/A	N/A	N/A	N/A	N/A	0.98	1.08	0.14
9	N/A	N/A	N/A	N/A	N/A	N/A	0.98	1.38	-0.22
10	0.96	1.13	-0.09	0.96	1.11	-0.08	0.9	1.51	-0.45

N/A: Not applicable due to no arterial sampling.

SUPPLEMENTAL REFERENCES

1. Wahlund LO, Barkhof F, Fazekas F, et al. A new rating scale for age-related white matter changes applicable to MRI and CT. *Stroke*. Jun 2001; 32(6):1318-1322.
2. Adamczuk K, Schaeverbeke J, Vanderstichele HM, et al. Diagnostic value of cerebrospinal fluid Aβ ratios in preclinical Alzheimer's disease. *Alzheimers Res Ther.* Dec 2015; 18;7(1):75.
3. Scheltens P, Weinstein HC, Leys D. Neuro-imaging in the diagnosis of Alzheimer's disease. I. Computer tomography and magnetic resonance imaging. *Clin Neurol Neurosurg*. 1992;94(4):277-289.