Interactively computing and visualizing functional and structural brain connectivity in real-time

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PURPOSE: In this new multimodality era, combining diffusion with functional MRI permits a unique way of exploring brain networks, especially when the users have access to the multiple parameters involved in such reconstructions. fMRI provides 4D whole-brain images that reflect changes in cortical blood flow, volume and oxygen as measured by the Blood-Oxygenation-Level-Dependant (BOLD) signal. The spontaneous low fluctuations (< 0.1 Hz) present in the BOLD signal allow the detection of temporally correlated spatial patterns, also known as Resting State Networks (RSNs) when the brain is at rest [1, 2]. The common way of exploring such networks is to extract the BOLD time course from an a priori region of interest (ROI) and compute the temporal correlation with all other voxels of the brain. The result is a seed-specific correlation map or a functional connectivity. What if a neurosurgeon is interested in looking at the underlying functional network associated to an intraoperative stimulated cortical site? It demands the preprocessing of correlation maps associated with every seed-voxel of the brain while taking into account that the seed-ROI can change in size, shape and position. Some have proposed a tool for voxel-wise brain connectivity visualization but the method requires the pre-calculation of a voxel to voxel correlation matrix to be held in memory [3]. Great effort was also made towards GPU implementation of functional connectivity exploration [4] or for pre-surgical planning [5]. The proposed methods however restrict the user from placing their seed-ROI at any point in the 3D space which greatly reduces the level of interactivity. The user is forced to move the ROI solely on 2D anatomical slices, thus only revealing activations present on displayed slices. The AFNI toolbox also proposes a joint method for combining rs-fMRI and dMRI which demands the precomputation of whole-brain tractography with fixed parameters [6-8]. In this work, we propose an interactive tool for the exploration of brain connectivity in a fully 3D fashion, which can be coupled with our existing real-time multi-peak fiber tractography (RTT) robust to crossings module implemented in the *Fibernavigator* [9]. We qualitatively demonstrate how the functional and structural modules can be merged together to explore brain connectivity in an interactive fashion on both a healthy volunteer and a tumor patient datasets.

METHODS: Our new real-time functional exploration tool is implemented on CPU and runs on a single core computer, which does not require any specific hardware. It works on any fMRI data (e.g. resting-state) that is preferably pre-processed (i.e. motion and slice time corrected, spatial and temporal filtered). For anatomical reference, the user has to first load a subject-specific anatomical image (e.g. T1, T2, FA, b0, etc). By placing a seed-ROI in the 3D environment (anatomical space), one can instantaneously activate the functional correlation module while dragging the seed-ROI anywhere in the brain. The mean BOLD signal is first extracted from the voxels encompassed in the seed-ROI, and then statistically compared to the rest of the brain. The correlation coefficient (ccoef) between voxels x and y is denoted as: $ccoef = cov(x,y)/ \sigma_x\sigma_y$, where $cov(x, y)$ is the covariance of any two signals and σ_x σ_y are the standard deviations of the time series.

fMRI visualization: Ccoef's are then normalized to z-scores and rendered at each voxel as small particles, which are depth-sorted in real-time according to the orientation of the viewing axis. To reduce cluttering, the opacity (alpha) and size of each particle are weighted by their associated z-score value. This way, regions showing high correlations are displayed predominantly over less correlated ones. Interactive z-threshold and cluster-level sliders are also available for visualization purpose. Finally, the user can save and export the generated activation map into a 3D nifti file. As one can see, the computation step is performed in the native space (i.e. fMRI space) while the rendering stage is done at the anatomical level using the scaling transformation matrix associated to the anatomical and rs-fMRI datasets.

Datasets: Continuous functional recording was carried out on a Siemens 1.5 Tesla (T) imaging system using a standard echo-planar imaging (EPI) sequence. 35 axial slices were obtained with a 64x64 matrix, TR/TE 2730/40 msec, for a voxel size of 3.4x3.4x4.2 mm. High angular resolution diffusion imaging (HARDI) data was acquired using a single-shot echo-planar (EPI) spin echo sequence (TR/TE = 11700/98 ms, GRAPPA factor 2), with b-value of 1000 s/mm² and 64 uniform directions (128x128, 2 mm isotropic spatial resolution, fiber orientation distribution function (fODF) upsampled to 1 mm³, spherical order = 8). NLM denoising was performed on the raw diffusion data. Dataset 1 (*D1*) consists of a healthy volunteer and dataset 2 (*D2*) consists of a tumor patient with astrocytoma of grade III located in the motor cortex. The study was performed according to the guidelines of the Internal Review Board of the Centre Hospitalier Universitaire de Sherbrooke (CHUS).

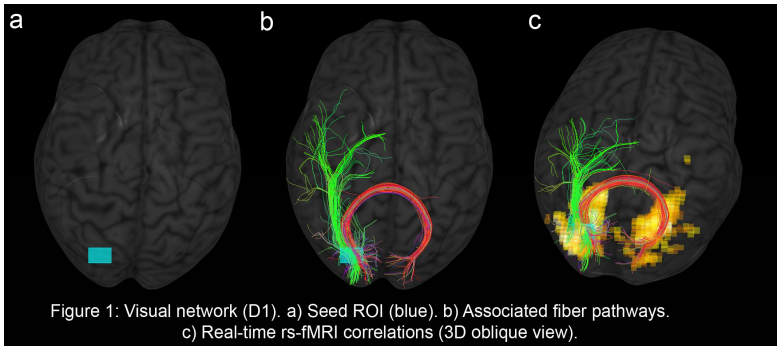

Figure 1: Visual network (D1). a) Seed ROI (blue). b) Associated fiber pathways. c) Real-time rs-fMRI correlations (3D oblique view).

RESULTS: Figure 1 demonstrates how the functional connectivity seed-ROI can be coupled with our existing RTT module [9], enabling the real-time reconstruction of the visual network by interactively placing a 10x12x8 mm seed-ROI within the visual cortex (z-score > 2.0, min. cluster size: 20 voxels, 1000 evenly distributed tractography seeds). Figure 2 illustrates how the method was applied for a neurosurgical intervention. A 10x10x10 mm ROI was interactively placed in the left lateral motor cortex, revealing associated right activations (known as the motor RSN, fMRI z-score > 2.0, min. cluster size: 20 voxels). The correlation map (28 000 voxels) was then directly injected as seed-ROI to the RTT module (1 seed per voxel), thus allowing the instantaneous reconstruction of the associated motor pathways. Tractography parameters were interactively set as the following (*D1*/*D2*): step size (mm) = 0.5/1.0, max angle (θ) = 35°, threshold (FA) = 0.2/0.15, min-max fiber length (mm) = 10-200, # of seeds = 1000/28 000. Experimentation was done on a laptop with the following specs: System: Linux Mint 32-bit, Video card: Geforce GT 640M memory 2GB, NVIDIA Driver: 306.97, CPU: Intel(R)Core(TM) i7-3632QM @ 2,20GHz, 16GB RAM. Mean frame-per-second (FPS) ratio remained above 20 when moving the seed-ROI in the 3D space which indicates acceptable interactivity level. It is important to note that the user has access to both tractography and rs-correlation parameters at all time during the interaction.

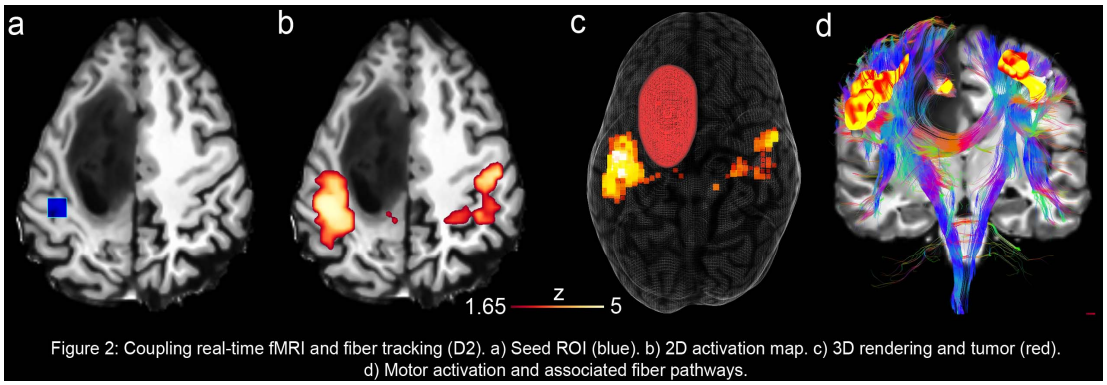

Figure 2: Coupling real-time fMRI and fiber tracking (D2). a) Seed ROI (blue). b) 2D activation map. c) 3D rendering and tumor (red). d) Motor activation and associated fiber pathways.

DISCUSSION & CONCLUSION: We presented here a new interactive exploration feature of the *Fibernavigator* [9] that allows fast reconstruction of functional and structural organization of the brain in a real-time 3D fashion. It gives convincing results on the fly and is an important tool to better understand how connections lie behind functional networks. It can also serve as a quality assurance tool at the individual level for close inspection of data prior to launching massive analysis. Tractography seeds are either initiated directly from the interactive seed-ROI or from the generated rs-fMRI correlation clusters. Alternatively, the end points of each streamline can also serve as seed-ROI for rs-connectivity. Finally, our real-time technique can be used for clinical applications and is achievable without complex GPU programming. Supplementary video data showing the real-time interactive tool in action can be found online at: *www.youtube.com/watch?v=ZDZUcJMhL_c*.

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