LARGE Lesion Brain Alignment with AFNI

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Introduction:

Alignment to a standard template is typically done in MRI and FMRI processing, facilitating statistical testing across subjects, analysis on atlas regions in the template space and permits a common set of coordinates. For many studies, this is a straightforward procedure, consisting of affine and nonlinear alignment to the template. Patient studies with surgical resection procedures such as hemispherectomy or lobectomy, and large stroke lesions present challenges to both standard volumetric and surface processing pipelines. Furthermore, edema on the contralesional hemisphere presents large distortions. Here, we introduce a new program, **lesion_align**, in the AFNI software for alignment of data with large lesions. We show examples of usage with extreme cases from a hemispherectomy dataset by moving atlas regions from the standard MNI template space to each subject's native space and computing a region of interest analysis in the native space. The key finding was an increase in the number of negative correlations only between regions in patients compared to controls indicating a form of resculpting connectivity perhaps as a means of post-surgical cortical reorganization.

Methods:

T1 data (1mm3) and BOLD EPI scans (3 6-min runs: 2mm isotropic, TR=2s) from 9 patients (with unilateral resection, 9-17 yo) and 9 age/sex-matched controls were used for validation.

The new program aligns the subject dataset to half a brain template with an option to determine the "good side". It proceeds first with an affine alignment for half the template brain to move the subject brain roughly to the template space. A slightly dilated mask of the full subject brain in affine template space is nonlinearly aligned to the template. Special considerations here allow for larger distortions. The atlas data is transformed from template to native space of the subject by inverting the transformations. Modal smoothing is done to improve contiguity of the atlas regions after distortion in the nonlinear and affine warps, where each voxel is replaced by the most common atlas region in a 2 voxel neighborhood.

Functional Connectivity (FC) of 22 HCP networks in native space were computed separately as positive and negative correlations, in healthy hemisphere in patients and in both hemispheres in controls. Leave-one-out testing was used to obtain the number of network pairs more than 2 standard deviations (SD) away from group mean in controls.

The program was further evaluated with data from the ATLAS database of 304 stroke subjects from a varied set of scanners and sites and with CT data from Oxford stroke subjects acquired as part of the Oxford Cognitive Screening study.

The program also provides a set of mirrored and "healed" lesion-free brains in the native and template spaces.
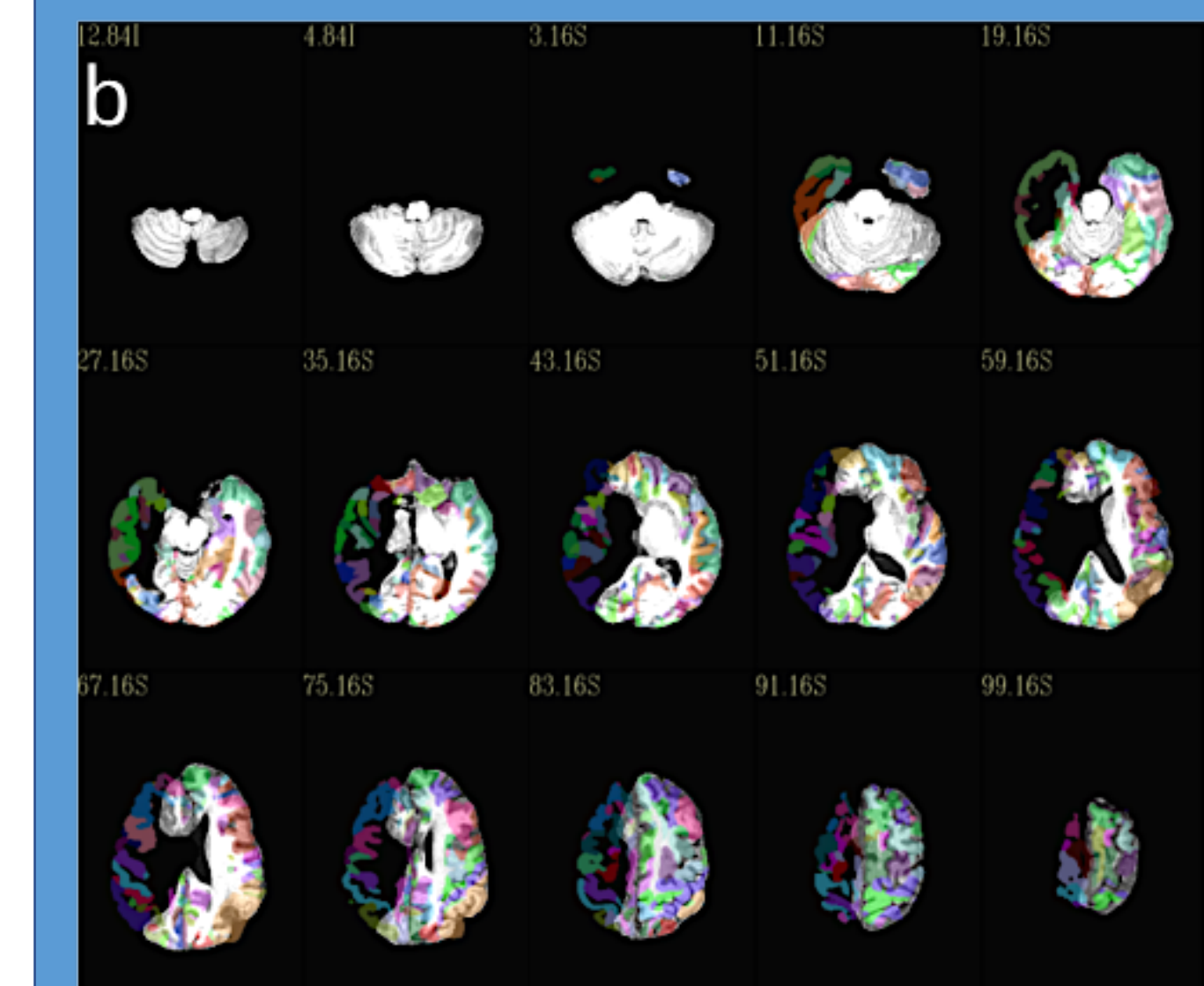
CT lesion alignment – HCP Glasser atlas brought to native space of CT using SCCT MNI CT template. CT data acquired as part of the Oxford Cognitive Screening study.

AFNI usage example:

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lesion_align –input Subj2+orig              \
        –base MNI152_2009_template.nii.gz   \
        –atlas MNI_Glasser_HCP_v1.0.nii.gz  \
        –outdir lesion_align –goodside right
```

Subject MRI → "good side" of template (MNI 2009c here)

Affine alignment

Affine-aligned Subject → template masked by dilated affine subject

Nonlinear alignment

Subject in template space (unifized and skullstripped) → Atlas (HCP Glasser here) in template space (modally smoothed)

Combine transformations

Invert transformations

"HEALING" BRAINS

a. MNI mirrored subject – subject "good side" mirrored in template space
b. Mirrored + filled – blends original subject with the full mirrored subject transformed from template space
c. Mirror filled - mirroring only in lesion to fill
d. Template-filled subject – template in subject "bad side"
e. Template-half subject - template values fill in lesion
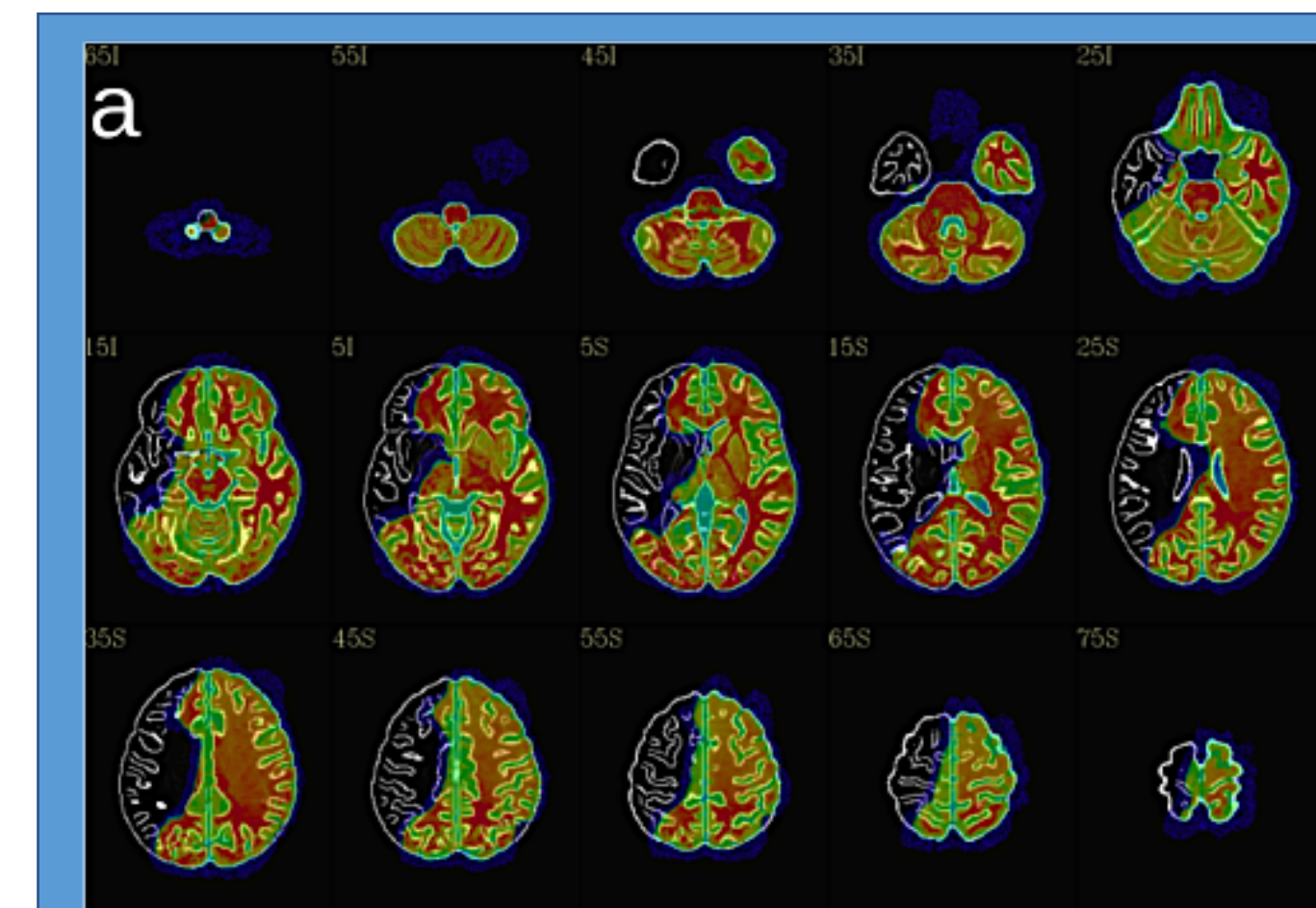
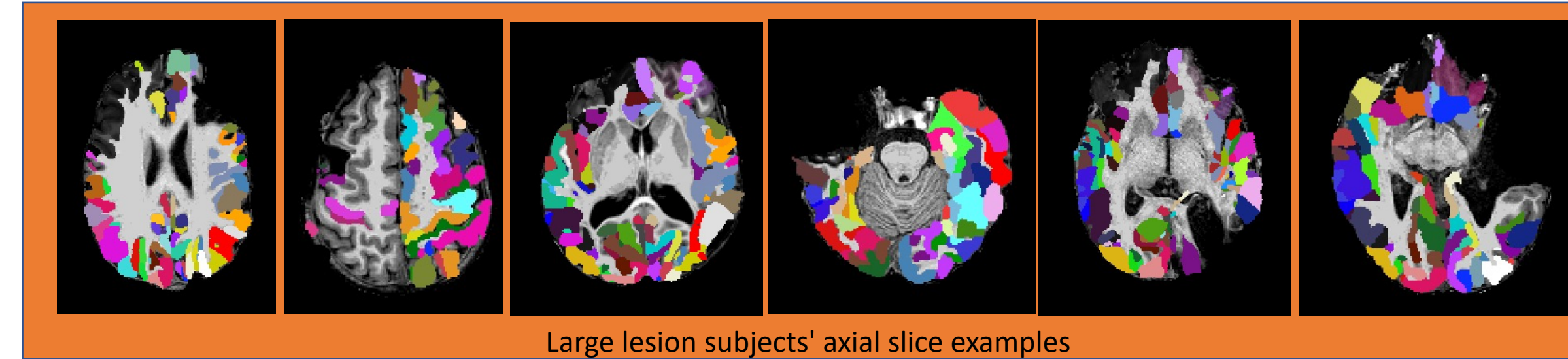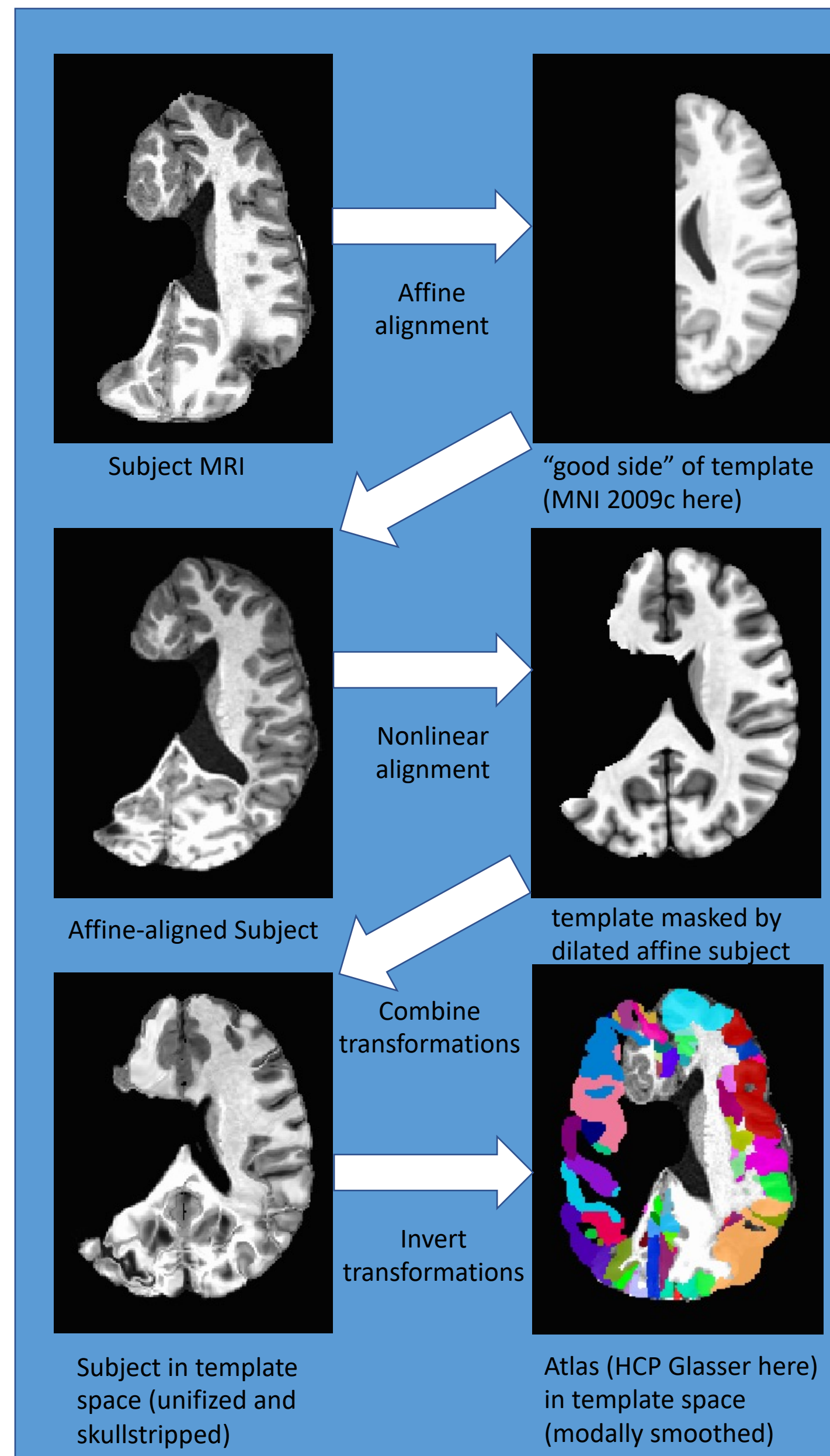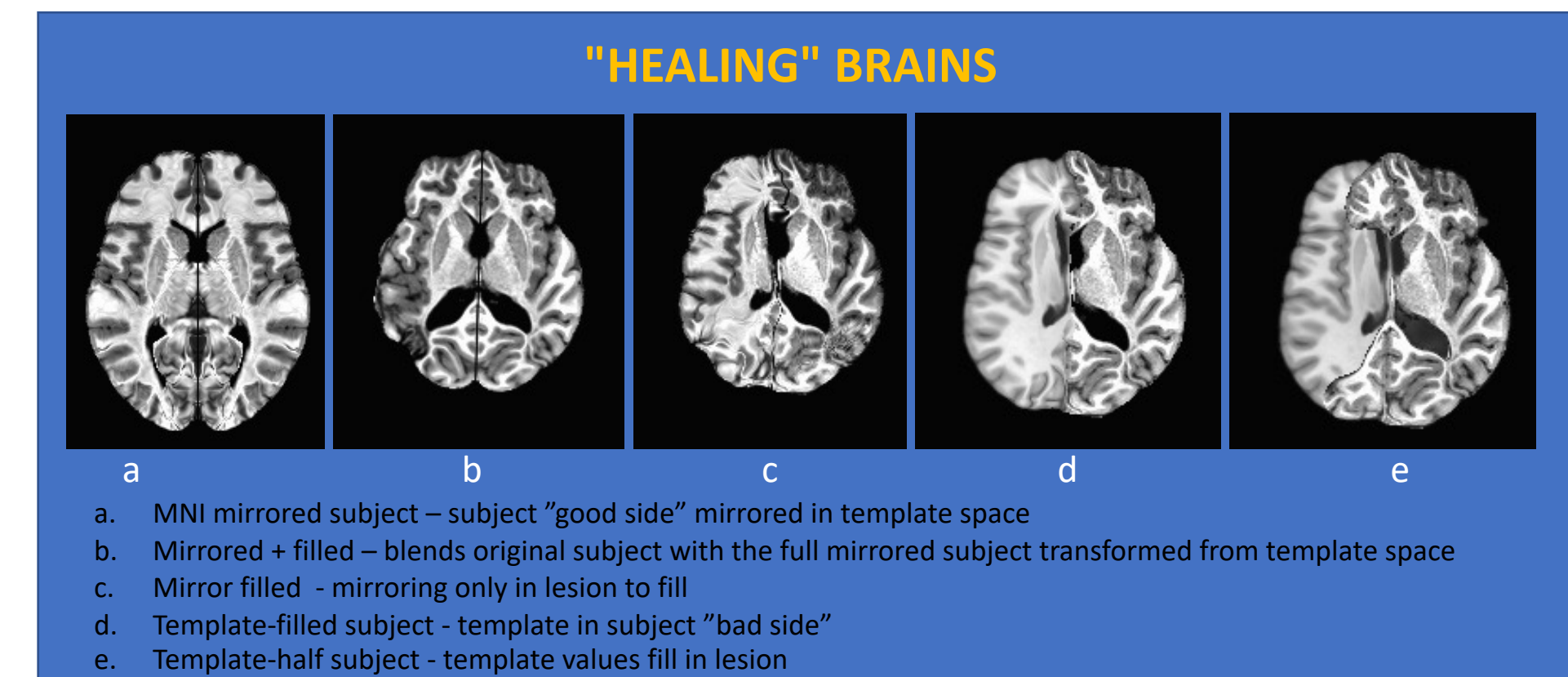Large lesion subjects' axial slice examples

Fig. 1. Lesion subject alignment – QC Report
a. alignment of patient dataset (in color) to template (white edges) in template space
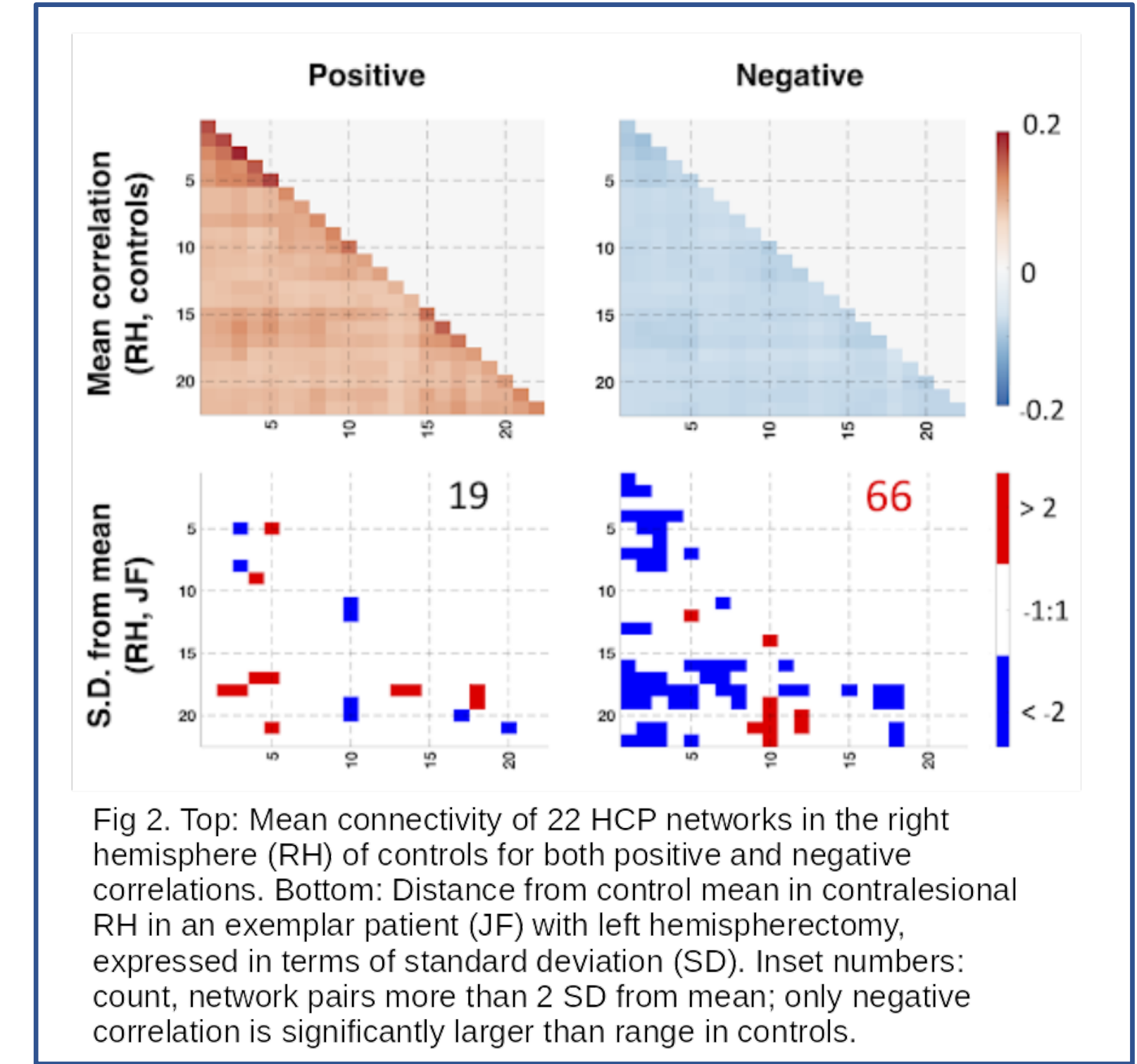b. alignment of atlas (HCP Glasser, in color) to subject native space (gray scale)

Fig 2. Top: Mean connectivity of 22 HCP networks in the right hemisphere (RH) of controls for both positive and negative correlations. Bottom: Distance from control mean in contralesional RH in an exemplar patient (JF) with left hemispherectomy, expressed in terms of standard deviation (SD). Inset numbers: count, network pairs more than 2 SD from mean; only negative correlation is significantly larger than range in controls.

Results:

The new procedure successfully aligned all large lesion subjects to the template. Fig 1a shows the transformation of a subject to template space. The template is shown only as edges in white with a T1 dataset in color. Fig 1b shows the HCP atlas in the native subject. Fig 2 shows the group mean of positive and negative FC (red, blue) in controls' right hemisphere. Differences in FC from an exemplar patient with left hemispherectomy are shown in terms of SD from mean. We found only the negative connectivity (66 alterations) was significantly greater than the expected range in controls.
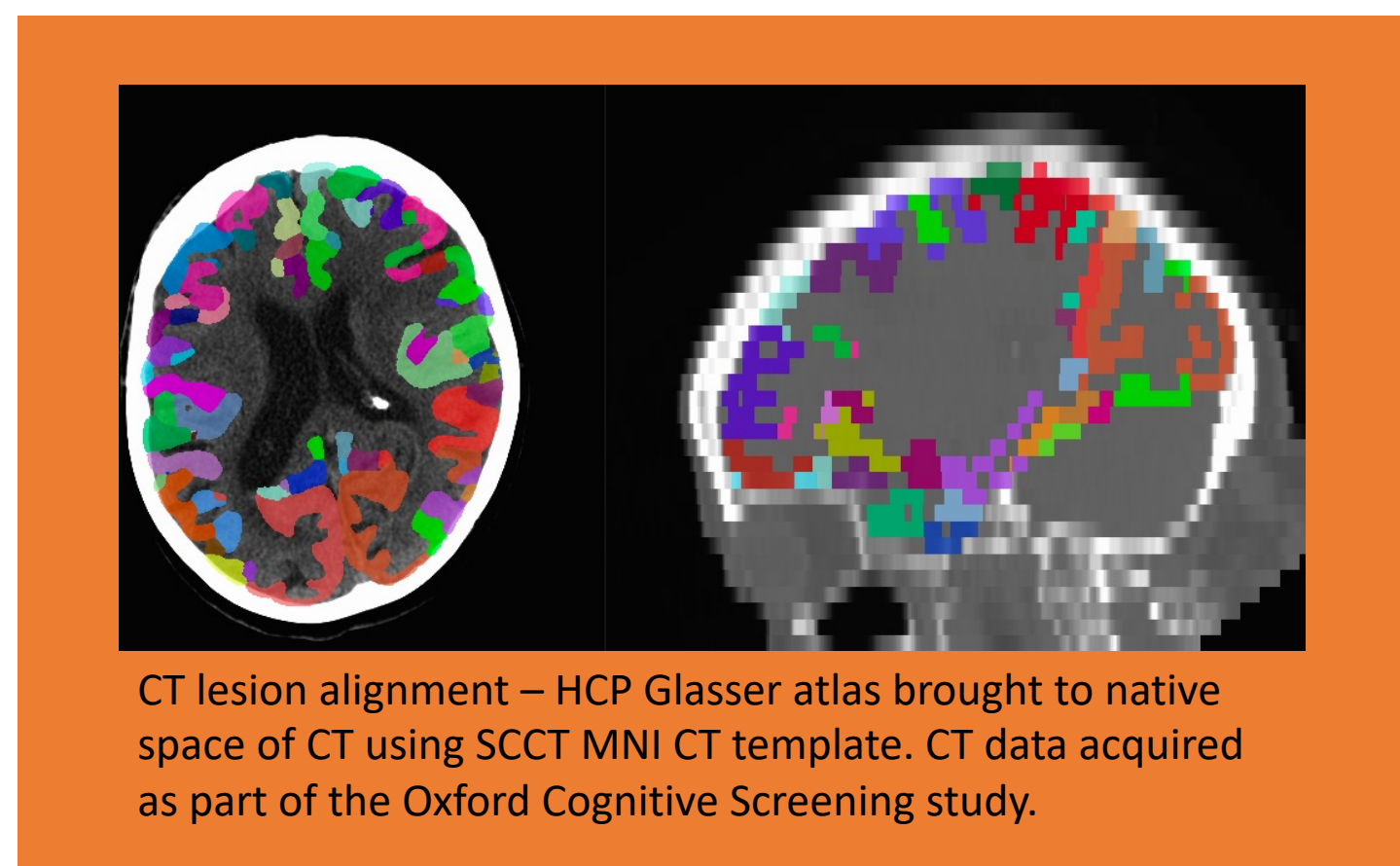
This procedure is robust to a wide variety of extreme lesions and resections. It uses half a template to match the original brain rather than mirroring (the "enantiomeric" solution). Both approaches take advantage of the usual situation that half the brain will be similar to a typical brain template. The program allows for analysis in standard or native space, depending on research goals.

While the program computes whole brain alignment including areas around the lesion, the regions on the lesion side will be suspect. Depending on lesion size, perilesional transformations can not be used for all but the most approximate region analysis. Here we use only good-side for analysis with minimal user intervention allowing reproducible work on images with large lesions.

Most stroke lesions are smaller than the hemispherectomy and lobectomy lesions, the main application of this program. With the ATLAS Stroke Lesion database, the program was able to provide good alignment for 90% of subjects using the lpa cost function for alignment and 95% with the nmi cost function. In comparison, the AFNI standard @SSwarper template alignment program was able to align all (100%) of the subjects. Unless the large distortion, the healing brain role of this program or a different template is needed, consider using @SSwarper instead for brains with smaller lesions, but lesion_align will do a reasonable job in most cases.

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