Tractography-driven resting-state fMRI for investigating inter-subject variability

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Introduction

In the past decade, the fusion between diffusion magnetic resonance imaging (dMRI) and functional magnetic resonance imaging (fMRI) has opened the way for the exploration of structure-function relationships in-vivo. Traditional ways of coupling fMRI and dMRI often come down to reconstructing fiber pathways between distant fMRI activation regions. This may be problematic for two reasons: First, it assumes that fMRI should lead to dMRI fiber reconstruction, but what about the other way around? That is, what do functional connectivity profiles look like when fMRI seed regions are determined via the end-points of key white-matter bundles? Secondly, the vast majority of structure-function studies are analyzed by assuming fixed fMRI and dMRI parameters across all subjects, despite the fact that this has been shown to lead to false-negatives [1]. To address these two points, we developed a new reconstruction technique called *tractography-driven resting-state*, and demonstrate how parameter selection alone may explain a large part of the inter-subject variability typically observed in the Default Mode Network (DMN).

Methods

Datasets (rs-fMRI, dMRI, T1) were obtained from 10 healthy volunteers. Acquisition and preprocessing details have been previously described in [2]. Our real-time tractography algorithm [1] performs the dense 3D integration along the fiber orientation distribution function peaks field. From there on, the 3D coordinates of the last 3 points of each streamline were back-

projected into fMRI-space to extract their associated BOLD signal and perform real-time correlations [3] with the rest of the brain (Figure 1). To assess inter-subject variability of the DMN, we first isolated the right cingulum (Cg) bundle of a single subject (S6) and used the end-points as seeds for resting-state connectivity. Cg was derived using the same parameters for each subject: FA threshold = 0.15, step size = 0.5 mm, max. angle = 35°, min. length = 60 mm, max. length = 200 mm with 1000 seeds evenly distributed within a 4 × 4 × 4 mm ROI located at the mid-coronal section of the Cg body. The rs-fMRI z-score and min. cluster size thresholds were 4.0 and 40 voxels, respectively. Since these parameters did not faithfully reconstruct the Cg and DMN in all subjects, we regenerated the Cg a second time by adjusting dMRI parameters until it matched its known anatomy. The DMN was then computed a second time and compared with previous.

Results

Figure 2 (middle) shows the reconstructed Cg for S6 with its associated DMN consisting of the medial prefrontal cortex, the precuneus, the left and right temporoparietal lobes and the parahippocampal gyrus [4-6]. Using the same parameters on other subjects yielded a Cg bundle and DMN map that varied dramatically (Figure 2, left panel). However, when interactively adjusting the tractography and rs-fMRI reconstruction parameters in a subject-specific manner, both the DMN and Cg were easily retrieved (Figure 2, right panel). Red circles indicate regions where one of the expected nodes could not be retrieved. Blue circles shows false-positive clusters successfully suppressed.

Conclusion

The morphology of a complex organ such as the brain differs from individual to individuals [7]. Most neuroimaging studies rely on using reconstruction parameters averaged across multiple subjects which specifically rule out most of the inter-individual variability. We assessed inter-subject variability associated to structure-function relationship by importing a set of fixed parameters from an individual to the rest of our subjects. By extracting the BOLD time series from the Cg terminal points and performing real-time correlations, we demonstrated that the DMN can be recovered, thus providing more insight on the structure-function relationship. The proposed technique yields results in real-time and is useful for assessing how functional networks underlay structural connections, especially when looking at inter-subject variability.

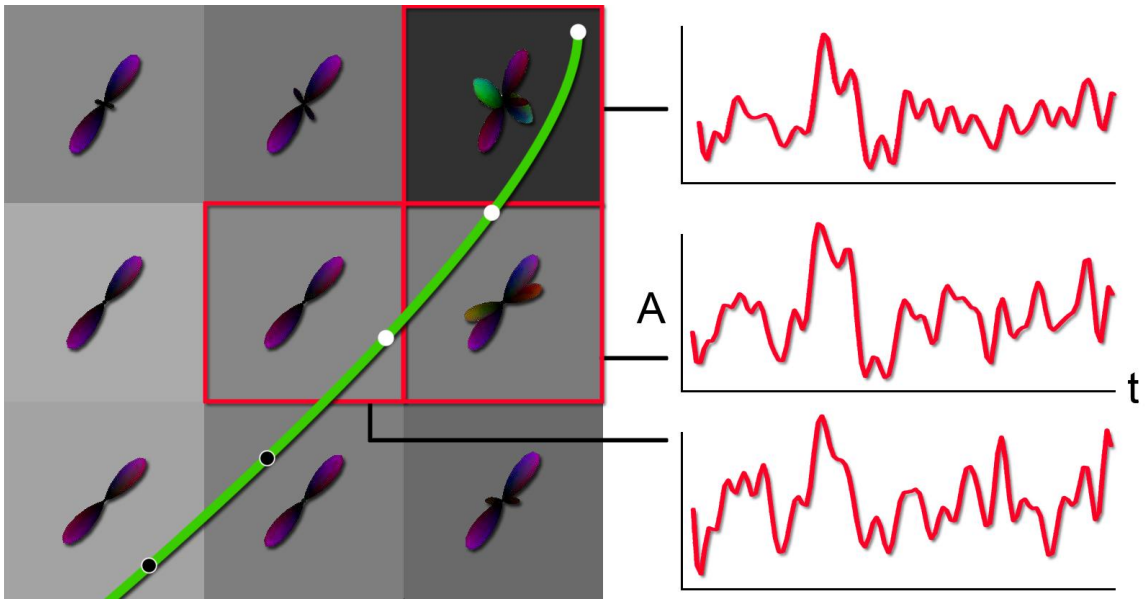

Figure 1: Principle behind the new tractography-driven resting-state fMRI connectivity correlation method. When a streamline hits the GM, its propagation is stopped. By looking at the underlying BOLD signal encompassed by the last n points of the streamline (3 in this case), the average BOLD signal is correlated with every other voxels of the brain.

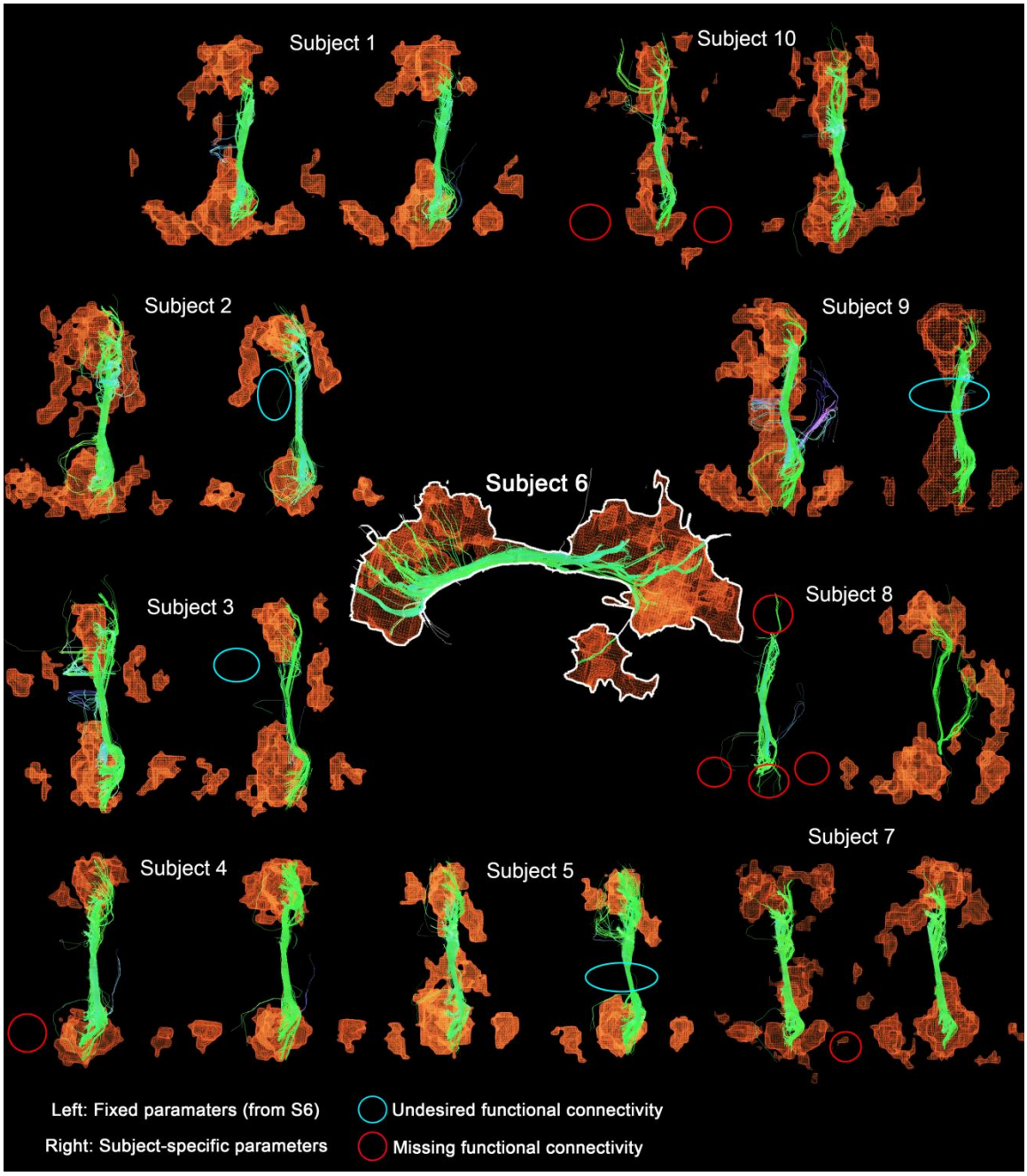

Figure 2: DMN and Cg-right displayed for all 10 subjects. Left: parameters extracted from reference subject (S6). Right: subject-specific parameters. Red circles indicate regions where one of the expected nodes could not be retrieved. Blue circles shows false-positive clusters successfully suppressed. Note the parahippocampal gyrus activation from S6.

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