Consensus between pipelines in whole-brain structural connectivity networks

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Audience Those interested in structural brain networks

Purpose A variety of image processing pipelines have been used to reconstruct whole-brain structural connectivity networks[1]. The choice of parcellation, registration and fiber tractography scheme can influence network connectivity measures and there is currently a lack of agreement upon which combinations result in networks of highest anatomical relevance[2]. For a given network reconstruction, determining which connections to retain or discard is also unclear[3]. To address these issues, we investigated the connection convergence in structural networks obtained using two independent 'state-of-the-art' reconstruction pipelines across a range of density thresholds, with the aim of identifying the core anatomical connections that occur robustly in both.

Methods Two T1-weighted images (3D FLASH) and three repeats of a 63-direction echo-planar diffusion weighted sequences were acquired at 1.5T from 28 young healthy subjects. Two pipelines (N/F) were applied to reconstruct whole-brain connectivity. These varied with respect to the parcellation, registration and fiber tractography schemes. T1-weighted images were skull-stripped, registered to improve signal to noise ratio and parcellated into 44/68 cortical regions, as defined in the Hammers/Desikan Atlas, using NiftySeg/Freesurfer software. The averaged structural image was non-linearly registered to the subjects *b*=0 image using NiftyReg/FSL registration tools. The voxel orientations of white matter fibers in diffusion-weighted images of $(2.5\text{mm})^3$ resolution were estimated using Constrained Spherical Deconvolution (CSD)/FSL-BEDPOSTX. 100 probabilistic streamlines were seeded from each grey matter boundary voxel and connectivity was quantified between all node pairs as the sum of connecting streamlines divided by the mean node boundary volumes. Native atlas node scales differed between pipelines (44/68), meaning a direct connection-wise comparison was not possible. Therefore, a merging scheme was implemented whereby the cortical parcels in both native parcellations were merged to an equivalent and common node scale of 34 nodes. Network convergence between pipelines was quantified over a range of network densities using the Percentage Convergence (PC[4]), defined as the percentage of supra-threshold edges found in both group networks (group networks were calculated by averaging connection weights across all subjects). The PC was calculated for 1000 bootstrap samples of the group networks.

Results PC of bootstrapped group networks was plotted as a function of network density (Fig. 1, a). Mean PC was high (≥ 67%) across the range of network densities and generally decreased with decreasing density. PC was lowest at a density of 0.05 (PC=67.0%), representing high convergence in the strongest 5% of connections between the pipelines. However, a local peak of mean PC was observed at a density of 0.22 (PC=85.8%). The convergent and divergent connections of group networks at this density are shown in Fig. 1. b. Local peak convergent connection streamlines corresponded closely with known white matter tracts in the literature (Fig. 1, c), whereas divergent connections corresponded with either longer or less plausible white matter tracts in our representative subject (Fig. 1, d).

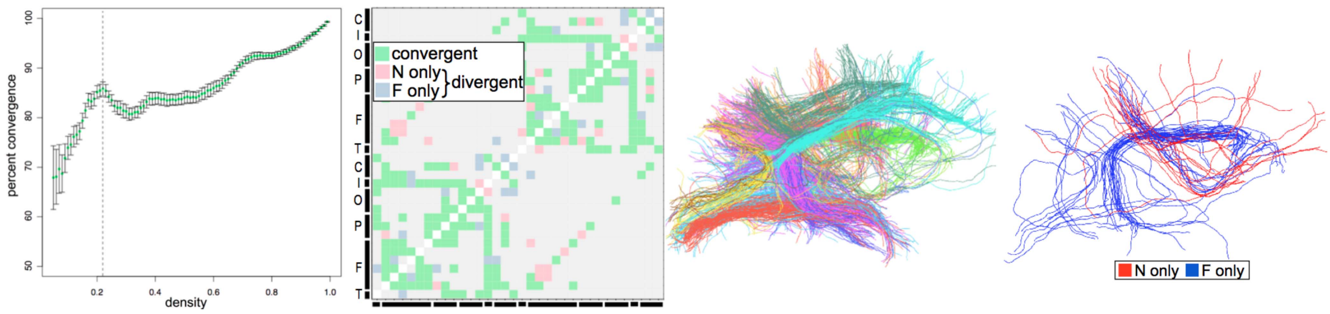

Fig. 1. (a) *PC between pipelines across density. A local peak PC is observed at a density of 0.22 (dotted line)* (b) *Convergent and divergent network connections at the local peak PC. Matrix entries describe the presence/absence of a connection between parcels. Rows/columns denote parcels belonging to temporal (T), frontal (F), parietal (P), occipital (O), cingulate (C) cortical lobes.* (c) *Inter-lobe convergent connections. Colours indicate streamline connection ownership.* (d) *Inter-lobe divergent connections.*

Conclusions We observed a high agreement between two independent state-of-the-art network reconstruction pipelines on a connection-wise basis for the first time. We identified the core connections which emerged most robustly in both. This common anatomical network-the 'consensus network' (Fig. 1, b), was derived by selecting the local peak convergence connections, which had both high connectivity and high convergence between reconstruction pipelines (dotted line, Fig. 1, a). We suggest this convergence was primarily driven by their ability to trace the true underlying fiber anatomy. The local peak convergence was observed at a density of 0.22, which is within the plausible range of sparsity found in brain networks in previous studies. This is a useful reference, given that the choice of density to analyse networks based on probabilistic fibers is both unclear and important for interpreting network topology. In the future, it would be interesting to investigate convergence at finer node scales as this would allow a more detailed analysis of the convergence structure.

References **[1]** Bullmore, E. & Sporns, O. 2009. *Nat. Rev. Neuroscience*. 10,186-198 **[2]** Bassett, D.S. *et. al*. 2011. *Neuroimage*. 54(2),1262-79 **[3]** Reus, A.M. & van den Huevel, M.P. 2013. *Neuroimage*. 70, 402-9 **[4]** Gong, G. et. al. 2012. *Neuroimage*. 59, 1239-48