AV-1451 processing methods

Susan Landau, Andy Horng, & William Jagust
Helen Wills Neuroscience Institute, UC Berkeley and Lawrence Berkeley National Laboratory

Summary

ADNI AV-1451 regional summary data are updated regularly and uploaded to LONI by our group. We use a native-space MRI scan for each subject that is segmented and parcellated with **Freesurfer (version 5.3.0)** to define a variety of cortical and subcortical regions of interest in each subject's native space. We then coregister each AV-1451 scan to its corresponding MRI and calculate the mean AV-1451 uptake within each Freesurfer-defined region.

Method

Acquisition of AV-1451 and MRI image data from LONI

We download AV-1451 data from LONI in the most fully pre-processed format (series description in LONI Advanced Search: "AV1451 Coreg, Avg, Std Img and Vox Siz, Uniform Resolution"). Each subject's pre-processed AV-1451 image is coregistered using SPM5 to the subject's MRI image (series description: ADNI 1 scans *N3;* and ADNI GO/2 scans *N3*) that was closest in time to the AV-1451 scan. Whenever possible we use MRI and PET images acquired within 3 months of each other, but when a concurrent MRI is not available we use an MRI scan acquired at another visit.

Calculation of AV-1451 SUVR

There is currently no consensus on the best way to quantify tau PET image data. The UC Berkeley AV-1451 dataset includes a broad set of AV-1451 means within Freesurfer-defined regions and their corresponding volumes (in mm^3). This set includes cortical, subcortical, WM regions of interest and candidate reference regions such as cerebellar grey matter.

In the same dataset we have provided several "Braak stage" region composite values (Braak and Braak, 1991) which are calculated using volume-weighted means of groups of FreeSurfer-defined regions, specified in the "Braak ROIs" section below. This Braak staging strategy has been validated recently [1]}.

Note that the regional AV-1451 data in the UC Berkeley dataset have been only roughly intensity normalized during pre-processing using an approximation of cerebellar cortex. ***To calculate intensity normalized SUVRs, we recommend dividing the Braak stage means or other AV1451 regions of interest (with or without an adjustment for regional volume) by the Freesurfer-defined cerebellar cortex mean or other reference region provided in the UC Berkeley dataset.***

Braak ROIs and corresponding Freesurfer region number from look up table

Braak 1
1006 L_entorhinal

2006 R_entorhinal

Braak 2

17 L_hippocampus
53 R_hippocampus

Braak 3

1016 L_parahippocampal
1007 L_fusiform
1013 L_lingual
18 L_amygdala
2016 R_parahippocampal
2007 R_fusiform
2013 R_lingual
54 R_amygdala

Braak 4

1015 L_middletemporal
10 L_thalamus
1002 L_caudantcing
1026 L_rostantcing
1023 L_postcing
1010 L_isthmuscing
1035 L_insula
1009 L_inferiortemporal
1033 L_temppole
2015 R_middletemporal
49 R_thalamus
2002 R_caudantcing
2026 R_rostantcing
2023 R_postcing
2010 R_isthmuscing
2035 R_insula
2009 R_inferiortemporal
2033 R_temppole

Braak 5

1028 L_superior_frontal
1012 L_lateral_orbitofrontal
1014 L_medial_orbitofrontal
1032 L_frontal_pole
1003 L_caudal_middle_frontal
1027 L_rostral_middle_frontal
1018 L_pars_opercularis
1019 L_pars_orbitalis
1020 L_pars_triangularis
11 L_caudate
12 L_putamen
1011 L_lateraloccipital

1031 L_parietalsupramarginal
1008 L_parietalinferior
1030 L_superiortemporal
13 L_pallidum
1029 L_parietalsuperior
1025 L_precuneus
1001 L_bankSuperiorTemporalSulcus
26 L_accumbens
1034 L_tranvtemp
2028 R_superior_frontal
2012 R_lateral_orbitofrontal
2014 R_medial_orbitofrontal
2032 R_frontal_pole
2003 R_caudal_middle_frontal
2027 R_rostral_middle_frontal
2018 R_pars_opercularis
2019 R_pars_orbitalis
2020 R_pars_triangularis
50 R_caudate
51 R_putamen
2011 R_lateraloccipital
2031 R_parietalsupramarginal
2008 R_parietalinferior
2030 R_superiortemporal
52 R_pallidum
2029 R_parietalsuperior
2025 R_precuneus
2001 R_bankSuperiorTemporalSulcus
58 R_accumbens
2034 R_tranvtemp

Braak 6

1021 L_pericalcarine
1022 L_postcentral
1005 L_cuneus
1024 L_precentral
1017 L_paracentral
2021 R_pericalcarine
2022 R_postcentral
2005 R_cuneus
2024 R_precentral
2017 R_paracentral

Partial Volume Correction for AV-1451

We have also provided the AV-1451 data corrected for partial volume effects using the Geometric Transfer Matrix approach [2]. A total of 81 non-overlapping regions were used as input for this method: 8 aggregated Freesurfer-defined regions listed in the "Aggregate PVC Input ROIs" section below, the remaining 70 individual Freesurfer-defined regions after

accounting for the aggregated ROIs, and 3 SPM-defined non-brain ROIs. These SPM12-defined regions were included with the goal of reducing the influence of tracer uptake in CSF, soft tissue, and bone. They were defined by the c3X.img (CSF), c4X.img (Soft Tissue) and c5X.img (Bone) tissue probability maps (created by SPM12 Segment) of the MRI image closest in time to the AV-1451 scan. Voxels are only included in those ROIs if the corresponding tissue probability is greater than 0.2 and no FreeSurfer ROI labels are assigned.

To calculate intensity normalized SUVRs, we recommend dividing the AV1451 PVC ROI values by a PVC reference region such a cerebellar grey matter to ensure standardized units.

Aggregate PVC Input ROIs and corresponding Freesurfer region number from look up table

Right orbitofrontal
2012 ctx-rh-lateralorbitofrontal
2014 ctx-rh-medialorbitofrontal
2032 ctx-rh-frontalpole

Right pars regions
2018 ctx-rh-parsopercularis
2019 ctx-rh-parsorbitalis
2020 ctx-rh-parstriangularis

Right middle frontal
2003 ctx-rh-caudalmiddlefrontal
2027 ctx-rh-rostralmiddlefrontal

Left orbitofrontal
1012 ctx-lh-lateralorbitofrontal
1014 ctx-lh-medialorbitofrontal
1032 ctx-lh-frontalpole

Left pars regions
1018 ctx-lh-parsopercularis
1019 ctx-lh-parsorbitalis
1020 ctx-lh-parstriangularis

Left middle frontal
1003 ctx-lh-caudalmiddlefrontal
1027 ctx-lh-rostralmiddlefrontal

Hemispheric White Matter
2 Left-Cerebral-White-Matter
41 Right-Cerebral-White-Matter
251 CC_Posterior
252 CC_Mid_Posterior
253 CC_Central
254 CC_Mid_Anterior

255 CC_Anterior

Other

5 Left-Inf-Lat-Vent
14 3rd-Ventricle
15 4th-Ventricle
24 CSF
28 Left-VentralDC
30 Left-vessel
44 Right-Inf-Lat-Vent
60 Right-VentralDC
62 Right-vessel
72 5th-Ventricle
77 WM-hypointensities
80 non-WM-hypointensities
85 Optic-Chiasm
1000 ctx-lh-unknown
1004 ctx-lh-corpuscallosum
2000 ctx-rh-unknown
2004 ctx-rh-corpuscallosum

References

1. Scholl, M., et al., *PET Imaging of Tau Deposition in the Aging Human Brain.* Neuron, 2016. **89**(5): p. 971-82.
2. Rousset, O.G., Y. Ma, and A.C. Evans, *Correction for partial volume effects in PET: principle and validation.* J Nucl Med, 1998. **39**(5): p. 904-11.

About the Authors

This document was prepared by Andy Horng and Susan Landau, PhD, Helen Wills Neuroscience Institute, UC Berkeley and Lawrence Berkeley National Laboratory. For more information please contact Susan at slandau@berkeley.edu.