ADNI Alzheimer's Disease Neuroimaging Initiative

Improved spatial normalization using PET templates of [^{18}F]florbetapir brain uptake of control and AD subjects

Nicholas Seneca, Cyrill Burger and Ioana Florea
PMOD Technologies, LLC., Zurich, Switzerland

Contents

Summary

Positron emission tomography (PET) radioligands selective for β-amyloid have high uptake in white matter, especially in controls which tend to have lower cortical uptake compared to patients with Alzheimer's disease. During a PET only image analysis workflow, a PET scan is spatially normalized to a template image such as a [^{15}O]H_2O scan. The uptake pattern of the β-amyloid PET radioligands in the white matter increases the likelihood of a normalization failure. For example, white-matter uptake is three times lower compared to gray matter for a [^{15}O]H_2O scan [1], whereas, [^{18}F]Florbetapir uptake in normal controls is ~1.6 times higher in white matter compared to gray matter. During a PET-MRI image analysis workflow, the MRI-based normalization may fail [2]. Additionally, not all studies include an MRI in the schedule of assessments. Therefore, a tracer specific template is preferable for the spatial normalization process [3, 4].

Methods

ADNI [^{18}F]Florbetapir PET data were used to create disease specific brain templates for a control group (n = 136, 73 females and 63 males, mean age 72 ± 5.0) and for an Alzheimer's disease patients group (n = 121, 51 females and 70 males, mean age 73 ± 7.0). The mini-mental status examination in the AD patients and controls scored 23.2 ± 2.0 and 29.1 ± 1.1 respectively. The pre-processed (i.e., co-reg, avg, standardized image and voxel size) [^{18}F]Florbetapir PET and the corresponding MRI baseline scans were downloaded from the ADNI-GO/-2 databases as available on and after September 30th 2016.

[^{18}F]Florbetapir Brain Template Creation

The templates construction was based on a workflow previously described for rodent brain images of various PET and SPECT radioligands [4]. The procedure was performed using the image fusion module (PFUSEIT) in the PMOD 3.8 software (PMOD Technologies LLC., Zurich, Switzerland).

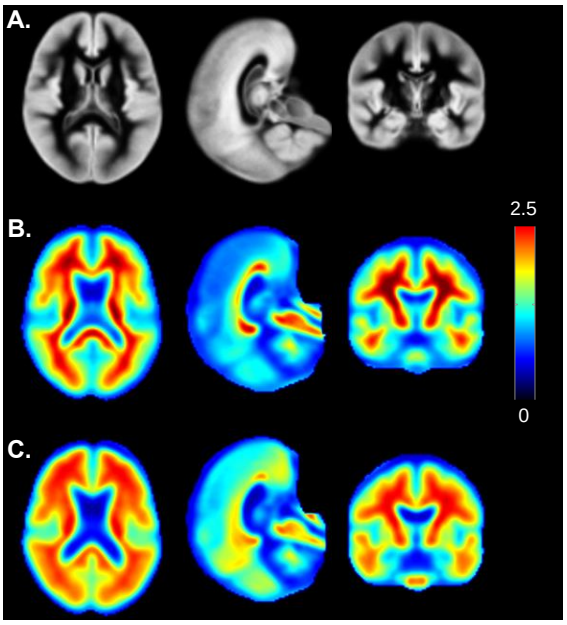

Figure 1. PET templates of [^{18}F]Florbetapir brain uptake in control and Alzheimer's disease subjects from ADNI imaging datasets. (A) Gray matter segmented MRI template. (B) High non-specific uptake in white matter from control subjects (n = 136). (C) Increased uptake in cortical brain regions as well as high uptake in white matter from Alzheimer's disease patients (n = 121). Images B and C are the final disease specific templates in MNI space shown in axial, sagittal and coronal planes.

Briefly, the template creation can be described in five main steps. First, a representative PET image was selected as "standard image" from the dataset. Each of the individual PET images was normalized to the standard image using the batch facility in the PFUSEIT module. Secondly, the normalized scans were averaged to obtain a first average PET (LR) in the space of the selected standard image, which might suffer from some asymmetry. Third, to compensate for asymmetry, the LR average was mirrored and normalized to LR, resulting an RL average. The LR and RL images were averaged to obtain the presumably symmetrical average PET image (LR_RL). Fourth, the LR_RL average was rigidly matched (RM) to the MRI image corresponding to the selected standard PET image. Fifth, the representative MRI image was normalized to the MNI MRI template using the three-tissue probability maps normalization (3TPM). Finally, the RM and the 3TPM transformations were combined and the symmetrical LR_RL average was transformed to the MNI space (Figure 1).

A schematic representation of the image analysis workflow is shown in Figure 2.

Dataset Information

This methods document applies to the following dataset(s) available from the ADNI repository:

Dataset Name	Date Submitted
ADNI database	September 30th, 2016

References

1. Zhang, K., et al. (2014). "Comparison of cerebral blood flow acquired by simultaneous [^{15}O]water positron emission tomography and arterial spin labeling magnetic resonance imaging." J Cereb Blood Flow Metab **34**(8): 1373-1380.
2. Brendel, M., et al. (2015). "Improved longitudinal [^{18}F]AV45 amyloid PET by white matter reference and VOI-based partial volume effect correction." Neuroimage **108**: 450-459.
3. Perani, D., et al. (2014). "Validation of an optimized SPM procedure for FDG-PET in dementia diagnosis in a clinical setting." Neuroimage Clin **6**: 445-454.
4. Vallez Garcia, D., et al. (2015). "A standardized method for the construction of tracer specific PET and SPECT rat brain templates: validation and implementation of a toolbox." PLoS One **10**(3): e0122363.

About the Authors

This document was prepared by Drs. Nicholas Seneca, Cyrill Burger and Ioana Florea from PMOD Technologies, LLC., Zurich, Switzerland. For more information please contact PMOD at +41 443504600 or by email at support@pmod.com.

Notice: This document is presented by the author(s) as a service to ADNI data users. However, users should be aware that no formal review process has vetted this document and that ADNI cannot guarantee the accuracy or utility of this document.

Figure 2. A schematic representation of the image analysis workflow for the creation of a disease specific reference [^{18}F]Florbetapir template.