







Salvadó G¹, Foley C², Grecchi E³, Cardoso MJ⁴, Lopes-Alves I⁵, Markiewicz P⁴, Falcon C¹, Battle M², Lammertsma AA⁵, Schmidt ME⁶, Barkhof F⁴,⁵, Molinuevo JL¹, Gispert JD¹, on behalf of the AMYPAD Consortium

1) Barcelonaβeta Brain Research Center (Spain), 2) GE Healthcare (United Kingdom), 3) IXICO (United Kingdom), 4) University College London (United Kingdom), 5) VU Medical Center (The Netherlands), 6) Janssen Pharmaceutica (Belgium)

Background

Multiple studies have shown that the selection of the reference region (RR) on amyloid (A β) PET quantification is critical. However, there is no universally optimal RR as it depends on study design and the radiotracer.

Aim of study

To compare the performance of different supratentorial white matter (sWM) reference regions with those of the Centiloid standard [1] for quantification of longitudinal [18F]Flutemetamol PET scans.

Methods

Sample: 125 subjects from the AIBL study [2] with longitudinal MRI and [18F]Flutemetamol PET images (577±55 days apart).

Preprocessing: Centiloid standard method was used to determine SUVr values in the target cortical VOI, with two pipelines:

- Cross-sectional: applying it to both time points independently
- Longitudinal: applying it to averaged image pairs

Reference regions:

- Atlas-based using different atlases and erosions levels
- Standard Centiloid RRs
- Subject-specific using SPM WM segmentation with successive erosions

Figures of merit:

- **Effect size** of longitudinal change (Cohen's d) tested in individuals with intermediate Centiloid values ([GZ] 15≤CL<30)
- **Plausibility** defined as the percentage of all subjects with non-negative Aβ changes
- SUVr mean percentage change per year in stable participants, defined as either positives (CL≥30), or negatives (CL<15) with changes below 0.04 in SUVr [3]



Discussion

Our results are in agreement with Landau *et al.* [4] that found that subcortical WM resulted more accurate to measure changes of Aβ with [¹8F]Florbetapir. On the other hand, Bullich *et al.* [5] found that cerebellar RRs were optimal for detecting Aβ changes with [¹8F]Florbetaben in MCI subjects. A possible drawback for sWM as RR is that WM is susceptible of display pathological alterations of vascular origin in older individuals and MCI/AD patients that could affect tracer binding. Finally, the pipelines have been implemented on SPM, which might have favored the SPM-based RR.

Conclusions

- ✓ sWM perform better than standard Centiloid RRs for longitudinal quantification
- ✓ Atlas-based sWM, which allow an easier automation, show equivalent performance as subject-specific RR
- ✓ The agreement between results with both pipelines suggest that our findings are generalizable to other pipeline implementations

Acknowledgements

Authors would like to acknowledge Dr. Christopher C. Rowe on behalf of AIBL for sharing [18F]Flutemetamol PET scans with the AMYPAD consortium.

References: [1] Klunk W. et al., Alzheimer's & Dementia (2014), [2] Ellis K.A. et al., International Psychogeriatrics (2009), [3] Jack C. Jr. et al., Neurology (2013), [4] Landau S.M. et al., J Nucl Med (2015), [5] Bullich S. et al. J Nucl Med (2017)

Contact: gsalvado@barcelonabeta.org