

Appendix 1

CL pipeline validation

Converting PIB SUVR to CL

To use the CL method, we must confirm that our image analysis pipeline fulfills the CL requirements. We downloaded the PIB and T1 MRI data (34 young controls and 45 AD) from the GAAIN website. Based on the CL guideline (21), a reorientation step is needed that requires reorienting the image so that the coordinate of the anterior commissure is within ~3 cm from the origin and the orientation is within ~15° of the Montreal Neurological Institute (MNI) space. We omitted this tedious process from our study, and just reset the origin as the image center without manually adjusting the anterior commissure-posterior commissure line before image registration. As suggested by the guideline (21), the downloaded MRI images were first registered to the MNI-152 template, and unified segmentation was then applied to the registered MRI images, which, in turn, generated transformation parameters. The downloaded PIB images were registered to the corresponding registered MRI images, and the spatial normalization process was applied to PET images with previously generated transformation parameters. Registration, segmentation, and spatial normalization were completed using SPM8 software (<https://www.fil.ion.ucl.ac.uk/spm/>). The SUVR was calculated on the spatially normalized PIB image using standard VOIs, which was also downloaded from GAAIN website (as shown in [Figure S1](#)). The target region is the global cortical cortex, and the reference region is the whole cerebellum. The PIB SUVR can be converted to CL using the following equation:

$$CL = 100 \times (SUVR_{IND} - SUVR_{YCO}) / (SUVR_{AD100} - SUVR_{YCO}) \quad [2]$$

where $SUVR_{IND}$ represents the individual PIB SUVR, $SUVR_{YCO}$ represents the mean SUVR of 34 young controls,

and $SUVR_{AD100}$ represents the mean SUVR of 45 patients with AD. According to the CL guideline, the pipeline accuracy can be validated by plotting the CL calculated by site against the GAAIN CL and calculating the results of linear regression. The percentage error of the average SUVR of AD and young controls between our results and the GAAIN results were within 2% (0.32% for AD, and 0.24% for young controls), and an excellent correlation ($R^2=0.99$) can be observed in the CL pipeline validation section.

Converting standard FBB SUVR to CL

After the pipeline evaluation, we then converted the standard FBB SUVR into the equivalent PIB SUVR or CL using a specific equation. To generate this equation, paired PIB and FBB images were downloaded from the GAAIN website. This data set contained 35 subjects, and detailed subject information can be found in a previous study (7). All images in this data set followed the aforementioned and validated image analysis pipeline; we have also calculated standard FBB and PIB SUVR. By plotting the standard FBB SUVR against the PIB SUVR and calculating the results of linear regression, the conversion equation can be expressed as $(\text{standard FBB SUVR}) = m_0 \times (\text{PIB SUVR}) + b_0$. Thus, the standard FBB SUVR can be converted into equivalent PIB SUVR by the equation

$$SUVR^{FBB} = m_0 \times SUVR^{PIB-Equiv} + b_0 \quad [3]$$

where the $SUVR^{PIB-Equiv}$ represents the equivalent PIB SUVR, $SUVR^{FBB}$ represents the standard FBB SUVR, b_0 is the intercept, and m_0 is the slope of the linear regression equation. The standard FBB SUVR can be additionally converted into CL using Eq. [2]. The percentage error of the average FBB and PIB SUVR between our and their results was also within 2% (0.32% for AD $SUVR_{FBB}$, 0.15% for young control $SUVR_{FBB}$, 0.24% for AD $SUVR_{PIB}$, and 0.06% for young control $SUVR_{PIB}$).

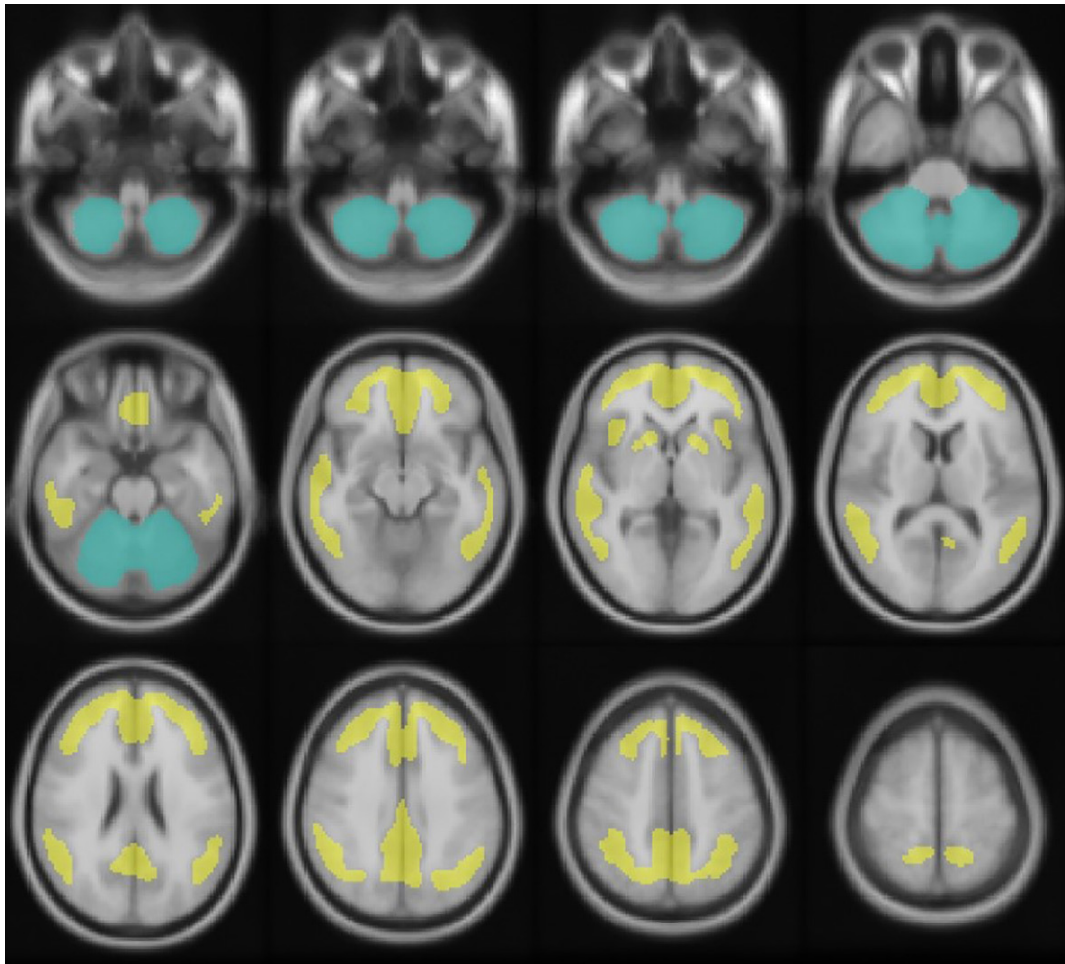


Figure S1 Standard GAAIN volumes-of-interest used for the CL method. The target region (yellow) and reference region (green) are mapped on the MNI-152 template. GAAIN, Global Alzheimer's Association Interactive Network; CL, centiloid; MNI, Montreal Neurological Institute.

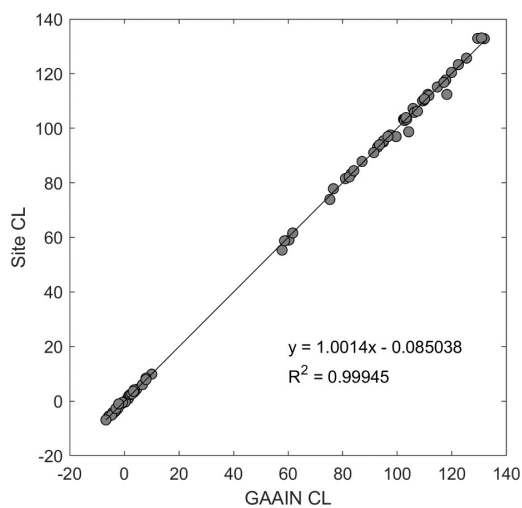


Figure S2 Linear regression between the site CL and GAAIN CL. CL, centiloid; GAAIN, Global Alzheimer's Association Interactive Network.

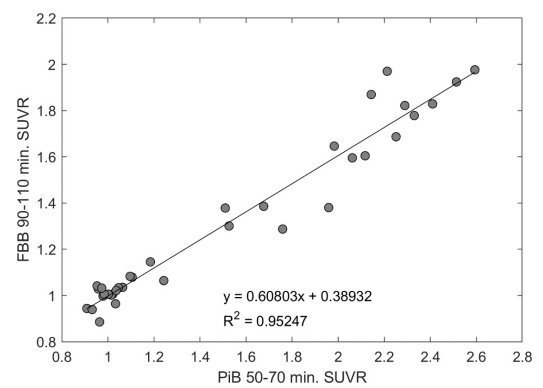


Figure S3 Linear regression between FBB SUVR and PIB SUVR. FBB, florbetaben; SUVR, standardized uptake value ratio; PIB, Pittsburgh compound B.