

Multivariate analysis of diffusion tensor imaging and cortical thickness maps in a traumatic brain injury (TBI) cohort using Advanced Normalization Tools (ANTs)

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Introduction

TBI is a complex disease process involving mechanical disruption of neurological tissues and activation of secondary injury cascades, culminating in loss of function. Multiple neuroimaging approaches have recently been developed to detect white matter (WM) and gray matter injury following TBI. It is hypothesized that a multivariate analysis of these two imaging modalities may provide insight into the alteration of cortical and WM circuits following TBI. To address this hypothesis, we employ a novel multivariate technique, sparse canonical correlation analysis (SCCA), to quantify traumatically induced disruption of WM and cortical networks.

Diffuse Traumatic Brain Injury Data

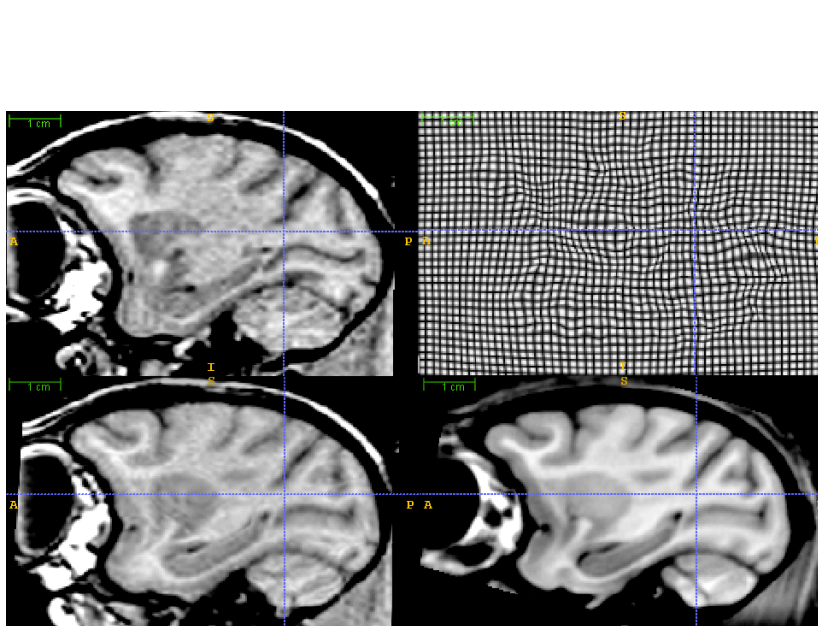
The TBI data used in this study is part of a larger effort investigating the relationship between various neuroimaging indices and cognitive and functional abilities in long-term survivors of TBI (principal investigator: John Whyte).

Description of cohort: 17 controls and 16 patients with TBI were used. Each patient had a history of non-penetrating traumatic brain injury of at least moderate severity defined by significant and well-documented loss or alteration of consciousness following injury in addition to meeting several other exclusionary criteria. The healthy volunteers were matched in terms of age, gender, ethnicity, handedness, and years of education.

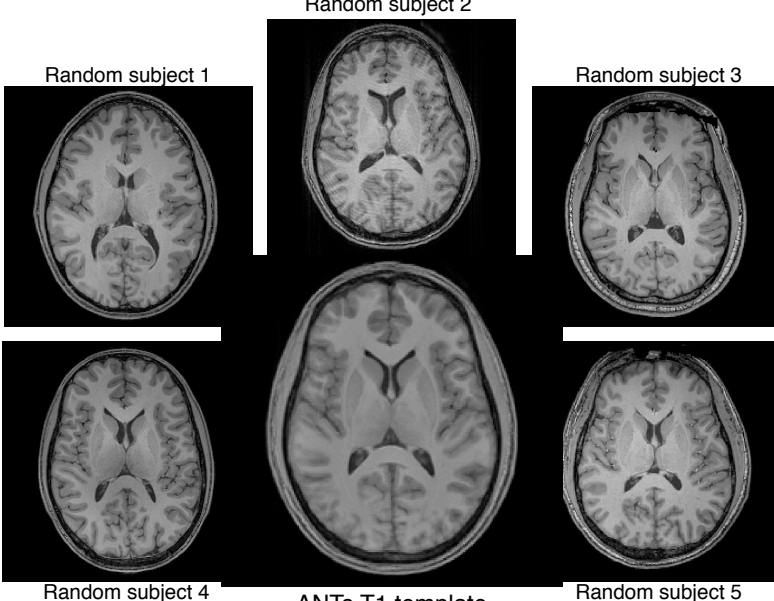
Image acquisition: High resolution T1-weighted anatomic images were obtained using a 3D MP-RAGE imaging sequence with the following acquisition parameters: TR = 1620 ms, TI = 950 ms, TE = 3 ms, flip angle = 15°, 160 contiguous slices of 1.0 mm thickness, FOV = 192 × 256 mm², matrix = 192 × 256, 1NEX with a scan time of 6 minutes, and voxel size = 1 mm³. 30-directional DTI images were also obtained.

Advanced Normalization Tools

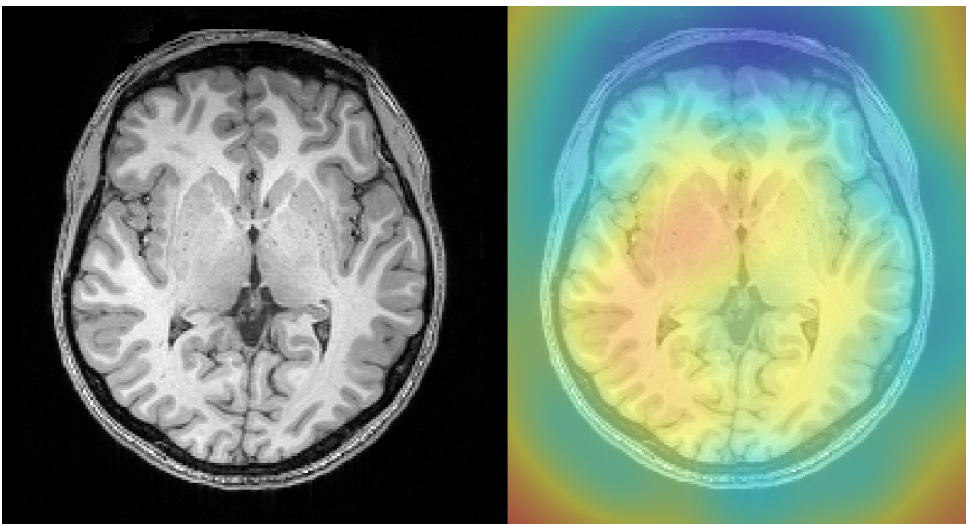
Processing



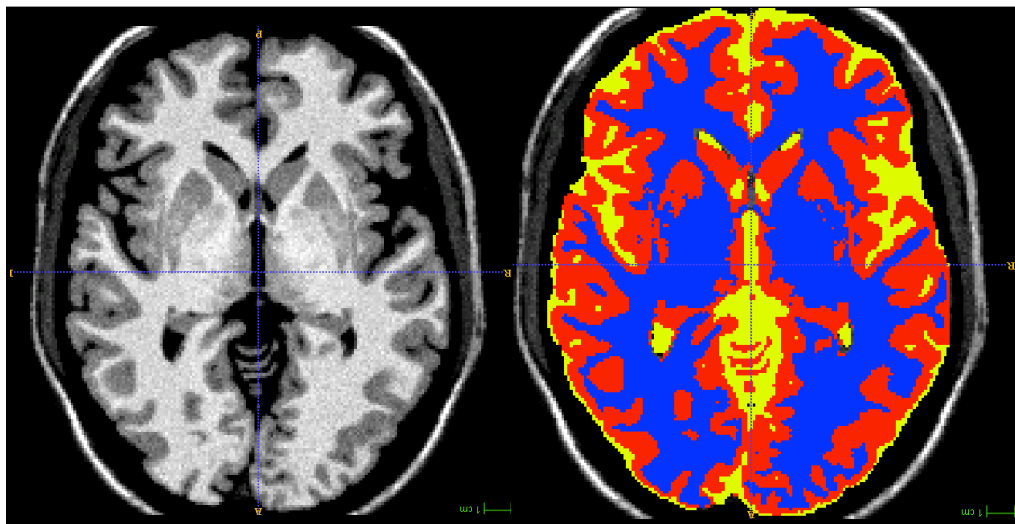
SyN normalization [2]



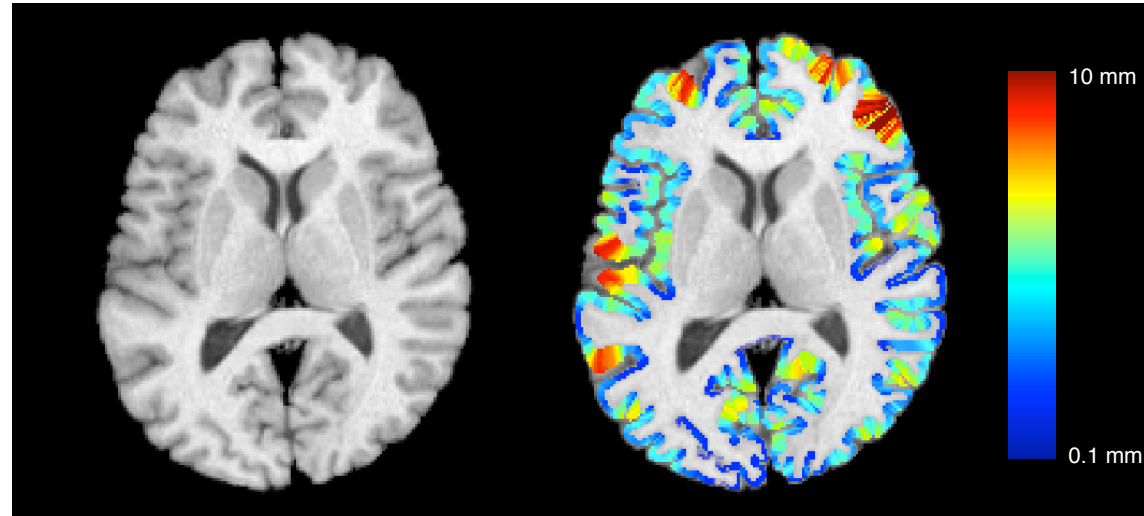
SyGN template building [4]



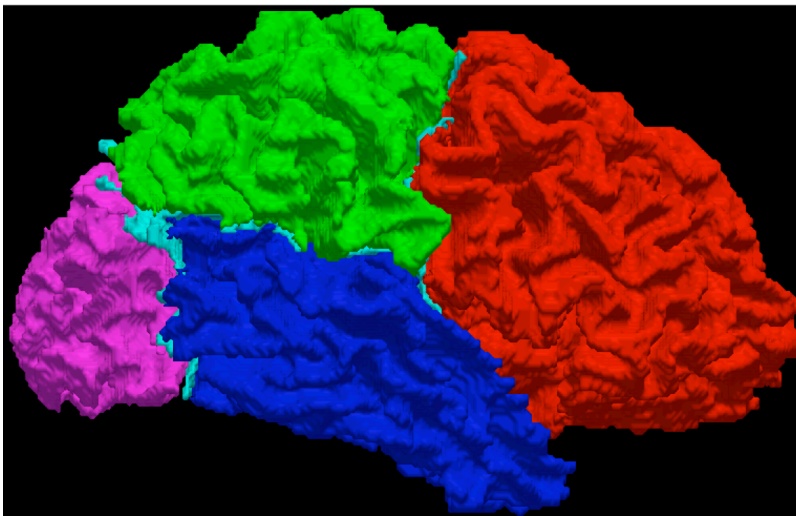
N4 bias correction [6]



Atropos *n*-tissue segmentation [3]

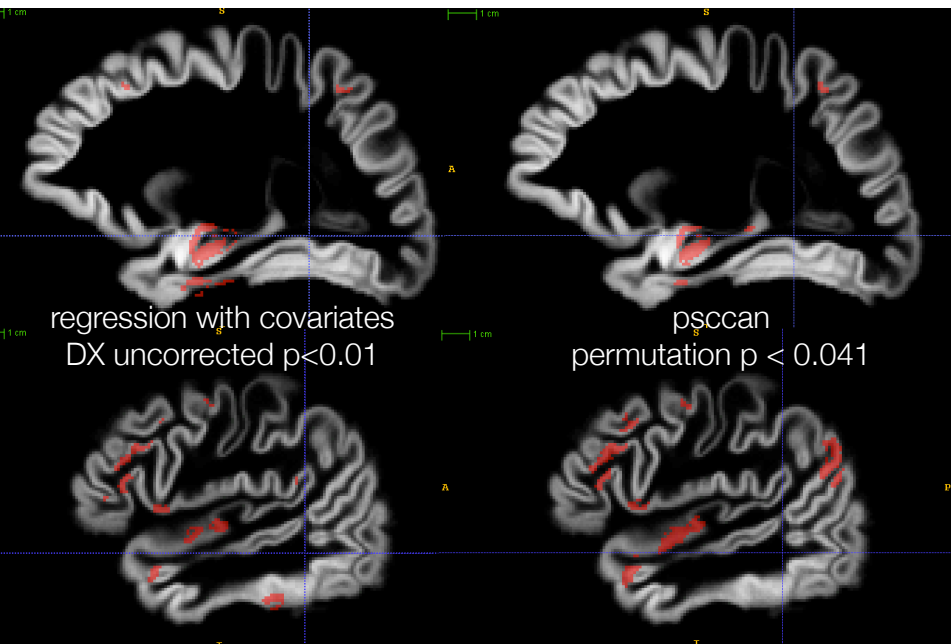


DiReCT cortical thickness [5]

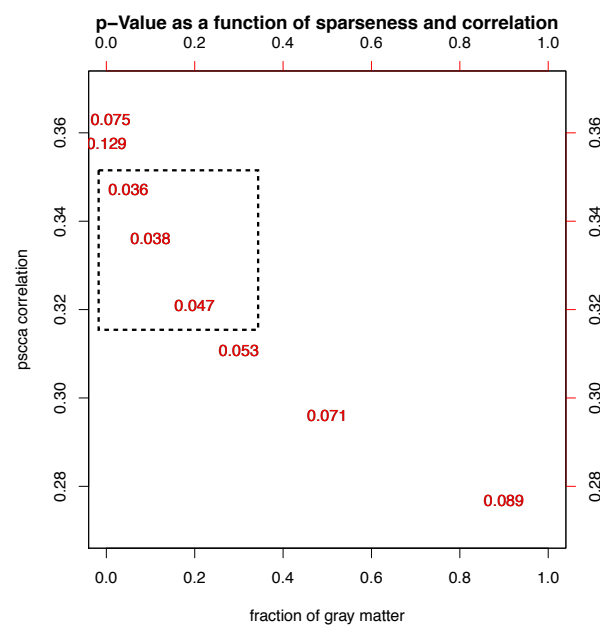


topological well-composedness [7]

Statistics

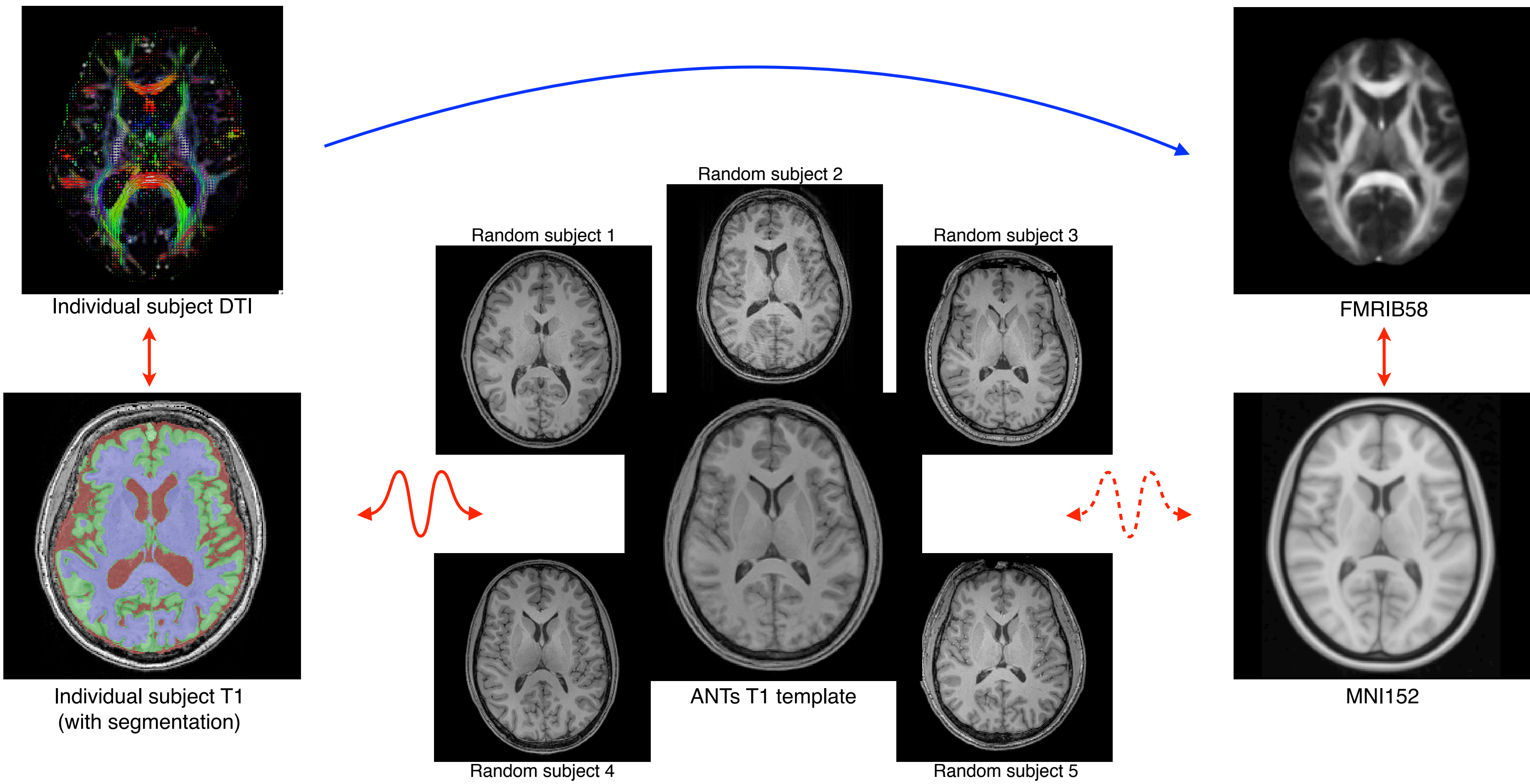


sparse canonical correlation analysis [1]



<http://www.picsl.upenn.edu/ANTs>

ANTs TBI Multivariate Processing Workflow



Results

Conclusions

SCCA demonstrates significant differences between the control and patient groups in both the FA ($p < 0.002$) and gray matter ($p < 0.01$) that are widespread but largely focus on thalamocortical networks related to the limbic system. Specific regional differences included the medial thalamic nuclei, hypothalamus, amygdala, hippocampus, anterior cingulate cortex, orbitofrontal cortex and fornix. Using these SCCA-identified regions, we demonstrate a strong correlation of the degree of injury in WM and GM within the patient group.

References

- [1] B. B. Avants, P. A. Cook, L. Ungar, J. C. Gee, and M. Grossman. Dementia induces correlated reductions in white matter integrity and cortical thickness: a multivariate neuroimaging study with sparse canonical correlation analysis. *Neuroimage*, 50(3):1004–1016, Apr 2010.
- [2] B. B. Avants, N. J. Tustison, G. Song, P. A. Cook, A. Klein, and J. C. Gee. A reproducible evaluation of ANTs similarity metric performance in brain image registration. *Neuroimage*, 54(3):2033–2044, Feb 2011.
- [3] B. B. Avants, N. J. Tustison, J. Wu, P. A. Cook, and J. C. Gee. An open source multivariate framework for n-tissue segmentation with evaluation on public data. *Neuroinformatics*, Mar 2011.
- [4] B. B. Avants, P. Yushkevich, J. Pluta, D. Minkoff, M. Korczykowski, J. Detre, and J. C. Gee. The optimal template effect in hippocampus studies of diseased populations. *Neuroimage*, 49(3):2457–2466, Feb 2010.
- [5] S. R. Das, B. B. Avants, M. Grossman, and J. C. Gee. Registration based cortical thickness measurement. *Neuroimage*, 45(3):867–879, Apr 2009.
- [6] N. J. Tustison, B. B. Avants, P. A. Cook, Y. Zheng, A. Egan, P. A. Yushkevich, and J. C. Gee. N4ITK: improved N3 bias correction. *IEEE Trans Med Imaging*, 29(6):1310–1320, Jun 2010.
- [7] N. J. Tustison, B. B. Avants, M. Siqueira, and J. C. Gee. Topological well-composedness and glamorous glue: a digital gluing algorithm for topologically constrained front propagation. *IEEE Trans Image Process*, 20(6):1756–1761, Jun 2011.