



# Geodesic Path Differences in Neural Networks in the Alzheimer's Disease Connectome Project (ADCP)



Nagesh Adluru<sup>1</sup>, Veena A. Nair<sup>1</sup>, Vivek Prabhakaran<sup>1</sup>, Shi-Jiang Li<sup>2</sup>, Andrew L. Alexander<sup>1</sup>, Barbara B. Bendlin<sup>1</sup> University of Wisconsin, Madison USA, <sup>2</sup>Medical College of Wisconsin, Milwaukee USA. Email: **adluru@wisc.edu** 

# Background

Neural networks derived from diffusion weighted imaging may shed light on disease progression and pathology propagation in Alzheimer's disease *in vivo*. In this work preliminary analysis of the path properties of such networks are presented. Geodesic or shortest paths are fundamental in understanding key network phenomenon such as the propagation rates of information, infection or pathology. For example, the ubiquitous small-worldness property of natural occurring biological and social networks is based on having short path lengths between any pair of entities in the network. Please move cursor over figures for additional details when viewing in Adobe. Poster checked for accessibility.

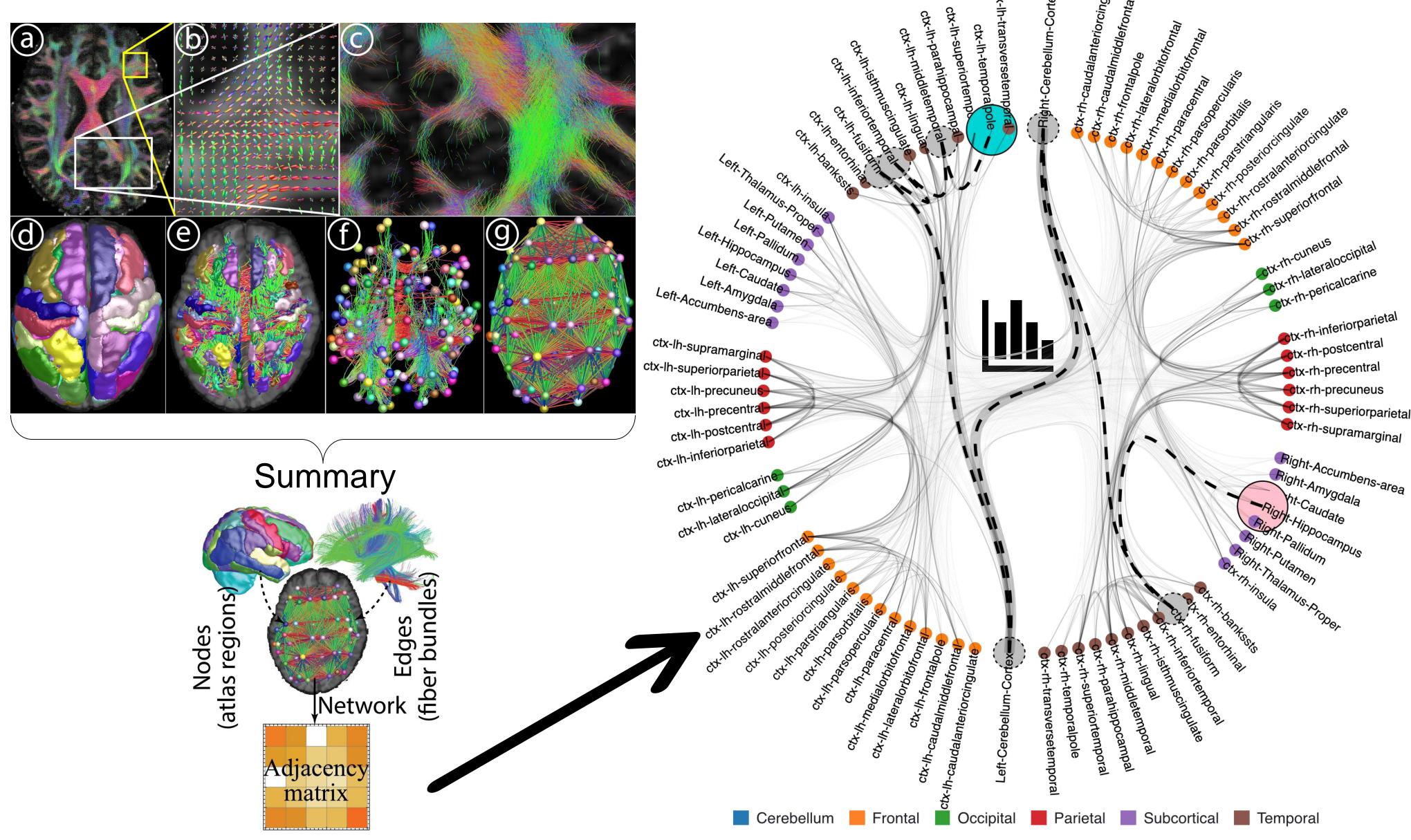
## Data

Consensus diagnosis	Cognitively unimpaired (CU)	Mild cognitive impairment (MCI)	Alzheimer's disease (AD) dementia
Sample size	n = 26	n = 24	n = 18
Sex	F(n = 15), M(n = 11)	F(n = 9), M(n = 15)	F(n = 10), M(n = 8)
Age	68.3 ± 8.19 [y]	71.9 ± 10.5 [y]	73.1 ± 7.77 [y]

**Table 1.** Sample characteristics of the data analyzed in this study.

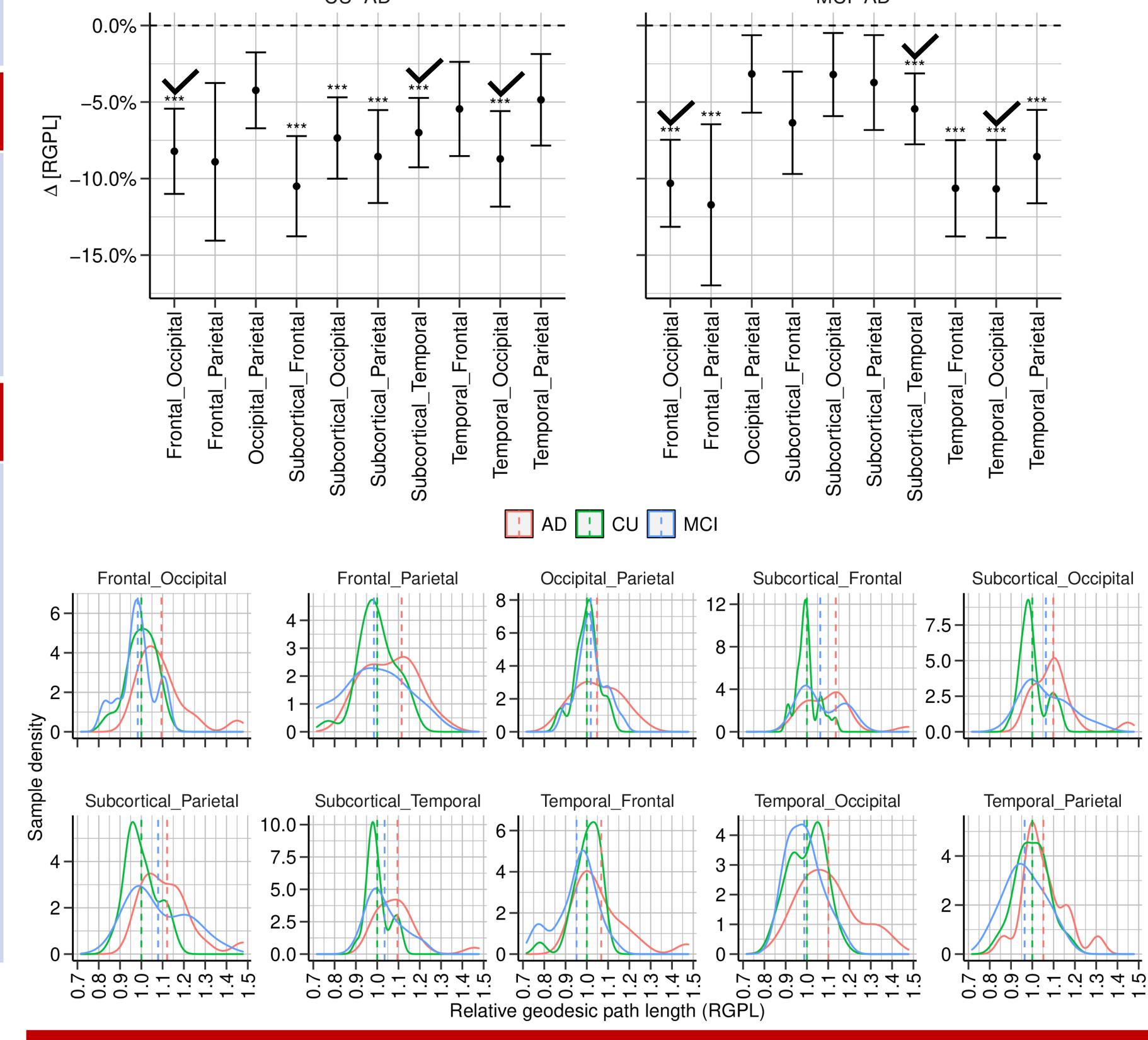
## Methods

Connectome protocol based multi-shell diffusion weighted MRI data acquired from n=68 participants were analyzed (Table 1). Neural networks were extracted from the data using state-of-the-art image processing and tractography algorithms available in the MRtrix3 package<sup>1-3</sup> (overview in Fig. 1). The average geodesic path lengths between frontal, temporal, parietal, occipital, subcortical regions were computed using Dijkstra algorithm<sup>4-6</sup>. The regions were identified based on the IIT Desikan gray matter atlas<sup>7</sup>. The paths can be used to reason about the average efficiency of communication of electrical signals or propagation of pathology between brain lobes. Statistical analysis was performed to test the geodesic path length differences between the CU, MCI and the AD groups controlling for age and sex. The path lengths were normalized so that they were at unity for the CU group, and the differences were considered statistically significant when  $p_s \le 0.05$ .



# Results

Statistical effects of the consensus diagnosis on the relative geodesic path length (RGPL) differences between lobes are shown in Fig. 2. 60% of the connections between the lobes showed statistically significant higher path lengths in AD compared to CU and MCI, with 30% overlapping. The distributions of the mean RPGL are shown in Fig. 3. For all the different pairs of lobes, the mean length was consistently higher for the AD group compared to both the CU and MCI groups.



## Conclusions

The path lengths between all the major lobes are longer for the AD group compared to both the CU and MCI groups. These findings suggest that network efficiency is reduced in AD and may explain cognitive dysfunction observed in the Alzheimer's clinical syndrome. Future work entails incorporating better constraints on tractography using structural  $T_1$  - weighted images and separating disease groups by AD-biomarker status.

#### References

1. Tournier, J.-D., Smith, R. E., Raffelt, D., Tabbara, R., Dhollander, T., Pietsch, M., Christiaens, D., Jeurissen, B., Yeh, C.-H. & Connelly, A. (2019). MRtrix3: A fast, flexible and open software framework for medical image processing and visualisation. Neurolmage, 202, 116137.

2. Smith, R. E., Tournier, J.-D., Calamante, F. & Connelly, A. (2015). The effects of SIFT on the reproducibility and biological accuracy of the structural connectome.

3. Dhollander, T.; Mito, R.; Raffelt, D. & Connelly, A. Improved white matter response function estimation for 3-tissue constrained spherical deconvolution. Proc Intl Soc Mag Reson Med, 2019, 555

- 4. Dijkstra, E. W. (1959). A note on two problems in connexion with graphs. Numerische Mathematik, 1: 269-271. doi:10.1007/BF01386390.
- 5. West, D.B. (1996). Introduction to Graph Theory. Upper Saddle River, N.J.: Prentice Hall.
- 6. Ognyanova, K. (2016). Network analysis with R and igraph: NetSci X Tutorial. Retrieved from www.kateto.net/networks-r-igraph.
  7. Peng, H., Orlichenko, A., Dawe, R. J., Agam, G., Zhang, S., & Arfanakis, K. (2009). Development of a human brain diffusion tensor template. Neuroimage, 46(4), 967-980

#### Acknowledgements

Thank you for the support from ADCP UF1-AG051216, UW ADRC AG033514, R01-AG037639, Waisman IDDRC U54-HD090256, the ADRC and Waisman staff, and the study subjects and families.