Repeatability and variability of graph metrics in a test-retest of whole-brain structural networks.

Jennifer Andreotti[1], Kay Jann[1], Lester Melie-Garcia[2], Thomas Dierks[1], and Andrea Federspiel[1]
[1]*Dept. of Psychiatric Neurophysiology, University Hospital of Psychiatry / University of Bern, Bern, Bern, Switzerland,* [2]*Neuroinformatics Department, Cuban Neuroscience Center, Havana, Havana, Cuba*

Purpose: Whole-brain network analysis of diffusion imaging tractography data is an important new tool for quantification of structural connectivity patterns across individuals and between groups. In order to construct the connectivity network, different weights and thresholds levels may be set but their effect on the graph organization and properties is not fully understood. In 2007, Estrada and Hatano [1], defined the concept of communicability to quantify the connectivity between two regions by all possible walks (AC) and not only the direct connections (SC). In our analysis we compared network properties as well as their stability and variability for AC and SC graphs of 19 healthy subjects (mean age ± SD: 26.1±2.7 years, 10 F, 9 M).

Methods: Diffusion Tensor Imaging (DTI) was performed on a Siemens Trio 3T scanner using a spin echo (SE-)EPI using two 180° pulses (TR/TE=6800/93ms, matrix size=128×128, FOV 256×256 mm^2, 50 slices, slice thickness=2 mm, gap thickness=0 mm, pixel bandwidth 1346 Hz/pixel, max b-value 1300 s/mm^2,42 non-collinear directions). Each subject underwent two consecutive DTI sessions. In addition, T1-weighted anatomical images were acquired with a 12-channel head coil (176 sagittal slices, slice thickness=1.0 mm, FOV 256×256 mm^2, TR/TE=7.92/2.48 ms, Flip angle=16°, inversion with symmetric timing (inversion time= 910 ms), fat saturation). Movement and eddy currents corrections were performed in FSL. After coregistration of diffusion weighted images with T1-weighted images an automated cortical parcellation was performed in FreeSurfer ('Destrieux' cortical atlas). The structures defined then served as ROIs for probabilistic fiber tracking in FSL. A connectivity map for each ROI was created starting from seeds placed in every voxel of the ROI considered (Tracking parameters: 5000 paths from each seed point, step size 0.5 mm, maximum trace length 500 mm and curvature threshold of ±80degrees). An index of connectivity was assigned to each brain voxel, representing the proportion of generated paths from the seed region that passed through it.

For each subject, whole-brain undirected weighted networks were created using 154 ROIs from the parcellation (lower temporal regions were excluded) as nodes. In the SC graph, an undirected arc a_{ij} between nodes i and j was established if a nonzero connectivity index was found to exist between the voxels of regions i and j. The arc weight was defined as the number of streamlines connecting the two ROIs corrected by ROIs' surface. Weighted communicability connectivity matrices (AC) were computed as the exponential $exp(D^{-\frac{1}{2}} A D^{-\frac{1}{2}})$, where A denotes the adjacency matrix of SC, $D^{-\frac{1}{2}}$ is the diagonal matrix with elements $1/\sqrt{\deg\_i}$ and $\deg\_i$ is the generalized degree of node i in SC [2]. A common threshold on density was applied to all matrices in order to obtain comparable graph metrics. Results are given for T=0.25, but thresholds between 0.15 and 0.35 were tested with no significant changes in the results.

Once the adjacency matrices were defined, global and local properties such as binary and weighted cluster coefficient, nodal strength, and small world property were analysed for every graph. Local properties were normalized over the total for all graphs in order to compare. In addition, the intra class correlation (ICC) and the coefficient of variation (CV) of each global and local property were considered in order to verify repeatability of the network metrics [5]. For this aim we also computed similarity between and within subject for raw connectivity matrices as the squared Pearson's correlation coefficient between edges' weights.

Results: The analysis showed increased similarity R^2 for AC weighted graphs (Mann-Whitney U test: within p=0.0006, between p<0.0001) as well as reduced variability in between subjects similarity (Levene's test: p<0.0001, see Fig.1). Also for node properties, between subject similarity is smaller than within subject. Variability measures (ICC and CV) are slightly better in AC, although results are good in all graphs showing mean ICC over 0.65 for all measures. In general, all nodes' graph measures show a larger variability for SC. Measures extracted from the two measurements correlate well (see Fig.1,Small world property SC R=0.92, AC R=0.83, AC/SC R=0.72), although between AC and SC a scaling factor exists.

Discussion: Results show that repeatability of graph metrics is overall good for all properties in SC and AC, although AC measures are slightly more robust. Variability is smaller within subjects than between subjects, indicating that the measures extracted can be used to characterize the individual network's structure. Also AC reduces variability between subjects for all properties, which may be good for group comparison. However, differences between SC and AC are also related to the different definition of connectivity and each of them may be more adequate for a specific analysis.

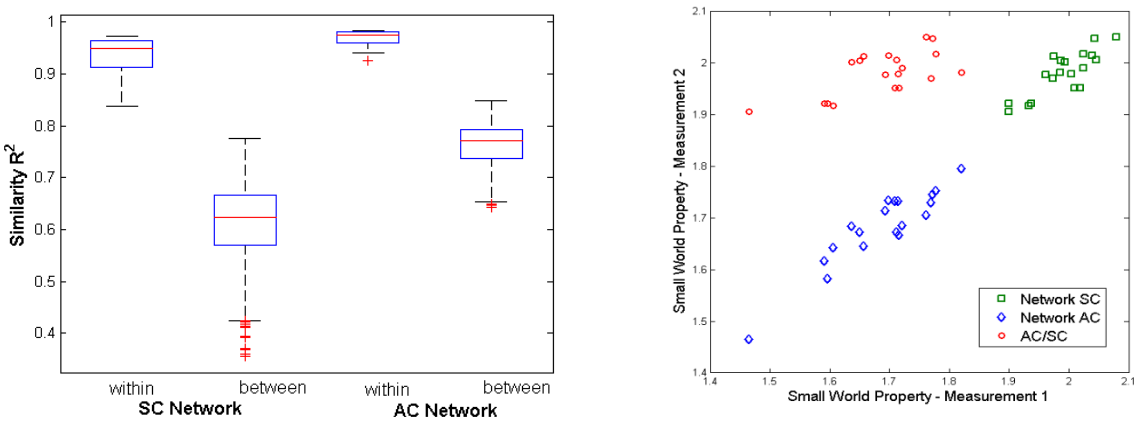

Fig.1: Left: similarity within and between subjects of raw connectivity matrices for all weightings. Right: scatter plot of small world property for all subjects and different weightings. For between weights, the average of both measurements is used.

References: [1] Estrada E. and Hatano N. *Phys. Rev.* 2008, E 77 [2] Crofts J. and Higham D. A *J. R. Soc. Interface*. 2009; 6: 411-414. doi: 10.1098/rsif.2008.0484 [3]Rubinov M. and Sporns O. *NeuroImage* 2010; 52:1059:1069 [4] Iturria-Medina et al., *NeuroImage* 2007; 36:645:660 [5] Bassett et al. *NeuroImage* 2011;54:1262-1279