

A new way of constructing edge weights of a structural connectivity matrix by considering direct and indirect connections of the fiber tracts

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Introduction: The human brain is a complex network of structure and function. Modeling the whole human brain as a network, the so-called human connectome [1], has obtained significant interest in the past decade. There are two distinct types of network connectivity, i.e. functional connectivity and structural connectivity. Functional connectivity describes how functionally specialized areas work in synchrony and interact with each other [2-3]. Structural connectivity uses diffusion tractography to find physical connections between brain regions and apply network analysis techniques to identify structural modules [4]. Correlation studies between functional connectivity and structural connectivity reported moderate associations. This may be attributed in part to the fact that functional connectivity not only involves brain regions that are directly connected, but also those that are connected indirectly. In this study, we proposed a novel definition of connectivity strength between pairs of brain regions and applied the conductance concept to build edge weights for connectivity matrices, including direct and indirect structural connections. A validation test was performed to assess the stability of the resulting connectivity matrices in a group of 20 healthy subjects.

Methods: The connectivity matrices were constructed based on a diffusion spectrum imaging (DSI) template and a tractatlas. The DSI template was built by coregistering DSI datasets of 122 healthy adults in the Montreal Neurological Institute (MNI) space [5]. The tractatlas consisted of 117 tract bundles reconstructed in the DSI template [6]. 74 regions of interest (ROIs) in cortical and subcortical regions were defined to indicate two ends of a reconstructed tract bundle. Mean generalized fractional anisotropy (mGFA) of a tract bundle was determined by averaging the GFA values along the path of the entire tract bundle. The direct structural connection $SC_1(i,j)$ between ROI(i) and ROI(j) was defined as the "conductance" of a tract bundle: $SC_1(i,j) = (A / L)$ mGFA, where A and L were tract number and bundle length of the tract bundle, respectively. The indirect connections via 2 tract bundles $SC_2(i,j)$ was determined by treating the "resistances" of 2 tract bundles as they were connected in series. The same principle applied to the indirect connection via 3 tract bundles $SC_3(i,j)$. Once SC_1 , SC_2 and SC_3 were determined, the summation of the direct and indirect connections was determined by treating SC_1 , SC_2 and SC_3 as 3 "resistances" in parallel. We hypothesized that the patterns of structural connectivity matrices varied among SC_1 , SC_2 and SC_3 , and that it became stable in the summation of SC_1 , SC_2 and SC_3 (SC_{1+2+3}) as compared to SC_1 only or the summation of SC_1 and SC_2 (SC_{1+2}). To test the stability of the connectivity matrices, DSI datasets of 20 healthy adults were selected to calculate their structural connectivity matrices. Pearson correlation coefficients were calculated between connection matrices defined in the DSI template and those calculated from individual subjects. DSI was performed on a 3T MRI system (TIM Trio, Siemens) using a twice-refocused balanced echo diffusion echo planar imaging (EPI) sequence, TR/TE = 9600/130 ms, FOV = 200 x 200 mm, image matrix size = 80 x 80, and slice thickness = 2.5 mm. A total of 102 diffusion encoding gradients with the maximum diffusion sensitivity $b_{max} = 4000$ s/mm² were sampled on the grid points in a half sphere of the 3D q-space with $|q| \leq 3.6$ units [7].

Results: The connectivity matrices of SC_1 , SC_{1+2} , and SC_{1+2+3} are showed in Fig. 1, Fig. 2, and Fig. 3, respectively. In SC_1 , the connection occurs between brain regions of ipsilateral hemisphere by association fibers, between cortical and subcortical regions by projection fibers, and between homotopic regions of bilateral hemispheres by commissural fibers. In SC_{1+2} , new connections occur in cortical-cortical connections, cortical-subcortical connections and subcortical-subcortical connections in the ipsilateral hemisphere. In addition, inter-hemispheric connections between cortical and subcortical regions were also found. In SC_{1+2+3} , new connections were found in inter-hemispheric heterotopic connections in both cortical and subcortical regions. The pattern of the connectivity matrices became stable after SC_{1+2+3} . Figure 4 shows the box plot of the Pearson correlation coefficients between connectivity matrices defined in the DSI template and those calculated from individual subjects. We can see that as 1st-degree and 2nd-degree indirect connections were added to the direction connection, the variance of the correlation coefficients decreased and the strength increased from 0.7064 to 0.9157

Discussion and Conclusion: Based on the cortical and subcortical parcellation and connecting tract bundles reconstructed in the DSI template, we presented a unique method to measure the connectivity between pairs of ROIs, including direct and indirect structural connection. We found that the summation of direct connection (SC_1) and indirect connections (SC_2 and SC_3) recovers a structural connectivity matrix that encompasses the majority of the known functional connectivity in the brain. Furthermore, the connectivity matrices of individual subjects became highly correlated to each other and with that defined in the DSI template when all the direct and indirect connections were taken into account. Taken together, it warrants further studies to show that our proposed method of measuring structural connectivity can improve the association between structural connectivity and functional connectivity.

References: [1] Sporns, O., et al., PLoS Comput. Biol. 2005;1(4):e42. [2] Friston, K., et al., Hum. Brain Mapp. 1993a;1:69–80. [3] Friston, K., et al., J. Cereb. Blood Flow Metab 1993b;13:5 –14. [4] Hagmann P., et al., PLoS Biol 2008;6:e159. [5] Hsu Y. et al., NeuroImage 2012;63:818-834. [6] Lo, Y.C. et al. Proc ISMRM (2013). [7] Wedeen V., et al., Magn. Reson. Med. 2005; 54:1377-1386.

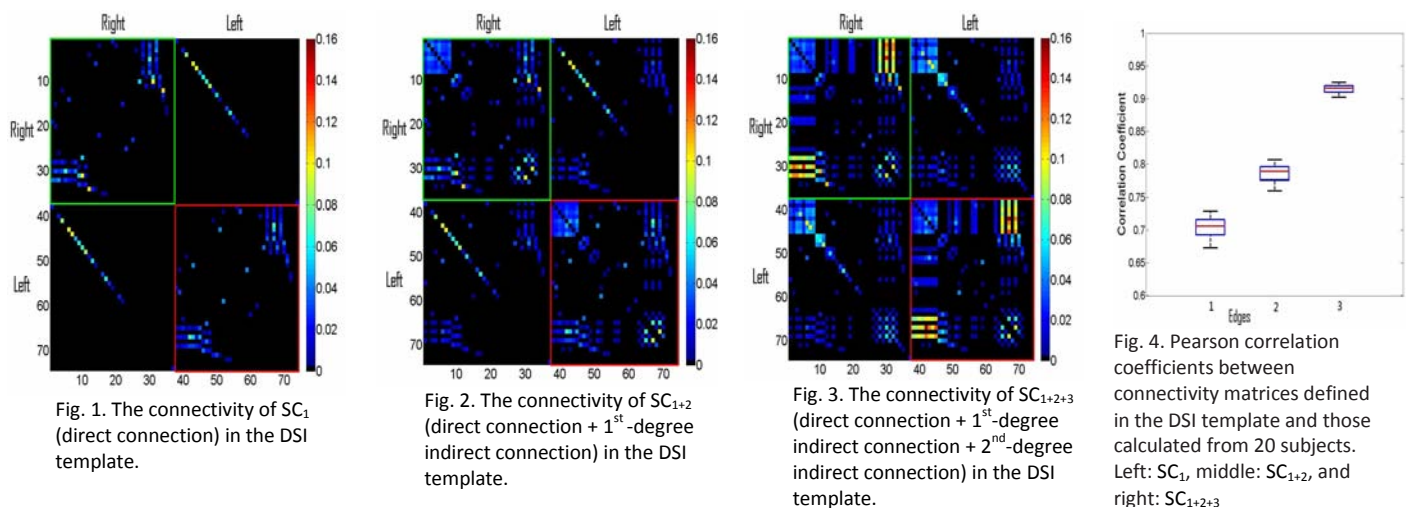


Fig. 4. Pearson correlation coefficients between connectivity matrices defined in the DSI template and those calculated from 20 subjects. Left: SC_1 , middle: SC_{1+2} , and right: SC_{1+2+3}