The Pons As Region of Reference For Intensity Normalization In Semi-Quantitative Analysis of Brain 18FDG PET: Application to Metabolic Changes Related to Ageing in Conventional and Digital Control Databases

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Short communication

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Abstract

**Background:** To define the most appropriate region for intensity normalization in brain $^{18}$FDG PET analysis through ageing.

Brain metabolic changes related to ageing were evaluated in two populations of healthy controls who underwent conventional (n=56) or digital (n=78) $^{18}$FDG PET/CT. The median correlation coefficients between age and the metabolism of each 120 atlas brain region were reported for 120 distinct intensity normalizations (according to the 120 regions). SPM linear regression analyses with age were performed on most significant normalizations (FWE, p<0.05).

**Results:** The cerebellum and pons were the two sole regions showing median coefficients of correlation with age less than -0.5. With SPM, the intensity normalization through the pons provided at least 1.7- and 2.5-fold more significant cluster volumes than other normalizations for conventional and digital PET respectively.

**Conclusions:** The pons is the most appropriate area for brain $^{18}$FDG PET intensity normalization for examining the metabolic changes through ageing.

**Background**

In brain 2-deoxy-2-$^{[18F]}$fluoro-D-glucose ($^{18}$FDG) PET, scaling of tracer uptake to a reference region is essential for data analyses. However, there is currently no genuine recommendation of guidelines for visual or semi-quantitative $^{18}$FDG PET analyses [1, 2]. Proportional scaling [3], i.e., intensity normalization based on the whole-brain and that related to specific brain areas, such as the cerebellum [4] and the pons [5], have been proposed, especially for the diagnosis of neurodegenerative disorders. Nevertheless, proportional scaling intensity normalization is biased in cases of diffuse hypometabolism leading to artefactual hypermetabolism [6]. The choice of other specific brain regions assumes that this reference region for intensity normalization is not physio-pathologically affected.

The gold standard method for brain intensity normalization remains the absolute quantification of brain glycolytic metabolism, but it is principally used for research purposes, and its non-applicability in routine is related to the invasive measures of radioactivity determined by sampling arterial blood [7]. The best way to define a reference region for semi-quantitative analysis could be based on these absolute quantification studies, which showed that the metabolic changes related to ageing affect the quasi-totality of brain regions in healthy subjects [7].

Meanwhile, digital PET technology provides significant advances in the quality of brain $^{18}$FDG PET images mainly through improvements in spatial resolution that could modify the choice of the reference region for intensity normalization with a better visualization of small anatomical structures [8]. For this purpose, we propose to define the most appropriate region for intensity normalization in semi-quantitative analysis of brain $^{18}$FDG PET given the well-known physiological metabolic changes related to ageing in
two different populations of healthy controls who underwent brain $^{18}$FDG PET with conventional and digital PET systems.

**Methods**

**Populations**

Two populations of healthy controls who received a brain $^{18}$FDG PET scan on a conventional system (Discovery ST, GE Healthcare®, APHM, La Timone, Marseille, France) or a digital system (Vereos, Philips®, CHRU Nancy, France) and who were free from neurological and psychiatric diseases were selected for this study (respective Clinical Trials Ref: NCT00987090 and NCT03345290).

**Brain $^{18}$FDG PET**

$^{18}$FDG was injected intravenously (150 MBq for the conventional system and 2 to 3 MBq/kg for the digital camera) while the subjects were in a resting state with their eyes closed in a quiet environment as recommended [1]. Image acquisition started 30 to 45 min after injection and ended 15 min later [1]. All PET images were reconstructed with iterative OSEM methods, as performed in clinical practice, and corrected for scatter, random and attenuation with a CT scan.

**Statistical and SPM analyses**

The $^{18}$FDG PET brain images were pre-processed using SPM12 (Wellcome Department of Cognitive Neurology, Institute of Neurology, London, UK) running on MATLAB 2018a (MathWorks Inc., Sherborn, MA). After an initial step of approximate manual reorientation and positioning to the MNI space, the spatial normalization of each PET image into the MNI space was performed using the MNI template for the conventional camera and an adaptive template for the digital camera. PET images were then smoothed with a post-Gaussian filter adapted to the spatial resolution of the system (8 mm of smoothing for the conventional camera and 4 mm for the digital camera). Marsbar software (http://marsbar.sourceforge.net/) was used to extract the metabolism values of the 116 areas of the Automated Anatomical Labelling (AAL, [9]) atlas with the whole grey matter, midbrain, pons and medulla provided by Pickatlas (https://www.nitrc.org/projects/wfu_pickatlas/) at the individual level.

Pearson coefficient correlations were determined between each of the 120 brain atlas regions and age using the 120 brain atlas regions for intensity normalization. The median and maximal correlation coefficients with age for each intensity normalization region were reported for both the conventional and digital PET systems. A focus was placed on the regions for which the medians of Pearson correlation coefficients with age were less than −0.5.

Then, these reference regions as well as the classically reported proportional scaling were used for intensity normalization [3]. PET images were normalized in intensity by dividing PET images with individual values of brain areas aforementioned and derived from the AAL atlas gathering all areas belonging to a defined brain structure when feasible (e.g., all areas of the cerebellum and the vermis for...
the cerebellum) to be the closest possible to the routine practice. Visual inspections of the images at the
different stages of the pre-processing procedure ensured the quality and convergence of the different
methods applied. The metabolic changes related to ageing were assessed through negative linear
correlations, with age and sex added in the model as covariates for each intensity normalization (p < 0.05
FWE corrected for the conventional PET system and equivalent corresponding T-voxel level for the digital
PET system, in order to take into account the distinct number of subjects in the two database that are
thus analyzed using the same T-score threshold).

Results
Population

The healthy control population whose scans were acquired on the conventional camera consisted of 56
subjects (50 ± 17 [min: 21; max: 78], years old, 33 women), whereas 78 controls (58 ± 16 [min: 22; max:
87], years old, 42 women) had their scans performed on the digital system.

Results provided by the different intensity normalization
regions

The correlation analyses between each of the 120 brain atlas regions and age using the 120 brain atlas
regions for intensity normalization are summarized in Table 1. The vermis 8 and the cerebellum 8L were
the brain atlas regions showing the highest median correlation coefficients of -0.51 and -0.63 for the
conventional and digital PET, respectively. Their respective maximal correlation coefficients were -0.76
for the vermis 8 region with conventional PET and -0.82 for the cerebellum 8L region with digital PET.
Interestingly, among the 120 atlas regions used for PET intensity normalization, only the pons in addition
to the cerebellum showed median correlation coefficients below -0.5 (maximal correlation coefficient of
-0.82) for digital PET.

As depicted in Fig. 1, the intensity normalization by the pons was, however, the best region after SPM
linear regression analyses for both cameras with respective significant cluster volumes of 143,330 (T-max
voxel at 10.2) and 453,080 (T-max voxel at 13.5) mm$^3$ for conventional and digital PET scanners. By
comparison, these linear regression analyses revealed only 41,528 (T-max voxel at 8.3) and 84,216 (T-
max voxel at 9.8) mm$^3$ significant cluster volumes for the whole brain and cerebellum intensity
normalization, respectively, for the conventional system and 63,079 (T-max voxel at 12.2) and 183,378 (T-
max voxel at 12.6) mm$^3$ significant cluster volumes, respectively, for the digital system.

Discussion

The present study shows that the pons is the best brain region for intensity normalization of brain $^{18}$FDG
PET scans for the detection of metabolic changes related to ageing. These findings are reinforced by the
fact that our results are duplicated in two independent populations of healthy controls with both conventional and digital PET systems.

Metabolic changes related to ageing, which are physiological changes that have been widely studied, have been highlighted in well-conducted studies involving absolute glycolytic quantification, which remains the gold standard for normalization in intensity of brain $^{18}$FDG PET images [7]. Even if these age-related changes affect the quasi-totality of brain areas [7], a more pronounced age-related effect is visualized in the frontal and temporal regions (Fig. 1), which is in accordance with previously reported results in semi-quantitative analyses [10]. Interestingly, our results indicate that the most suitable regions for intensity normalization of brain $^{18}$FDG PET scans are the pons and the cerebellum (Table 1), these two regions being known to be poorly affected by age-related changes. Among both regions, intensity normalization by the pons exhibits the best performances after SPM analyses (Fig. 1). This region has previously been proposed as a reference for the detection of Alzheimer’s disease [5]. As long as the pons is free of any pathological involvement, this region should be recommended for visual as well as semi-quantitative analyses of brain $^{18}$FDG PET imaging related to other conditions.

Histogram-based methods have been also recently proposed to improve the intensity PET normalization. These results were however obtained in healthy subjects with artificial introduced hypometabolisms [12]. These data-driven methods need group of patients whereas the pons allows the intensity normalization of brain PET images at the individual level, easily applicable for the visual analysis in clinical routine.

Our results are strengthened by the fact that they have been obtained twice, after regional correlation analyses and voxel-to-voxel analyses. Moreover, these results are visualized in two different populations for which brain $^{18}$FDG PET scans have been acquired with two different PET technology systems.

Of note, more significant results were observed when using the population having performed a brain $^{18}$FDG PET with the digital camera than those having performed brain PET images with the conventional system (Table and Fig. 1). These results are in accordance with the higher performance parameters provided with the new digital PET systems when compared to conventional PET systems [8], even if the spatial normalization method and post-filter smoothing of images have been adapted for digital PET technology. In addition, the intensity normalization by the pons showed better correlation performances with age when using the digital system. This highlights that digital PET technology modifies the results of PET intensity normalization with its ability to delineate small anatomical structures such as the pons.

**Conclusions**

In conclusion, the current study proposes to use the pons as a reference region for intensity normalization of semi-quantitative analysis of brain $^{18}$FDG PET with both conventional and digital PET technologies. This method is currently reported for the detection of metabolic changes related to ageing but should be proposed in future guidelines for visual as well as semi-quantitative analyses of brain $^{18}$FDG PET
imaging related to other pathophysiological mechanisms as long as the pons region is free of any pathological involvement.

Declarations

Ethics approval and consent to participate

This work has been performed in accordance with the Declaration of Helsinki, with written consent of patients and approval of local ethics committee (ClinicalTrials.gov: NCT00987090 and NCT03345290).

Consent for publication

Informed consent was obtained from all individual participants included in the study.

Availability of data and materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors’ contribution

All authors contributed significantly to the analysis and interpretation of the data (AV, MD, JY, EG), to the writing of the manuscript (AV, EG) and to the revision of the manuscript (MD, EG).

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References

1. Varrone A, Asenbaum S, Vander Borght T, et al. EANM procedure guidelines for PET brain imaging using [18F]FDG, version 2. Eur J Nucl Med Mol Imaging. 2009;36:2103–10. https://doi.org/10.1007/s00259-009-1264-0.

2. Nobili F, Festari C, Altomare D, et al. Automated assessment of FDG-PET for differential diagnosis in patients with neurodegenerative disorders. Eur J Nucl Med Mol Imaging. 2018;45:1557–66. https://doi.org/10.1007/s00259-018-4030-3.
3. Drzezga A, Riemenschneider M, Strassner B, et al. Cerebral glucose metabolism in patients with AD and different APOE genotypes. Neurology. 2005;64:102–7. https://doi.org/10.1212/01.WNL.0000148478.39691.D3.

4. Kim EJ, Cho SS, Jeong Y, et al. Glucose metabolism in early onset versus late onset Alzheimer’s disease: an SPM analysis of 120 patients. Brain J Neurol. 2005;128:1790–801. https://doi.org/10.1093/brain/awh539.

5. Minoshima S, Frey KA, Foster NL, Kuhl DE. Preserved pontine glucose metabolism in Alzheimer disease: a reference region for functional brain image (PET) analysis. J Comput Assist Tomogr. 1995;19:541–7. https://doi.org/10.1097/00004728-199507000-00006.

6. Yakushev I, Landvogt C, Buchholz H-G, et al. Choice of reference area in studies of Alzheimer’s disease using positron emission tomography with fluorodeoxyglucose-F18. Psychiatry Res. 2008;164:143–53. https://doi.org/10.1016/j.psychresns.2007.11.004.

7. Petit-Taboué MC, Landeau B, Desson JF, et al. Effects of healthy aging on the regional cerebral metabolic rate of glucose assessed with statistical parametric mapping. NeuroImage. 1998;7:176–84. https://doi.org/10.1006/nimg.1997.0978.

8. Salvadori J, Imbert L, Perrin M, et al. Head-to-head comparison of image quality between brain 18F-FDG images recorded with a fully digital versus a last-generation analog PET camera. EJNMMI Res. 2019;9:61. https://doi.org/10.1186/s13550-019-0526-5.

9. Tzourio-Mazoyer N, Landeau B, Papathanassiou D, et al. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. NeuroImage. 2002;15:273–89. https://doi.org/10.1006/nimg.2001.0978.

10. Van Der Gucht A, Verger A, Guedj E, et al. Age-related changes in FDG brain uptake are more accurately assessed when applying an adaptive template to the SPM method of voxel-based quantitative analysis. Ann Nucl Med. 2015;29:921–8. https://doi.org/10.1007/s12149-015-1022-2.

11. Yanase D, Matsunari I, Yajima K, et al. Brain FDG PET study of normal aging in Japanese: effect of atrophy correction. Eur J Nucl Med Mol Imaging. 2005;32:794–805. https://doi.org/10.1007/s00259-005-1767-2.

12. López-González FJ, Silva-Rodríguez J, Paredes-Pacheco J, et al. Intensity normalization methods in brain FDG-PET quantification. NeuroImage. 2020;222:117229. https://doi.org/10.1016/j.neuroimage.2020.117229.

Tables

**Table 1**

Median and highest Pearson correlation coefficients between PET metabolism and age for the 120 brain atlas regions of intensity normalization, in both conventional and digital PET systems. Regions with median correlation coefficients less than -0.5 are highlighted in red.
| Region for intensity normalization | Conventional PET | Digital PET |
|-----------------------------------|------------------|-------------|
|                                   | Strongest         | Median of    | Strongest         | Median of    |
|                                   | correlation       | correlation  | correlation       | correlation  |
|                                   | coefficient      | coefficients| coefficient      | coefficients|
| Precentral_R                      | -0.573688445     | 0.279184148 | -0.581382052     | 0.293280215 |
| Precentral_L                      | -0.622302284     | 0.232181965 | -0.628568612     | 0.266985128 |
| Frontal_Sup_R                     | -0.600980191     | 0.319870899 | -0.690629185     | 0.242280289 |
| Frontal_Sup_L                     | -0.547693637     | 0.405334595 | -0.599914817     | 0.443110434 |
| Frontal_Sup_Orb_R                 | -0.629579861     | 0.084998269 | -0.700581666     | -0.108439103|
| Frontal_Sup_Orb_L                 | -0.547437357     | 0.192820744 | -0.703649178     | -0.033764917|
| Frontal_Mid_R                     | -0.553053145     | 0.349833531 | -0.584128133     | 0.463018236 |
| Frontal_Mid_L                     | -0.551382331     | 0.315606715 | -0.610512904     | 0.39907714  |
| Frontal_Mid_Orb_R                 | -0.55913071      | 0.098969813 | -0.684911592     | -0.036623595|
| Frontal_Mid_Orb_L                 | -0.445475539     | 0.255947537 | -0.680085738     | 0.1323272  |
| Frontal_Inf_Oper_R                | -0.403554772     | 0.451057221 | -0.584413796     | 0.431311318|
| Frontal_Inf_Oper_L                | -0.346777766     | 0.545425764 | -0.542003107     | 0.481079751|
| Frontal_Inf_Tri_R                 | -0.549174379     | 0.296954014 | -0.608717652     | 0.267245207|
| Frontal_Inf_Tri_L                 | -0.558387379     | 0.286348933 | -0.653848914     | 0.273189928|
| Frontal_Inf_Orb_R                 | -0.52705298      | 0.333803877 | -0.6524112       | 0.21577136 |
| Frontal_Inf_Orb_L                 | -0.464517096     | 0.368956454 | -0.628902165     | 0.32330541 |
| Rolandic_Oper_R                   | -0.566697841     | 0.243996131 | -0.678571105     | 0.095847239|
| Rolandic_Oper_L                   | -0.618467447     | 0.211708259 | -0.723144101     | -0.112062758|
| Supp_Motor_Area_R                 | -0.517843026     | 0.180772399 | -0.460519688     | 0.426544183|
| Supp_Motor_Area_L                 | -0.696169862     | -0.02036436 | -0.73268581      | 0.039897831|
| Olfactory_R                       | -0.388765983     | 0.487926686 | -0.657210451     | 0.105375048|
| Olfactory_L                       | -0.528013879     | 0.384147962 | -0.721491098     | -0.122749257|
| Frontal_Sup_Medial_R              | -0.358836732     | 0.524163102 | -0.488283894     | 0.489288049|
| Frontal_Sup_Medial_L              | -0.573032908     | 0.423672249 | -0.735839552     | 0.25158455 |
| Frontal_Med_Orb_R                 | -0.484358087     | 0.39321911  | -0.615616599     | 0.337668074|
| Frontal_Med_Orb_L                 | -0.50075176      | 0.376511335 | -0.74510263      | 0.041807974|
| Region         | X   | Y   | Z   | V   |
|---------------|-----|-----|-----|-----|
| Rectus_R      | -0.55071263 | 0.351304466 | -0.635567564 | 0.035246613 |
| Rectus_L      | -0.604668295 | 0.259112277 | -0.671649932 | -0.154421386 |
| Insula_R      | -0.626506716 | 0.161993577 | -0.734040284 | -0.072023968 |
| Insula_L      | -0.443959797 | 0.496975678 | -0.56772327 | 0.513856619 |
| Cingulum_Ant_R| -0.275972126 | 0.634247449 | -0.400842278 | 0.640119849 |
| Cingulum_Ant_L| -0.692031912 | 0.350939125 | -0.78453279 | 0.189981663 |
| Cingulum_Mid_R| -0.615009986 | 0.262411063 | -0.579931165 | 0.467563092 |
| Cingulum_Mid_L| -0.664484269 | 0.167834424 | -0.730987309 | 0.232708068 |
| Cingulum_Post_R| -0.526277264 | 0.019893397 | -0.624772162 | 0.120155957 |
| Cingulum_Post_L| -0.555623248 | 0.02657322 | -0.634707019 | 0.240298045 |
| Hippocampus_R | -0.74488582 | -0.158224441 | -0.776691477 | -0.178442999 |
| Hippocampus_L | -0.792432684 | -0.401600367 | -0.794914907 | -0.355792507 |
| ParaHippocampal_R | -0.547796599 | 0.135694163 | -0.741894049 | -0.03170524 |
| ParaHippocampal_L | -0.691581684 | -0.020746522 | -0.774862984 | -0.184001347 |
| Amygdala_R    | -0.690685381 | -0.050409819 | -0.738301387 | -0.264093722 |
| Amygdala_L    | -0.675326502 | -0.09187106 | -0.738046871 | -0.344906004 |
| Calcarine_R   | -0.597218653 | 0.004930533 | -0.59736577 | 0.209424087 |
| Calcarine_L   | -0.641938573 | -0.076213494 | -0.693935653 | -0.086552086 |
| Cuneus_R      | -0.726146822 | -0.154685879 | -0.621177518 | 0.096712726 |
| Cuneus_L      | -0.785087897 | -0.348003457 | -0.666285592 | -0.124622161 |
| Lingual_R     | -0.634614302 | -0.097770865 | -0.643697071 | -0.046781064 |
| Lingual_L     | -0.685486599 | -0.166388559 | -0.670109744 | -0.04623892 |
| Occipital_Sup_R | -0.701641346 | -0.194678777 | -0.646231705 | -0.064989794 |
| Occipital_Sup_L | -0.741727211 | -0.306092732 | -0.597199679 | 0.127544711 |
| Occipital_Mid_R | -0.727813649 | -0.364255804 | -0.647178347 | -0.059276144 |
| Occipital_Mid_L | -0.718730655 | -0.244437115 | -0.672193986 | 0.035856165 |
| Occipital_Inf_R | -0.723331225 | -0.386129463 | -0.668353467 | -0.211046407 |
| Occipital_Inf_L | -0.745424761 | -0.389693675 | -0.689600876 | -0.207004321 |
| Fusiform_R    | -0.726536142 | -0.195906801 | -0.760147469 | -0.312002428 |
| Structure            | X-Coordinate | Y-Coordinate | Z-Coordinate | T-Coordinate |
|----------------------|--------------|--------------|--------------|--------------|
| Fusiform_L           | -0.737547599| -0.265574857| -0.756777592| -0.30482379  |
| Postcentral_R        | -0.709883189| 0.024251053  | -0.626583194| 0.099793863  |
| Postcentral_L        | -0.76459292 | -0.110140116| -0.734129726| -0.048775906 |
| Parietal_Sup_R       | -0.710966862| -0.163768876| -0.600734839| 0.175798905  |
| Parietal_Sup_L       | -0.639227666| -4.90902E-05 | -0.542532856| 0.337939446  |
| Parietal_Inf_R       | -0.620798761| 0.113031765  | -0.541267618| 0.442951513  |
| Parietal_Inf_L       | -0.554435839| 0.25511845   | -0.519628   | 0.459809369  |
| SupraMarginal_R      | -0.642901203| 0.143077102  | -0.631066657| 0.16035289   |
| SupraMarginal_L      | -0.67010586 | 0.198101079  | -0.629274111| 0.305772909  |
| Angular_R            | -0.637290184| -0.021187495 | -0.576971854| 0.223955824  |
| Angular_L            | -0.611346979| 0.099585441  | -0.577059191| 0.293618718  |
| Precuneus_R          | -0.745445943| -0.14394911  | -0.687422118| 0.094901913  |
| Precuneus_L          | -0.757202509| -0.219708792 | -0.708572999| 0.033021343  |
| Paracentral_Robule_R | -0.778348539| -0.344721681 | -0.702759859| -0.103953847 |
| Paracentral_Robule_L | -0.784491443| -0.417984838 | -0.794021505| -0.424682684 |
| Caudate_R            | 0.307397852 | 0.497272916  | 0.398152235 | 0.640465612  |
| Caudate_L            | -0.524293718| 0.387711671  | -0.711582026| 0.385198422  |
| Putamen_R            | -0.602942275| 0.125257327  | -0.701652279| -0.198897079 |
| Putamen_L            | -0.630316648| -0.007083048 | -0.70161431 | -0.11815898  |
| Pallidum_R           | -0.510633293| 0.20883992   | -0.770671936| -0.407366194 |
| Pallidum_L           | -0.448907585| 0.271878766  | -0.709597016| -0.223370032 |
| Thalamus_R           | -0.507908201| 0.263313022  | -0.67710738 | 0.302515492  |
| Thalamus_L           | -0.654566592| -0.060126393 | -0.74406809 | -0.109863951 |
| Heschl_R             | -0.485771916| 0.298329103  | -0.55866801 | 0.43147372   |
| Heschl_L             | -0.472564385| 0.35518222   | -0.503638686| 0.575685721  |
| Temporal_Sup_R       | -0.625069091| 0.254407932  | -0.624234384| 0.348479101  |
| Temporal_Sup_L       | -0.68587206 | 0.168621993  | -0.652154125| 0.302844751  |
| Temporal_Pole_Sup_R  | -0.331232941| 0.425860523  | -0.44600523 | 0.406669675  |
| Temporal_Pole_Sup_L  | -0.363542986| 0.354619085  | -0.500438422| 0.380854532  |
| Region                  | x     | y     | z     | w     |
|------------------------|-------|-------|-------|-------|
| Temporal_Mid_R         | -0.690671811 | 0.044779431 | -0.658061148 | 0.11769236 |
| Temporal_Mid_L         | -0.697074384 | 0.064873746 | -0.638795334 | 0.231016521 |
| Temporal_Pole_Mid_R    | -0.451855567 | 0.225791623 | -0.646963344 | 0.035810993 |
| Temporal_Pole_Mid_L    | -0.457567288 | 0.245337503 | -0.704001434 | 0.029743346 |
| Temporal_Inf_R         | -0.68436998 | -0.104670403 | -0.696015575 | -0.063048755 |
| Temporal_Inf_L         | -0.669764664 | -0.031455074 | -0.689992535 | 0.035977061 |
| Cerebelum_Crus1_R      | -0.600476473 | -0.004144622 | -0.644696334 | 0.035810993 |
| Cerebelum_Crus1_L      | -0.666707111 | -0.13413203 | -0.68045527 | -0.193184819 |
| Cerebelum_Crus2_R      | -0.681004608 | -0.302210346 | -0.679835366 | -0.196911931 |
| Cerebelum_Crus2_L      | -0.687555117 | -0.232091696 | -0.684717528 | -0.150689558 |
| Cerebelum_3_R          | -0.631993976 | -0.168105517 | -0.69448275 | -0.107741771 |
| Cerebelum_3_L          | -0.576269744 | -0.009951379 | -0.647040809 | -0.007816927 |
| Cerebelum_4_5_R        | -0.650573984 | -0.181355372 | -0.687937783 | -0.21895484 |
| Cerebelum_4_5_L        | -0.663071101 | -0.077466212 | -0.730497017 | -0.12346168 |
| Cerebelum_6_R          | -0.677921489 | -0.155131146 | -0.710308279 | -0.303651351 |
| Cerebelum_6_L          | -0.735262898 | -0.279267569 | -0.716515286 | -0.28440532 |
| Cerebelum_7b_R         | -0.704269564 | -0.332758809 | -0.738855392 | -0.40011216 |
| Cerebelum_7b_L         | -0.743454724 | -0.403805093 | -0.729542146 | -0.333328681 |
| Cerebelum_8_R          | -0.729481495 | -0.437717362 | -0.812531147 | -0.61846924 |
| Cerebelum_8_L          | -0.753248363 | -0.500101319 | -0.823696914 | -0.630973003 |
| Cerebelum_9_R          | -0.695106139 | -0.36420094 | -0.79927817 | -0.503436315 |
| Cerebelum_9_L          | -0.744673144 | -0.476228635 | -0.811756228 | -0.579151524 |
| Cerebelum_10_R         | -0.548985851 | -0.118360681 | -0.717244723 | -0.333550516 |
| Cerebelum_10_L         | -0.571047001 | -0.201373641 | -0.541209852 | 0.039102255 |
| Vermis_1_2             | -0.644498893 | -0.180633313 | -0.732799769 | -0.208601441 |
| Vermis_3               | -0.584677906 | -0.134242733 | -0.671825282 | -0.096599336 |
| Vermis_4_5             | -0.577923911 | -0.137586851 | -0.642737286 | -0.089295963 |
| Vermis_6               | -0.531525033 | -0.04047739 | -0.610495443 | -0.101942777 |
| Vermis_7               | -0.578924525 | -0.093968004 | -0.662218149 | -0.224039981 |
|        |        |        |        |        |
|--------|--------|--------|--------|--------|
| Vermis_8 | -0.756376798 | -0.506853104 | -0.790218976 | -0.616443676 |
| Vermis_9 | -0.742895596  | -0.469781549  | -0.753866317  | -0.457157983  |
| Vermis_10 | -0.667363951  | -0.342948819  | -0.714105274  | -0.232058498  |
| Midbrain | -0.71649863   | -0.13811898   | -0.748687248   | -0.13147618   |
| Pons    | -0.718410905  | -0.385970718  | -0.818592258  | -0.547892778  |
| Medulla | -0.737949443  | -0.406080404  | -0.776357698  | -0.371013333  |
| Whole grey-matter | -0.738042818 | 0.124152213 | -0.734258642 | 0.16754782686138 |