PROBABILISTIC HUMAN BRAIN ATLAS: PART 1, A SURROGATE FOR MANUAL VOI DEFINITION

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Introduction

Quantitative region-based analysis is important in functional imaging, however, manual VOI definition for determining regional uptake values on PET/SPECT scans can be time-consuming and is operator dependent (subject to intra/interobserver variability).

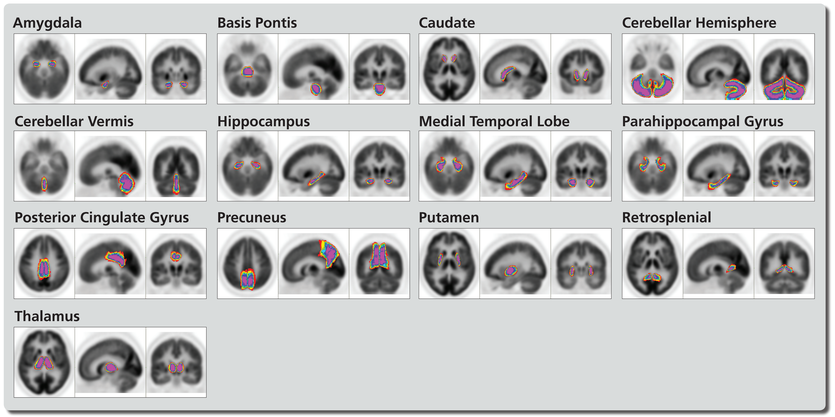
Objectives

The purpose of this study was to evaluate the use of automatically generated VOIs from a probabilistic anatomical human brain atlas[1] to address these limitations in determining regional uptake values by serving as a surrogate for manual VOI definition on co-registered MRI images.

Methods

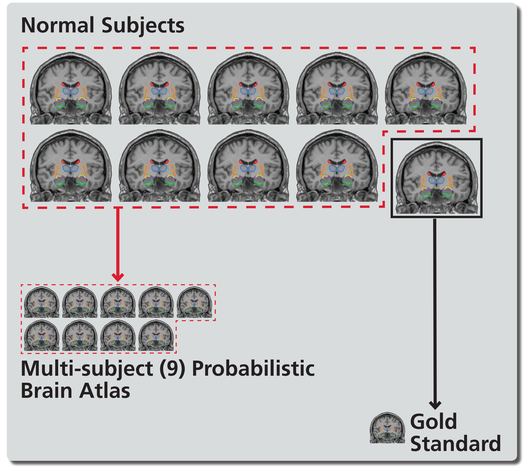
- 10 subjects received T1-weighted MRI scans. Four subjects also received 11C-DTBZ PET scans and six received FDG-PET scans.
- 13 VOIs were manually defined on each subject MR as the consensus opinion of three physicians and a neuroanatomist.
- The segmented MRI scans were co-registered to the PET scan for each patient. Each PET scan was registered to a template volume using the MIMneuro deformable registration[2]. After registration, the VOIs from each patient were transformed into template space (Figure 1).
- Leave-one-out validation was performed (Figure 2):
  - VOIs from 9 subjects formed a probabilistic atlas
  - Remaining subject served as the reference – "gold standard"
  - Median value calculated from the different probabilistic atlas levels were compared to the "gold-standard" VOIs
  - Process was repeated using a different subject as the reference each time.
- Average error resulting from a 1.4mm PET/MR fusion misalignment was used for reference.
- To evaluate the effect of error from atlas estimation of the VOI using statistical power analysis, an example study with effect size of 1, alpha 0.05, and desired power of 0.8 was used. This study would require 28 subjects to enroll for these conditions to be met.

Figure 1
Multi-subject Probabilistic Atlas



Multi-subject probabilistic atlas comprised of all 10 subjects showing each VOI defined. Each color of the 10 step color scale represents a different probabilistic level ranging from 1/10 (red) where the VOI is comprised of all of the voxels that at least 1 out of 10 subjects had in common to 10/10 (purple) where the VOI is made of all of the voxels that 10 out of 10 subjects had in common.

Figure 2
Leave One Out Scheme



One subject is used as the gold standard for comparison to the probabilistic atlas comprised of the nine remaining subjects.

Figure 3
Error in Probabilistic Atlas Estimation

	Level	% Error	Max % Error	N
Basis Pontis	9	4.7	10.9	
Cerebellar Vermis	4	1.6	3.9	28
Amygdala	2	2.5	6.0	30
Caudate	1	6.7	18.3	32
Cerebellar Hemisphere	8	1.4	2.7	28
Hippocampus	4	2.8	7.6	32
Medial Temporal Lobe	4	1.8	4.5	28
Parahipocampal Gyrus	6	2.5	7.5	30
Posterior Cingulate Gyrus	3	4.3	11.0	30
Precuneus	7	2.8	6.6	28
Putamen	3	1.9	4.7	28
Retrosplenial	2	5.3	9.4	34
Thalamus	6	3.5	8.1	38

Probabilistic atlas regional uptake value estimation typically resulted in minor errors. The largest errors were typically for smaller regions which border CSF. These same regions are likely to also suffer from errors with manual VOI definition which were not considered here. Most regions required no more than four additional enrollees to maintain the statistical power of the example study used.

Results

The average error from using atlas regions for VOI definition was less than twice as significant as the error from the fusion misalignment between the PET and MR for most regions.

Eight regions had error distributions with standard deviations <3% and only two regions exceeded 5%. Three regions had max error >10%. (Figure 3)

Atlas estimation typically had a minimal effect on the number of subjects required to enroll in the sample study. For example, using the probabilistic atlas for segmenting the hippocampus increased the required number from 28 to 32 to maintain the same statistical power (the required effect size decreased to 0.91). (Figure 3)

Conclusions

Using the probabilistic atlas has the advantage of not requiring MRIs to be obtained or contoured for region analysis, saving both time and money while requiring only a modest increase in subject enrollment for a study to maintain the same statistical power.

Future Directions

In the future, measuring the effect of inter- and intra-observer variation in manual VOI definition will be important to more accurately quantify errors in atlas estimation. It is possible, for some regions, that the atlas estimation errors may in fact be smaller or comparable in magnitude to variation in manual definition.

References

[1]Nelson AS, Piper JW, Friedland RP, Freeman B. Probabilistic human brain atlas for functional imaging: Comparison to single brain atlases. J Nucl Med. 2007;48 Suppl 2:S403.
[2]Piper, JW. Quantitative Comparison of Spatial Normalization Algorithms for 3D PET brain scans. J Nucl Med. 2007;48 Suppl 2:S403.