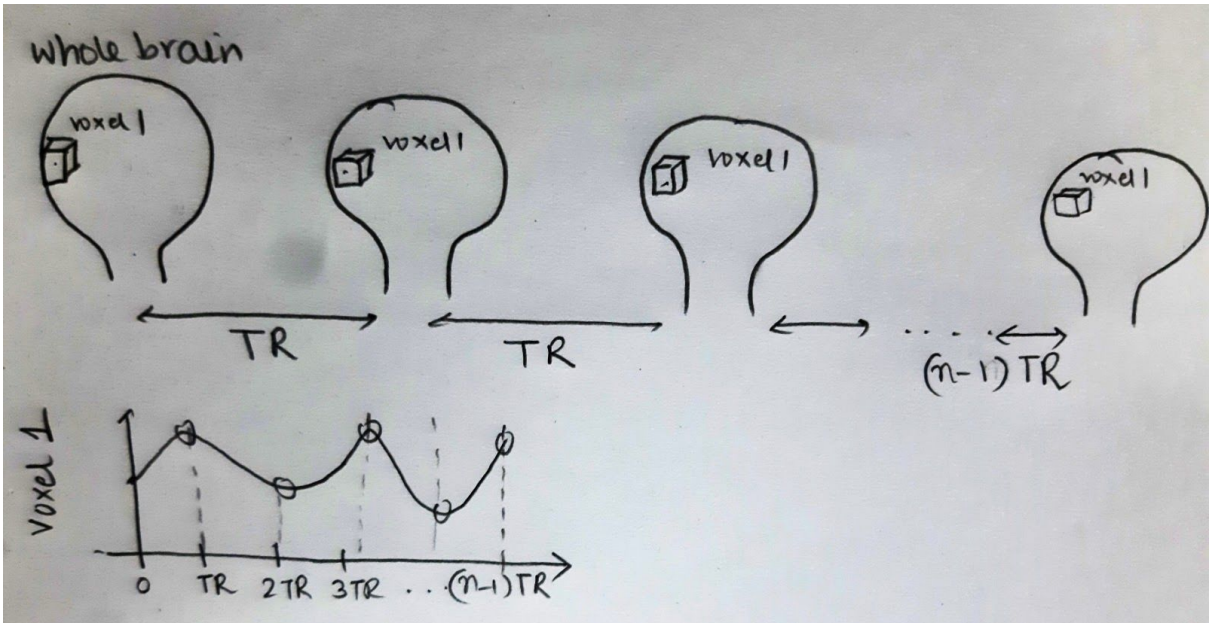
Slide 26: Steps within the fMRI Pipeline:



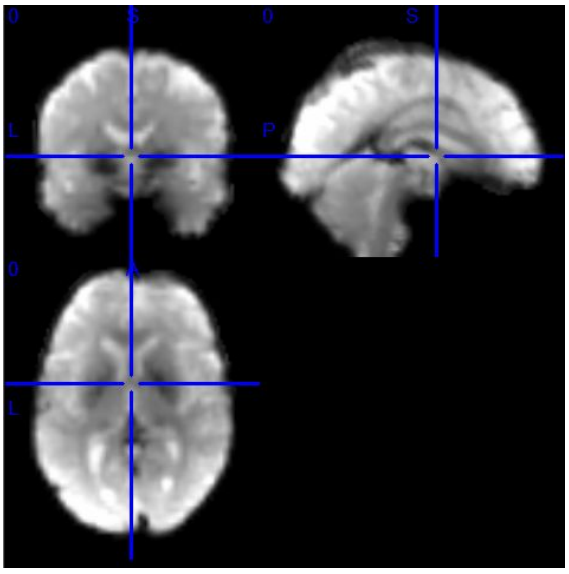
Before we begin, the above image depicts a very simplistic idea of what a whole brain fMRI scan entails.

- Several whole brain images are collected at **TR (time of repetition)** intervals.
- Each whole brain volume is built up of several **voxels (**volume pixels).
- The BOLD activity of each voxel, measured at each TR, is strung together to create the time series for that voxel

Returning to the slide:

1. The first step mentioned here is to generate something called a **'reference volume'.**
    a. Even though fMRI scans are generally done with the head fixed in place, the subject is likely to move his/her head slightly in the course of the scan. As seen in the above image, **if the position of the voxel itself changes from one volume to the next**, the time course of that voxel will no longer be reliable.
    b. To ensure all the head volumes are aligned with each other (can be perfectly overlaid on one another), we need to **pick one volume to align all other volumes to.** This is the reference volume. In fmriprep, this is automatically the middle volume in the scan.
    c. To ensure a clean reference image, we get rid of the parts of the middle volume that are not important to our analysis. This includes the skull and other surrounding tissue, thus only leaving the brain. This is called **skull**

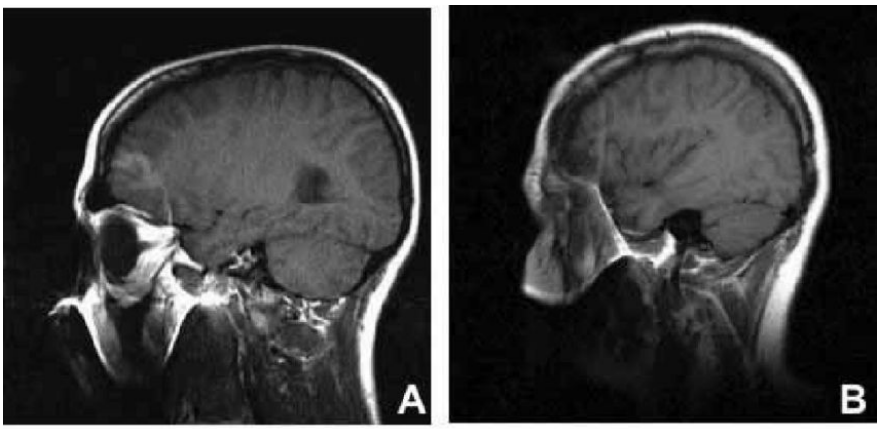
stripping. A skull stripped BOLD volume has been shown in the figure below.



2. Once the BOLD reference volume has been skull stripped, the next step is to **align the reference with the T1(structural) image.** The spatial resolution of a BOLD image is quite poor when compared to a T1 image. Registering the BOLD reference to the T1 image will allow the **overlaying of activity onto a highly structured image.** This will make the process of head motion correction and normalization that follow much more accurate. *The tool fmriprep uses for this is FSL's FLIRT tool.*

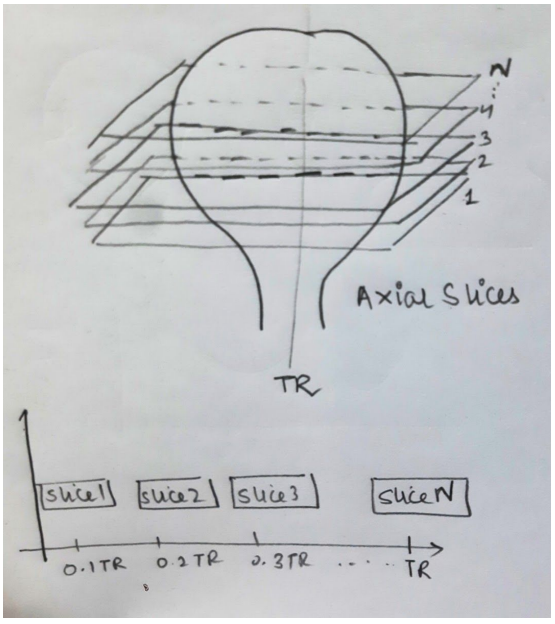
3. Now that the skull stripped, T1 aligned BOLD reference volume is ready, the next step is to compute how much, and in what way, each volume will have to be transformed (rotation, translation etc.). FMRIprep computes these matrices and stores them using a tool called McFLIRT from FSL. **It doesn't apply them yet.**

4. **The magnetic field lines within a scanner can be distorted depending on the magnetic susceptibility of the objects within it.** This can in turn cause distortions in the recorded BOLD activity, from what would have been if the field had been uniform. Using fieldmaps - which are intuitively snapshots of what the magnetic field looks like inside the scanner at a given point, these distortions can be corrected. This is called **Susceptibility distortion correction.** Fmriprep computes and stores the changes that will have to made to each volume, but **doesn't apply them yet.**



Susceptibility distortion caused due to dental implants - https://www.researchgate.net/figure/A-Sagittal-T1-weighted-MR-image-clearly-showing-distortion-around-jaw-from-gold-crown_fig1_24214125

5. Following the computation of the head motion and susceptibility distortion correction parameters, fmriprep computes **slice timing correction parameters**.



   a. Due to MR Physics constraints, scanners cannot collect the whole brain's BOLD activity at the same instant. It is instead collected in **2D slices,** which are generally **axial** in nature.
   b. As there is a time lag from moving from one slice to the next, **each slice is recorded in a different period within the TR period** (as shown in the illus. above)
   c. However, our definition of a time series **assumes each voxel in a volume is collected at the exact same time instant** (the end of 1 TR).
   d. Thus, to avoid a time lag in recording the activity of different voxels within the same volume, slice timing correction parameters are computed **to interpolate the time series such that it seems as if all voxels in a volume were recorded in the same instant.**
   e. **These slice timing parameters are both computed and applied at this stage.**

6. Now, either the 6th or 7th step (only 1) as described in the slide, is applied. If we choose to sidestep the normalization, a **concatenated matrix of the head motion and susceptibility distortion correction matrices is applied in one shot.**

7. If we choose to go forward with the normalization, the normalization parameters are also computed, concatenated with the aforementioned transformation matrices and applied in one go. **Normalization is the process of aligning the subject's brain scan to a standard brain (generated by averaging several brains - 152 in the MNI152 template), so that comparisons between subjects can be performed**. In the absence of normalization, the preprocessed scan will remain in the subject's native space.

Slide 27: fmriprep Supplementary Files - Self Explanatory

Slide 28: Functional Output Files:

Fmri-Prep generates 3 functional intermediate and output files:

1. The middle volume that has been chosen as **reference** (prior to the skull stripping and T1 registration)
2. The **functional brain mask** - as the final preprocessed BOLD file is not skull stripped, fmriprep provides a brain mask to perform skull stripping additionally at the end, if your analysis requires this. This can be done with **FSL's BET tool:** https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/BET/UserGuide
3. The final preprocessed functional file.

It is a good idea to open these files up in fslview to see if they look right. Particularly, the functional brain mask can be overlaid on the subject's T1 to see if the alignment is correct.

Slide 29 & 30 : Structural Output Files:

Fmriprep provides several intermediate structural files - particularly the GM, WM and CSF images prior to and post MNI registration. Additionally, it provides brain contour images that can be used to skull strip the T1 separately if required.

Slides 31 to 34: Visual Quality Assessement Reports

This is the link to the documentation that details how Visual Quality Assessment Reports can be analyzed: https://fmriprep.org/en/stable/outputs.html

Slide 35: Common Errors and Troubleshooting

This is the link to the list of common errors I encountered in running fmriprep: https://docs.google.com/document/d/1d5750a3RG245S5ME4fcds9z_lGkMTYqAxF4jlXwJ3sc/edit?usp=sharing