A new proposed workflow for processing high spatial resolution MRI data with multiple sessions

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Abstract:

In recent years, there has been a surging interest in high spatial resolution (high-res) fMRI at 7T, given the obvious benefits of increased BOLD contrast and spatial resolution compared to 3T fMRI. Even though 7T high-res fMRI is often limited to partial brain coverage and has mostly been applied to primary cortices, a growing interest has arisen to image sub-cortical regions, such as the hippocampus. Unfortunately, inter-session registration of high-res fMRI data remains challenging, as high-res fMRI is extremely sensitive to differences in head position and orientation, which can result in distortions, as well as regions of dropouts and artefacts. Here, we present a workflow that has been developed for the preprocessing of small field-of-view, multi-session and sub-millimetre resolution fMRI data of non-neocortical structures. Using two metrics to evaluate the quality of image registration, we show that our pipeline performs exceptionally well on multi-session high-res fMRI data acquired over the course of two days. In addition, the pipeline was successfully applied to all subjects, allowing for a meaningful analysis of hippocampus layers.

Keywords: 7T fMRI; high spatial resolution; spatial navigation; hippocampus

Introduction

With the advent of 7T scanners, researchers are now able to image the human brain at an unprecedented mesoscopic scale. One growing body of research work has been devoted to investigating and validating layer-fMRI under various experimental settings, such as during episodic memory tasks, language processing or working memory (Maass et al., 2014; Sharoh et al., 2019; Finn et al., 2019). Most research studies have examined activity in cortical layers in the primary cortices due to a well-established correspondence between cortical depths and cytoarchitectonic cortical laminae (Finn et al., 2021). By contrast, laminar fMRI studies targeting subcortical brain sites are limited, due to acquisition and analysis challenges in addition to the inherent variability in the human brain between relative cortical depth and underlying neuronal layers.

Despite impressive demonstrations of sub-millimetre fMRI imaging, there is still a noticeable lack of readily-available packages that can accurately preprocess ultra high-field resolution fMRI data, particularly when small fields-of-view are involved and data is acquired over multiple sessions. In addition, preprocessing pipelines that have been used in the literature are most often custom-tailored to the needs of each specific project, and, therefore, tricky to generalise to other datasets. A robust pipeline that can be empirically evaluated is, thus, of paramount importance.

We present a stable and robust containerised BIDS-compliant pipeline that requires minimal input from the user and that can be applied to a multitude of ultra high-resolution datasets building upon our previous work (Kashyap et al., 2021). The integrated workflow primarily uses ANTs (http://www.github.com/ANTsX/ANTs) for a majority of registration steps, as well as tools from community standard neuroimaging software (such as, Freesurfer, SPM, AFNI, FSL) for various intermediate steps such as skull-stripping and denoising.

Methods

In order to test our pipeline, we used four high-resolution functional MRI datasets from an ongoing spatial navigation study, collected on a 7T MRI Siemens Magnetom Terra scanner.

Subjects were scanned during the course of two days. On the first day, an anatomical 3D-MP2RAGE (voxel size = 0.75 mm^3, TR = 6 s, TE = 0.002 s, TI1 = 0.8 s, T2 = 2.7 s, FOV = 192 x 255, flip angle = 5°, no. of slices = 340) and TSE (voxel size = 0.44 x 0.44 x 1.5 mm, TR = 8 s, TE = 0.08 s, FOV = 225 x 225, flip angle = 160°, no. of slices = 40) scans were acquired, followed by two functional imaging runs (voxel size = 0.8 mm^3, TR = 2.5 s, TE = 0.03, FOV = 192 x 192, flip angle = 14°, no. of slices = 38, acceleration factor = 4 with GRAPPA reconstruction) and their corresponding opposing phase-encoding scans. On the second day, four additional functional runs were acquired (same parameters as above), giving a total of 6 functional runs per subject.

During the functional runs, subjects had to perform a spatial navigation task (Kunz et al., 2015). In short, six occluded objects were scattered across a circular virtual arena and subjects were instructed to navigate to each of them in separate trials (3 repetitions per object, giving a total of 18 trials; see Fig. 1).

Briefly, our workflow initially realigns the functional and opposite phase-encoded data and subsequently performs distortion correction using ANTs for each run in each session. Inter-session alignment is done using the corrected run-wise data and the transformation from functional to anatomical space is estimated using the boundary-based registration (BBR) algorithm (Greve & Fischl, 2009) in FSL, as it outperforms typical cost functions in data with the signal dropouts and artefacts (e.g., in ventral/medial temporal lobes). All matrices andwarps are preserved and are concatenated and applied in a single resampling step to reduce interpolation errors. Motion and QC plots are generated using Python. For layer-fMRI analysis, we used HippUnfold (DeKraker et al., 2022) to extract hippocampal layers (Figure 3) and in-house Matlab scripts.

Results & Discussion

To evaluate the quality of the inter-session registration we calculated two commonly estimated image quality metrics for our example participant. First, the structural similarity index measure (SSIM) between intra and inter-session aligned images was shown to be 0.92 and 0.87, respectively, which is suggestive of a high-degree of similarity between the images (a value of 1.0 indicates perfect alignment). Similarly, the normalised root mean squared error (NRMSE) between the two images was 0.041 and 0.065 for intra- and inter-session, respectively, indicating a very small difference between images (a value of 0 indicates perfect alignment).

After preprocessing all subjects using our pipeline we proceeded with the analysis of the spatial navigation task for the different hippocampal layers (Figure 3). As shown in Figure 4, we were able to show that distinct navigation strategies were differentially related to subregion-specific laminar profiles.

Using state-of-the-art ANTs functionality, the results of this study showed that our proposed pipeline for preprocessing ultra high-field resolution fMRI data provided a very accurate registration between functional and anatomical scan, and a very good alignment of the hippocampus over runs, despite the relatively small FOV used in the present study. Importantly, accurate results were obtained regardless of whether registration was performed within sessions (on same-day runs) or between sessions (between different-day runs), and the resulting preprocessed images enabled a meaningful analysis of hippocampal laminar activity.

In sum, our pipeline is a robust and reliable tool to the preprocessing of 7T high-res fMRI data, regardless of FOV size or number of sessions. Being built as a Docker-based containerised pipeline, all software dependencies are managed internally, simplifying and facilitating its usage, which we believe will appeal to the wider neuroscience community.

Figures

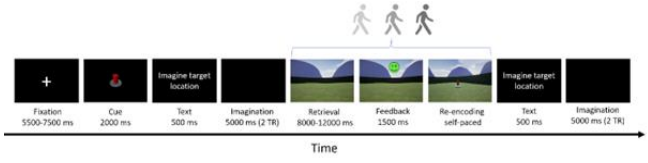

Figure 1: Overview of the paradigm. Each trial began with presentation of a fixation cross. This was followed by displaying an object (cue) which subjects had to place accurately in its correct location later in the retrieval phase. They were asked to imagine the target location, navigate, and drop the object. Feedback was provided based on drop error (Euclidian distance between drop location and the correct location of the object). When the object was shown at its correct location, they re-encoded it by walking to that location. Trials were ended by a second round of imagination. Two putative navigation strategies were derived based on participants' movement in the navigation phase i.e., straightness index (SI) and median deviation to boundary (MDB).

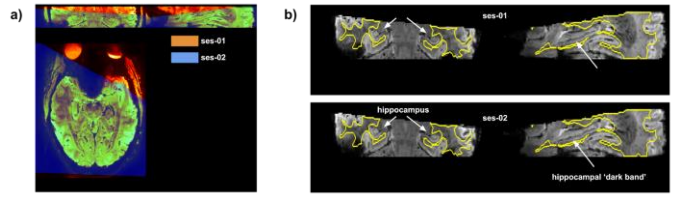

Figure 2: (a) Example subject with a slab orientation discrepancy between scan sessions. The pre-processed native space output for session 01 (ses-01) and session 02 (ses-02) are shown here in orange and blue shades, respectively. The hippocampal ROI is fully captured in both sessions. (b) White matter boundary from T1w data overlaid on the motion- and distortion-corrected mean EPI in native space. Arrows highlight the hippocampus ROI, and preservation of anatomical features after preprocessing in EPI data (dark band).

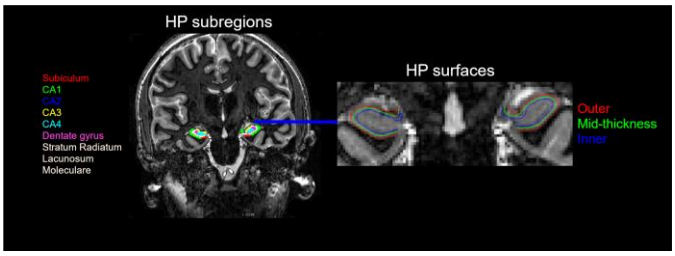

Figure 3**:** Hippocampal layers after running HippUnfold

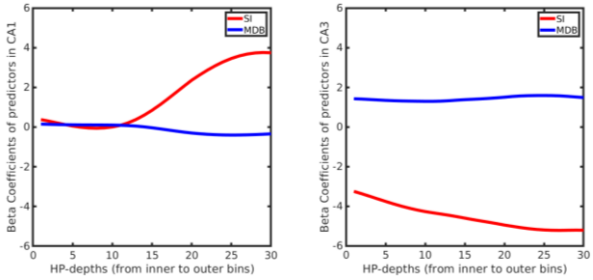

Figure 4: Straightness Index (direct divided by observed path length per trial; SI) positively correlated with laminar activity towards to outer bins of CA1, while showing a negative linear decrease across the laminae of the CA3. Conversely, Median Deviation Boundary (direct minus observed distance per trial; MDB) does not seem to vary across depth of CA1 and CA3

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