Supplementary Materials
Ambivert degree identifies crucial brain functional hubs and improves detection of Alzheimer's Disease and Autism Spectrum Disorder

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1 Functional MRI Preprocessing Pipeline for ADNI dataset

For each of the fMRI scans for a subject, the following preprocessing was performed. First, a reference volume and its skull-stripped version were generated and the BOLD reference was co-registered to the T1w reference using `bbregister` (FreeSurfer). Head-motion parameters with respect to the BOLD reference (transformation matrices, and six corresponding rotation and translation parameters) are estimated before any spatiotemporal filtering using `mcflirt` [1]. BOLD runs were slice-time corrected using `3dTshift` from AFNI [2]. The BOLD time-series were resampled onto their original, native space by applying a single, composite transform to correct for head-motion and susceptibility distortions.The BOLD time-series were resampled to `MNI152NLin2009cAsym` standard space, generating a preprocessed BOLD run in MNI152NLin2009cAsym space. Principal components are estimated after high-pass filtering the preprocessed BOLD time-series. The BOLD time-series, were resampled to the fsaverage5 surface. Gridded (volumetric) resamplings were performed using antsApplyTransforms (ANTs), configured with Lanczos interpolation to minimize the smoothing effects of other kernels [3]. Non-gridded (surface) resamplings were performed using `mri_vol2surf` (FreeSurfer).

2 Change in path length for different network hubs

For the nodes in each subject's network, we computed the ambivert degree, betweenness centrality, intra-module degree z-score, participation coefficient, gateway betweenness coefficient, gateway ambivert coefficient and gateway degree coefficient to detect different types of hubs. To compute network hubs, we give equal weights to the node's modular hub scores and the respective connector hub score. Accordingly, we removed the nodes with top 20% scores (in steps of 2.5%) and inspect the change in the network path length l on their removal. We performed comparison for change in path length for removal of different types of connector hubs for a given modular hub for varied percentiles (S1). For all the modular hubs, we found that the different gateway coefficients (betweenness, ambivert, degree) have a very similar increase in path length, which was in all the cases either similar to or lower than increase in path length with participation coefficient.

We plot the diffference in the anatomical locations of ambivert degree and participation coeffcient hubs, and intra-modular degree and participation coeffcient hubs in Figure S2.

3 Disruption of brain hubs in Alzheimer's Disease and Autism Spectrum Disorder

We computed the network hubs given by ambivert degree and participation coefficient hubs for the diseased (ASD and AD) subjects and their healthy counterparts. We noticed widespread disruption in the hub locations in case of both AD and ASD as compared to the normal controls at different thresholds (refer figures S3 and S4).

4 Acknowledgment

The ADNI was launched in 2003 as a public-private partnership, led by Principal Investigator Michael W. Weiner, MD. The primary goal of ADNI has been to test whether serial magnetic resonance imaging (MRI), positron emission tomography (PET), other biological markers, and clinical and neuropsychological assessment can be combined to measure the progression of mild cognitive impairment (MCI) and early Alzheimers disease (AD).

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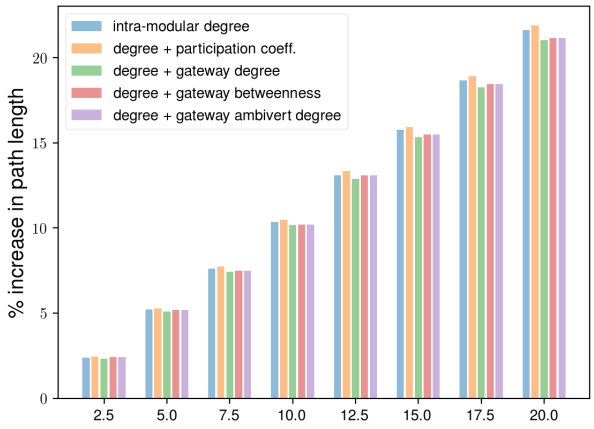
References

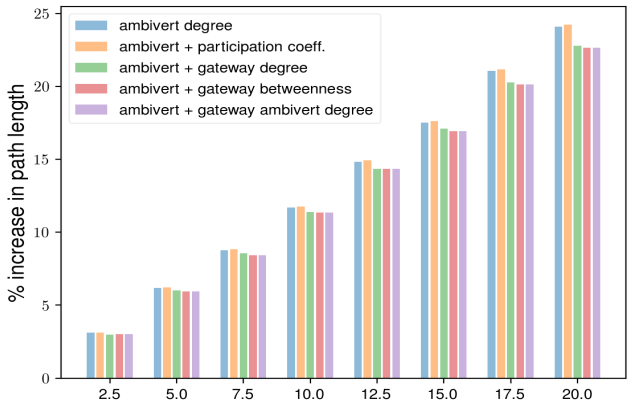
[1] M. Jenkinson, P. Bannister, M. Brady, and S. Smith, "Improved optimization for the robust and accurate linear registration and motion correction of brain images," *NeuroImage*, vol. 17, no. 2, pp. 825–841, 2002.

[2] R. W. Cox and J. S. Hyde, "Software tools for analysis and visualization of fMRI data," *NMR in Biomedicine*, vol. 10, no. 4-5, pp. 171–178, 1997.

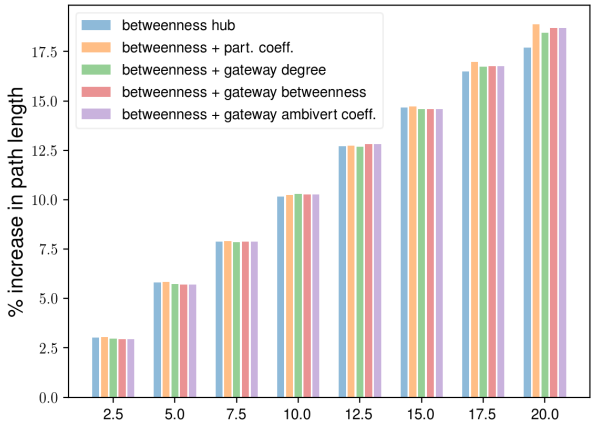
[3] C. Lanczos, "Evaluation of noisy data," *Journal of the Society for Industrial and Applied Mathematics Series B Numerical Analysis*, vol. 1, no. 1, pp. 76–85, 1964. [Online]. Available: http://epubs.siam.org/doi/10.1137/0701007



(a) Intra-modular Degree



(b) Ambivert Degree



(c) Betweenness

Figure S1: The increase in the path length after artificial lesioning of different percentiles of network hubs determined by (a) intra-modular degree modular hubs, (b) ambivert modular hubs and (c) betweenness centrality modular hubs along with different connector hub measures.

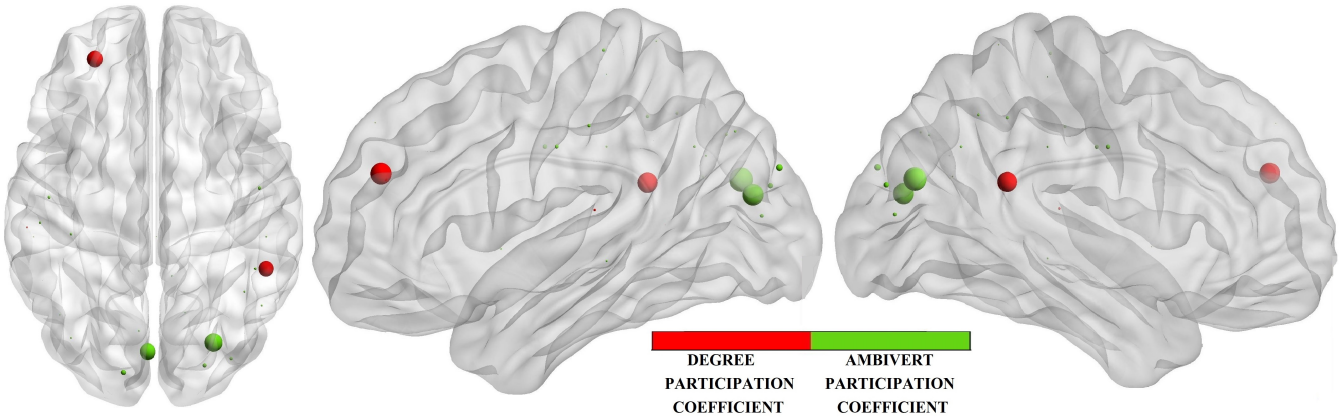
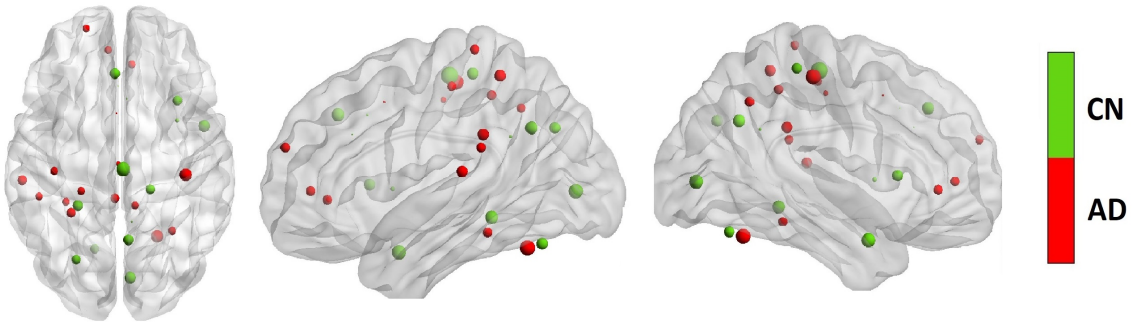
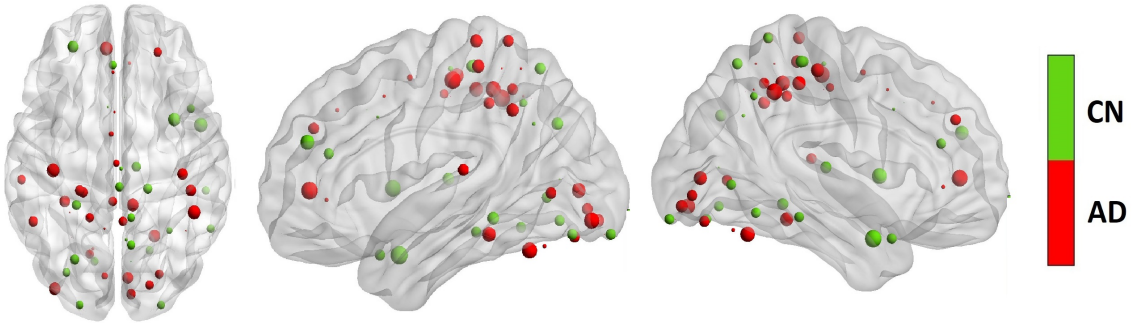


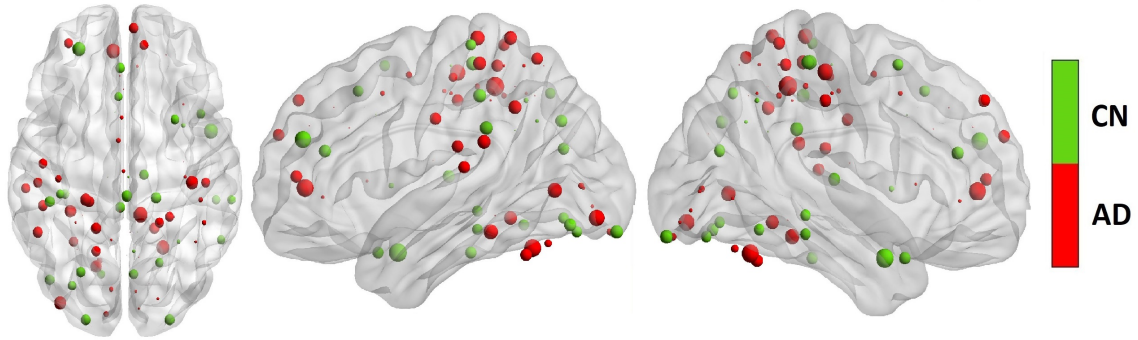
Figure S2: The figure depicts the different nodes that are identified as hubs using ambivert degree and participation coefficient, and using intra-modular degree and participation coefficient. The regions in red were identified using intra-modular degree and participation coefficient hubs but not with ambivert degree and participation coefficient hubs, and vice versa for the regions in green.



(a) Top 5%

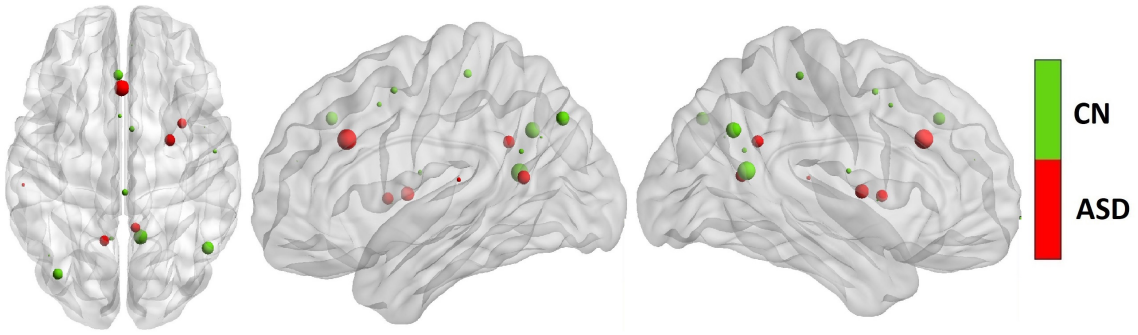


(b) Top 15%

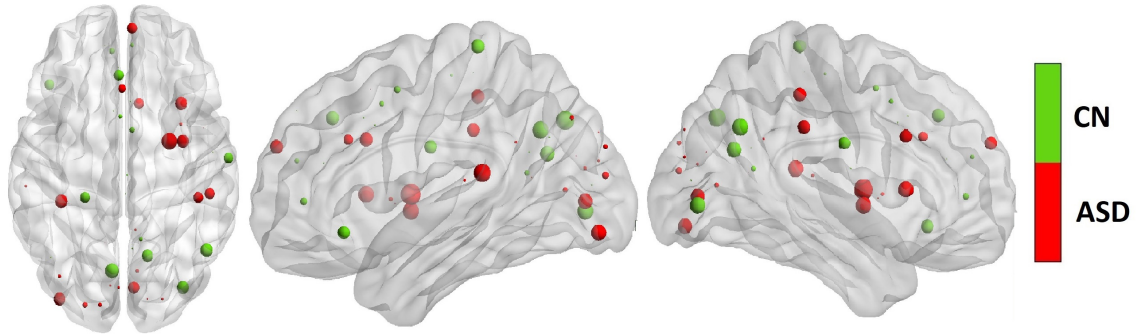


(c) Top 20%

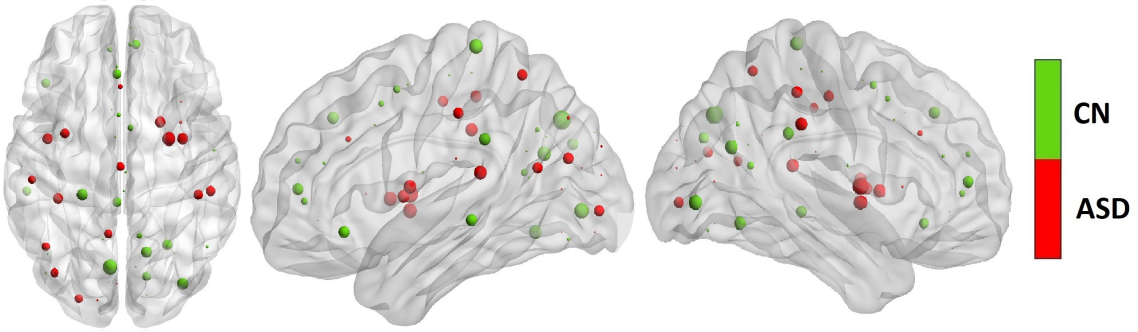
Figure S3: The figure depicts the difference between nodes that are identified as hubs using ambivert degree and participation coefficient in cognitively normal (CN) and AD subjects for different percentiles. The regions in red were identified as hubs in the AD subjects but not in CN subjects, whereas the regions in green were identified as hubs in CN subjects but not in the AD subjects.



(a) Top 5%



(b) Top 15%



(c) Top 20%

Figure S4: The figure depicts the difference between nodes that are identified as hubs using ambivert degree and participation coefficient in cognitively normal (CN) and ASD subjects for different percentiles. The regions in red were identified as hubs in the ASD subjects but not in CN subjects, whereas the regions in green were identified as hubs in CN subjects but not in the ASD subjects.