Variability of Basal Ganglia Morphology After Spatial Normalization: Implications for Group Studies

Jingyun Chen[1], Martin J. McKeown[2], Mirza Faisal Beg[1]

SFU SIMON FRASER UNIVERSITY THINKING OF THE WORLD

MIAL MEDICAL IMAGE ANALYSIS LAB

UBC

Brain Research Centre

[1] School of Engineering Science
Faculty of Applied Science
Simon Fraser University
8888 University Drive
Burnaby, BC, Canada V5A 1S6

[2]Brain Research Centre
2211 Wesbrook Mall
Vancouver, BC
Canada V6T 2B5

J. Chen: jingyunc@sfu.ca *M. J. Mckeown: mmkeown@interchange.ubc.ca*
M. F. Beg: mfbeg@ensc.sfu.ca

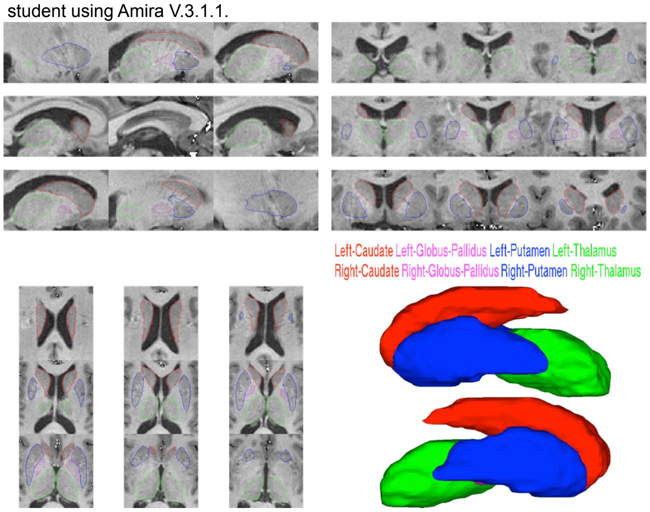
Introduction

- Spatial normalization - spatially transforming different brain magnetic resonance (MR) scans to a standard space.
- Standard low dimensional methods for spatial normalization can result in significant mis-registration, particularly for smaller structures such as those of the basal ganglia.
- Here we rigorously assess the **residual anatomical variability (RAV)** in basal ganglia structures after standard spatial normalization.

Method

Data Acquisition:

- 27 T1-weighted brain MR scans: 14 Parkinson's Disease (PD) subjects and 13 age-matched control subjects with no known neurological or psychiatric conditions.
- MR scanner: Philips Achieva 3.0T; Philips Medical Systems, Netherlands.
- Four basal ganglia regions of interest (ROIs): putamen, caudate, thalamus, globus pallidus in each hemisphere, manually labeled by a trained neuroscience student using Amira V.3.1.1.



Spatial Normalization Methods:

- The 12-parameter affine registration to the Talairach space implemented in Freesurfer work flow (autorecon1).
- SPM5's default spatial normalise module, including affine and 7x8x7 nonlinear basis functions.
- Freesurfer-initialized LDDMM (FS+LDDMM) registration[1], with the deformation fields applied to the ROIs of each subject.

Variability Measurement:

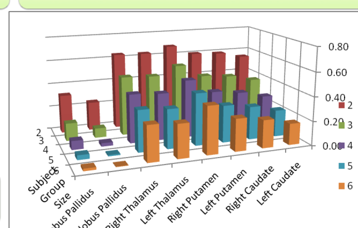
$$DSC = n \times V\left(\bigcap_i S_i\right) / \sum_{i=1}^{n} V(S_i)$$

where S_i, $(i=1,2\ldots n)$ are ROIs. $V(S_i)$ is the number of non-zero voxels of of S_i (i.e. the volume of ROI S_i), and n is the number of subjects to overlay, which we will refer to as the group size.

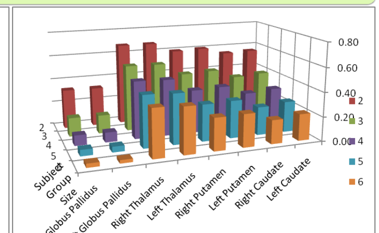
When $n=2$, $DSC(A,B)=2V(A\cap B)/[V(A)+V(B)]$, a measure commonly used to assess segmentation similarity, sometimes referred to as the similarity index. kappa coefficient, or mean overlap.

For complete overlap between two segmentations, DSC=1, and for no overlap, DSC=0. We computed the average DSC of normalized ROIs using Nieto-Castanon's scheme[2]. Average DSCs were computed over all possible subject combinations.

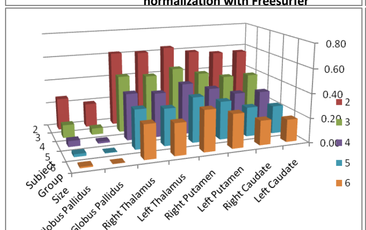
Results



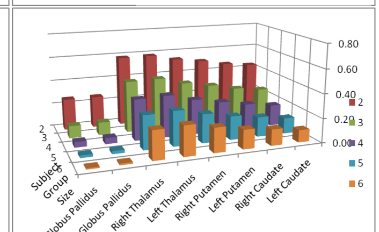
Average DSC's of Control Subjects after spatial normalization with Freesurfer



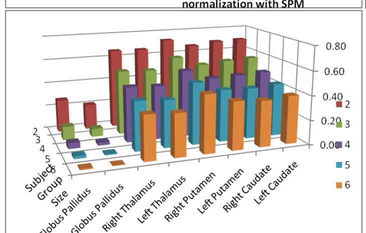
Average DSC's of PD Subjects after spatial normalization with Freesurfer



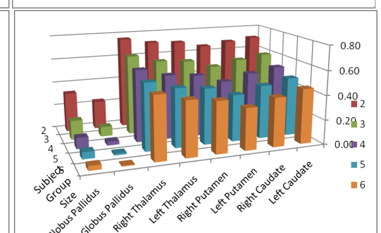
Average DSC's of Control Subjects after spatial normalization with SPM



Average DSC's of PD Subjects after spatial normalization with SPM



Average DSC's of Control Subjects after spatial normalization with LDDMM



Average DSC's of PD Subjects after spatial normalization with LDDMM

Discussion & Conclusion

- Manual segmentation is generally consistent. RAV mainly arises from mis-registrations after the spatial normalization process.
- RAV generally increases as subject group size increases.
- Less RAV with FS+LDDMM registration than the other two low-dimensional methods.
- More RAV in smaller basal ganglia ROIs, such as golbus pallidus.
- In fMRI analyses, time series from different subjects are concatenated together **under the assumption that there is a perfect correspondence at the voxel level across subjects after normalization.** Often data are spatially smoothed to make this assumption less rigid, but this degrades the spatial resolution.
- A high-dimensional registration method such as LDDMM is necessary to reduce the RAV before further processing.

ROI	Manual	FS+LDDMM	FS	SPM
Left Caudate	0.87±0.02	0.7±0.03	0.55±0.05	0.56±0.06
Right Caudate	0.85±0.02	0.69±0.03	0.59±0.05	0.57±0.05
Left Putamen	0.84±0.03	0.67±0.04	0.60±0.07	0.59±0.07
Right Putamen	0.86±0.03	0.73±0.04	0.68±0.07	0.64±0.07
Left Thalamus	0.87±0.20	0.66±0.03	0.64±0.06	0.61±0.06
Right Thalamus	0.85±0.02	0.66±0.02	0.64±0.05	0.62±0.06
Left Pallidum	0.69±0.01	0.21±0.01	0.24±0.05	0.20±0.04
Right Pallidum	0.55±0.01	0.27±0.02	0.32±0.04	0.27±0.04

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[1] A. R. Khan, L. Wang, M. F. Beg, "Freesurfer-initiated fully-automated subcortical brain segmentation in mri using large deformation diffeomorphic metric mapping", *NeuroImage*, vol. 41(3), pp. 735-746, 2008.

[2] A. Nieto-Castanon, S. S. Ghosh, J. A. Tourville, F. H. Guenther, "Region of interest based analysis of functional imaging data", *NeuroImage*, vol. 19(4), pp. 1303-1316, 2003.