Genetic factors influence on connectome fingerprints and functional networks

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Introduction: The current revolution in fMRI data analysis points toward the development of personalized medicine. Many studies have demonstrated that functional connectivity profiles are sufficient to identify an individual[1,2]. Importantly, the ability to discriminate between subjects seems to depend on the high intersubject variability and low intrasubject variability[3]. With this in mind, we investigated the contribution of highly distinctive networks among the individuals in twin pair identification, to possibly establish whether these networks variabilities rise from the genetic code.

Materials and Methods: *Dataset:* The data used is provided by the Human Connectome Project (HCP). We used resting-state functional and structural MRI data of 246 monozygotic twins. The technical details of this dataset are available at http://protocols.humanconnectome.org/. *Preprocessing:* The HCP dataset was preprocessed by using the standard and conservative pipeline of the toolbox CONN[4]. *Parcellation:* We applied two parcellation schemas: Shen[5] and Gordon[6]. Importantly, both atlases attribute each node to a functional system, which allowed further analysis of the contribution of each network to individual and twin identification.

Individual identification analysis: The identification analysis was based on previous work[1]. In summary, a dataset was created containing all the functional connectivity matrices for each run (rest1 and rest2). The individual identification was determined by computing the correlation between each individual connectivity matrix from one run and all the other connectivity matrices. The predicted identity was that with the maximal Pearson correlation score. Additionally, we also investigated the contribution of single networks to identification accuracy by sub-sectioning the functional connectivity matrices into sub-matrices of single networks.

Twins identification: Twin pair identification algorithm was obtained by few alterations of the individual identification analysis. The second run of the target subject was removed, and if the chosen maximum correlation value belongs to their twin, the prediction was considered correct.

Results: The individual identification accuracy obtained by comparing a target matrix (rest1) against all the other connectivity matrices from the database (rest2) was well above chance (1/246=0.4%) by using both parcellation schemas, Shen (97.6%) and Gordon (99.6%). Based on the networks' definition of Shen's schema, the medial frontal (93.1%) and frontoparietal (92.7%) were the most successful for individual identification. On the other hand, the dorsal attention (99.6%) and default mode (99.2%) networks based on Gordon's schema were the most distinctive networks. For the twin identification analyses, the whole-brain based identifications were similar (Shen, 60.8%; Gordon, 61.3%). Finally, the medial frontal (23.1%) and subcortical-cerebellum (32.1%) networks (Shen's schema), and the default (13.3%) and dorsal attention (13.9%) networks (Gordon's schema) were the most successful networks for twin pair prediction.

Discussion: Our results are in agreement with previous studies[1-3], supporting the fact that individual's connectivity profile is a reliable individual's marker. The high accuracy, well above chance (0.4%), obtained on whole-brain based twin identification might point to the importance of genetic factors on functional connectome individualities, despite the lower accuracy on network-based identification. Nonetheless, highly discriminant networks for individual identification demonstrated to be the most similar functional networks between a pair of twins, reflecting the importance of genetic factors on these networks.

Conclusion: Connectivity profiles are a promising source for further individual's genetic studies, as the distinctiveness of a functional network might also be determined by genetic factors.

References: [1] doi:10.1038/nn.4135; [2] doi:10.1371/journal.pone.0111048; [3] doi:10.3389/fnins.2017.00085; [4] doi:10.1089/brain.2012.0073; [5] doi:10.1016/j.neuroimage.2013.05.081; [6] doi:10.1093/cercor/bhu239.