

Medical/Bio Research Topics II: Week 05 (05.10.2023)

Structural MRI: practice in data processing

(구조 자기공명영상: 데이터 처리 실습)

Alzheimer's Disease and Mild Cognitive Impairment

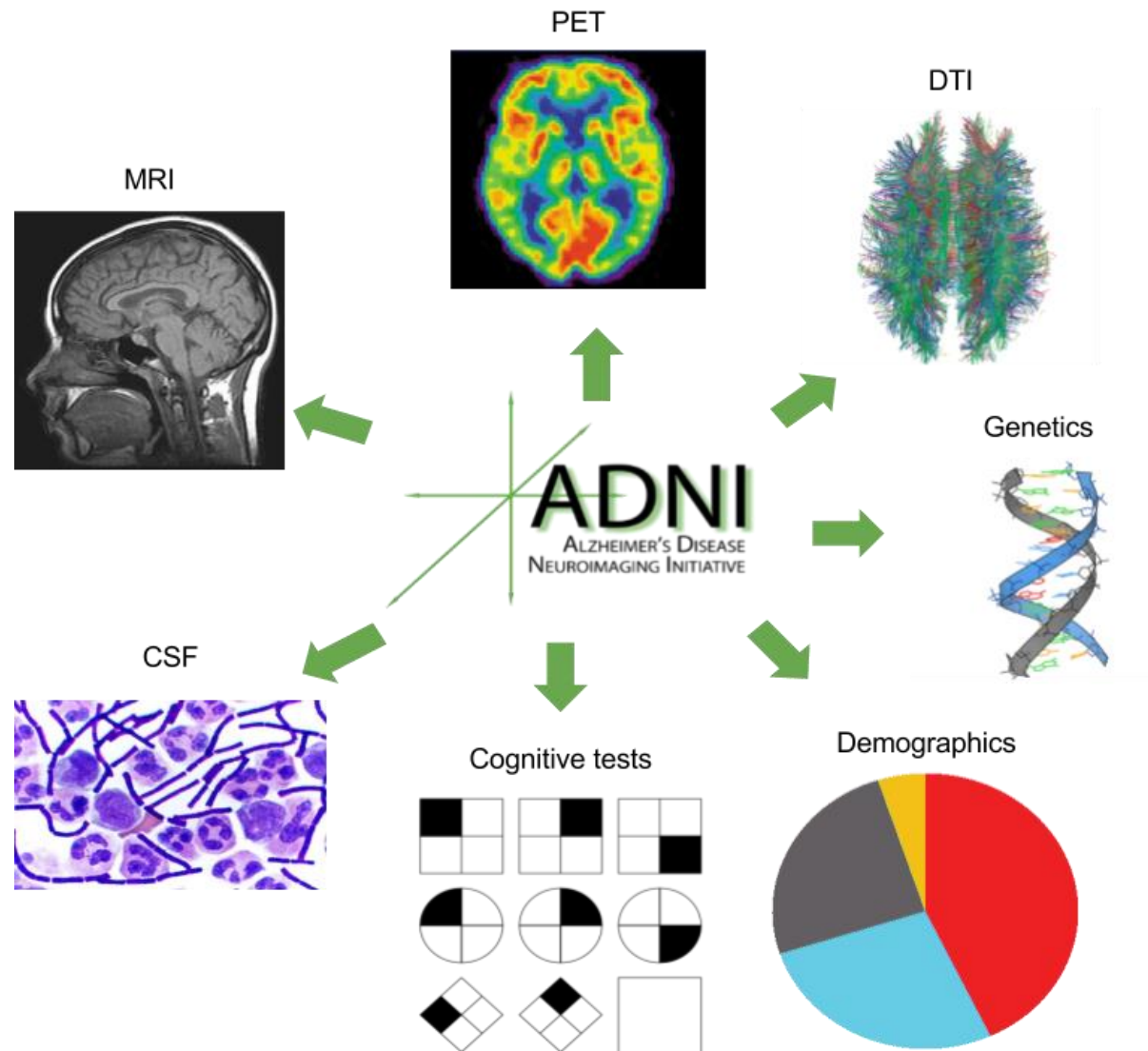
- Alzheimer's disease
 - Neurodegenerative disease that usually starts slowly and progressively worsens
 - As of 2020, approximately 50 million people worldwide with Alzheimer's disease
 - Most common cause (60% to 70%) of dementia
 - While the causes of Alzheimer's disease are not yet fully understood, there are many environmental and genetic risk factors associated with its development

- Characterized by the accumulation of amyloid beta ($A\beta$) and hyperphosphorylated tau, and loss of neurons and synapses in the cerebral cortex and certain subcortical regions, resulting in gross atrophy of the affected regions, including degeneration in the temporal lobe and parietal lobe, and parts of the frontal cortex and cingulate gyrus
 - Known to target the hippocampus which is associated with memory
- Memory impairment is the key symptom of Alzheimer's disease, and memory gets worse and other symptoms develop as the disease progresses

- A probable diagnosis is based on the history of the illness and cognitive testing, with medical imaging and blood tests to rule out other possible causes
 - Clinical and cognitive measures lack both sensitivity and specificity to detect the pathology of Alzheimer's disease
- No treatments can stop or reverse the progression of Alzheimer's disease, though some may temporarily improve or slow the progression of symptoms

- Mild cognitive impairment (MCI)
 - Related to the notion that the progression of Alzheimer's disease can be defined by three broad time periods from the preclinical phase, to MCI, followed by Alzheimer's disease dementia
 - Often found to be a transitional stage between normal aging (expected decline in memory or other thinking skills that happens with age) and dementia (more serious decline in memory or other thinking skills)
 - Estimated that between 5% and 20% of people aged over 65 have MCI
 - Symptoms are not severe enough to interfere significantly with daily life
 - Not a type of dementia, but has a significant risk of developing dementia

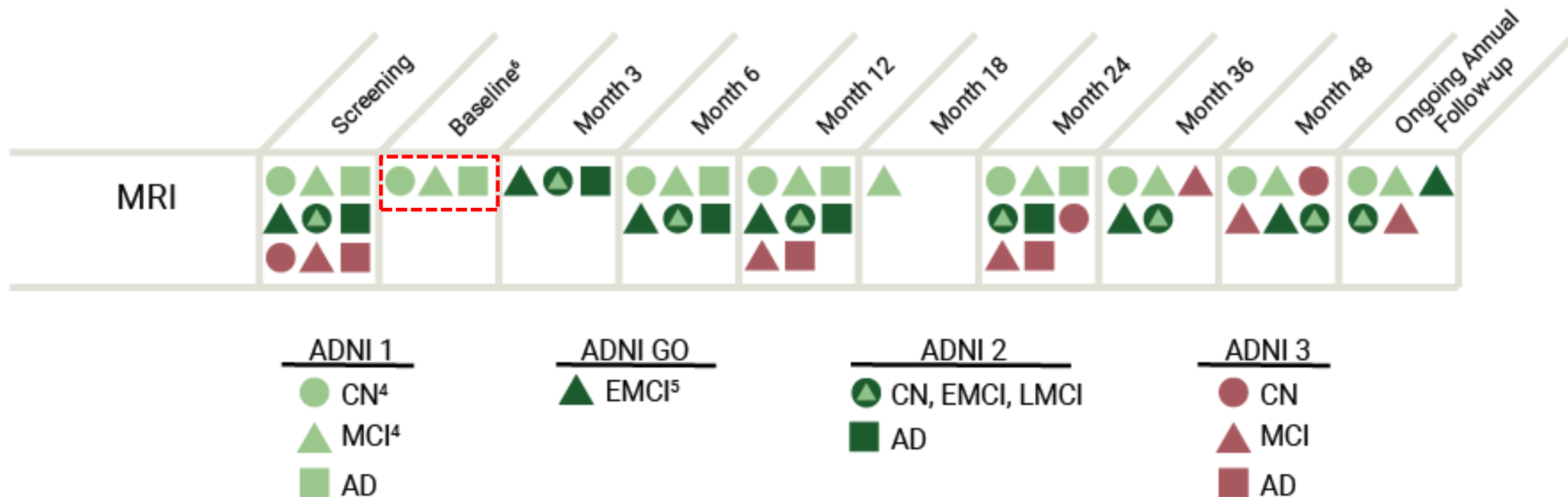
- Alzheimer's Disease Neuroimaging Initiative (ADNI) study (<https://adni.loni.usc.edu/>)
 - Launched in 2004
 - Collects, validates, and utilizes data, including MRI and PET images, genetics, cognitive tests, cerebrospinal fluid, and blood biomarkers as predictors of Alzheimer's disease
 - Aimed at determining the relationships between clinical, cognitive, imaging, genetic, and biochemical biomarkers across the entire spectrum of Alzheimer's disease



[\[https://tadpole.grand-challenge.org/Data/\]](https://tadpole.grand-challenge.org/Data/)

Data collected through the ADNI study

- MRI data collected through the ADNI study
 - Structural MRI (sMRI)
 - Diffusion-weighted MRI
 - Perfusion MRI
 - Resting state functional MRI



[\[https://adni.loni.usc.edu/data-samples/data-types/mri/\]](https://adni.loni.usc.edu/data-samples/data-types/mri/)

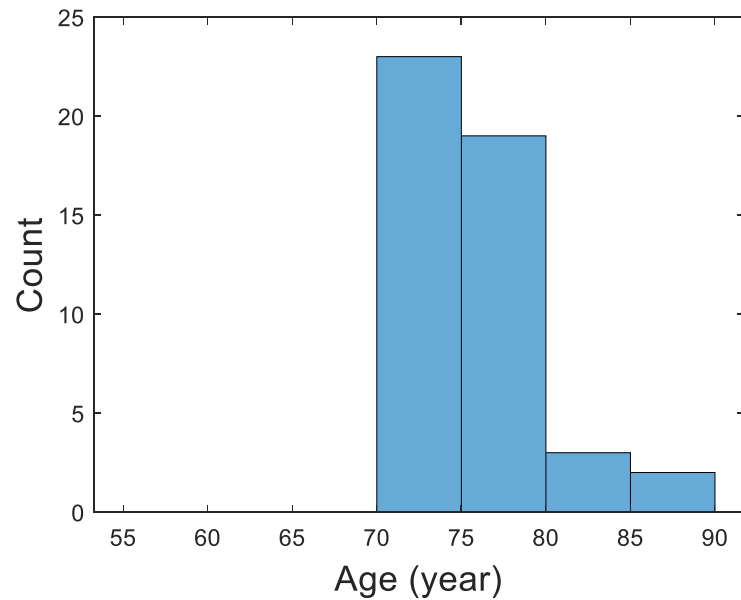
Collection of MRI data through the ADNI study

Dataset

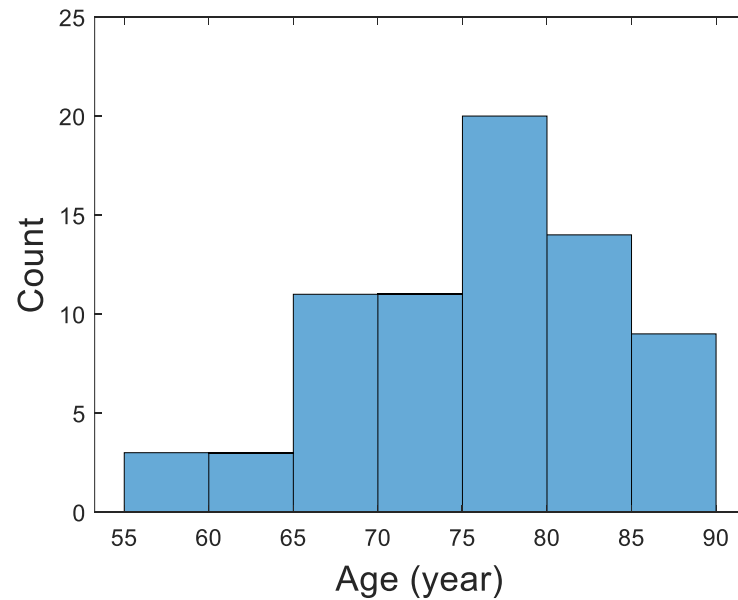
- Baseline of the ADNI1 study
 - CN (healthy elderly individuals): $n = 47$
 - Age: 75.1 ± 3.9 years
 - Sex: 29 women and 18 men
 - MCI (individuals with mild cognitive impairment): $n = 71$
 - Age: 75.1 ± 8.1 years
 - Sex: 26 women and 45 men

– AD (individuals with Alzheimer's disease): $n = 33$

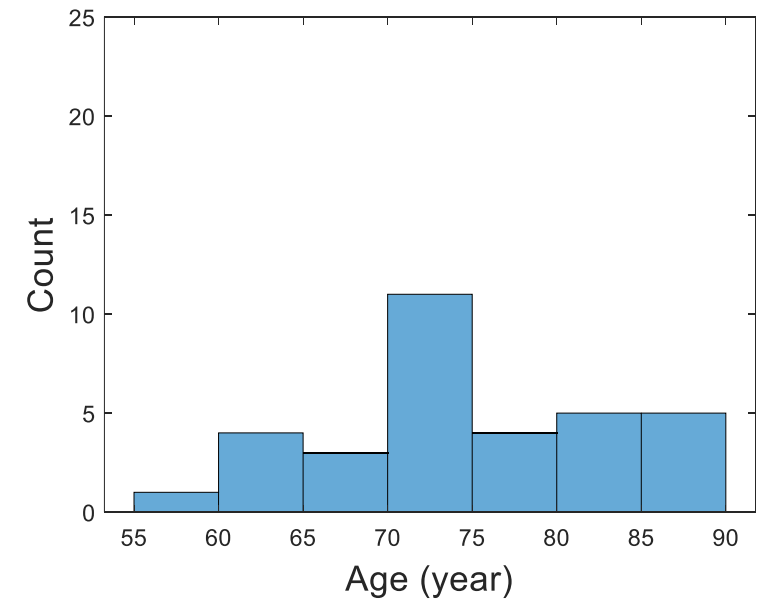
- Age: 74.0 ± 8.1 years
- Sex: 22 women and 11 men



CN



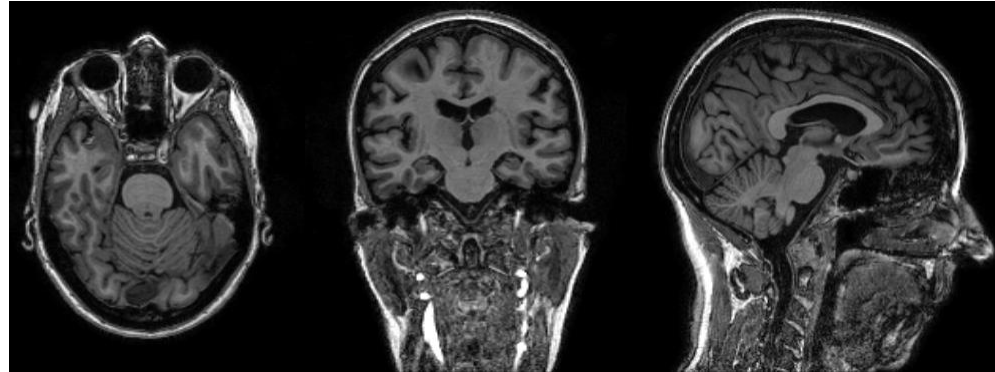
MCI



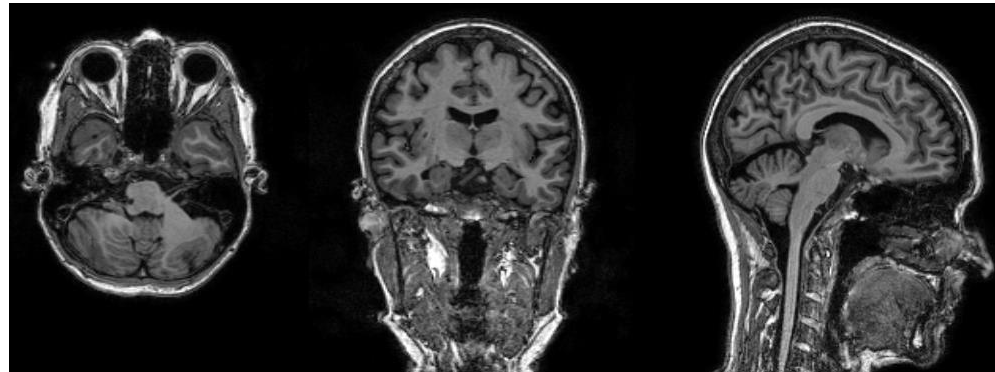
AD

- sMRI data
 - Magnetization prepared rapid gradient echo (MP RAGE): three-dimensional, T1-weighted, gradient-echo sequence
 - Dimensions: $(256 \times 256 \text{ sagittal plane}) \times 170 \text{ slices}$
 - Voxel depth: 32-bit float
 - Voxel size: $1.0 \text{ mm} \times 1.0 \text{ mm} \times 1.2 \text{ mm}$

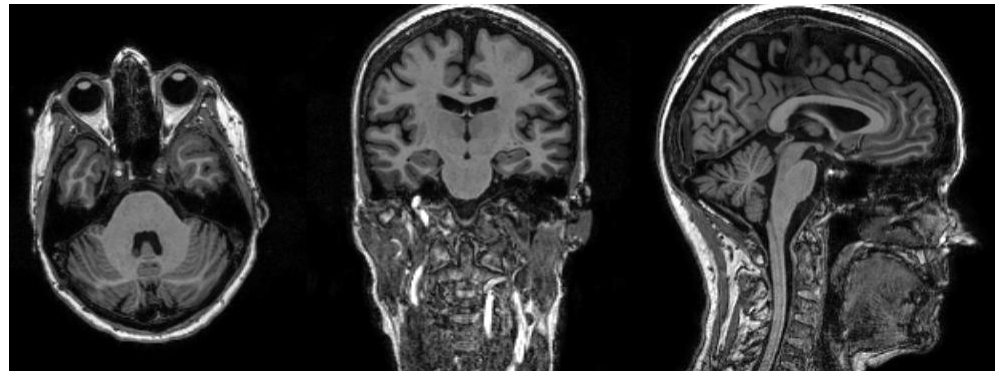
CN



MCI



AD



Processing of sMRI Data

1. Reorganization of files: `reorganize.py`

`data/ADNI1_Baseline_CN`
`data/ADNI1_Baseline_MCI`
`data/ADNI1_Baseline_AD`



`data/ADNI/CN`
`data/ADNI/MCI`
`data/ADNI/AD`

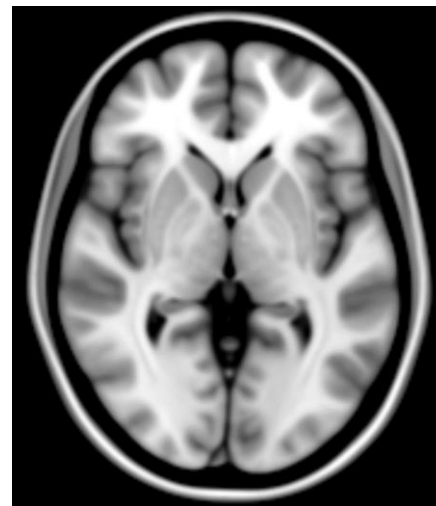
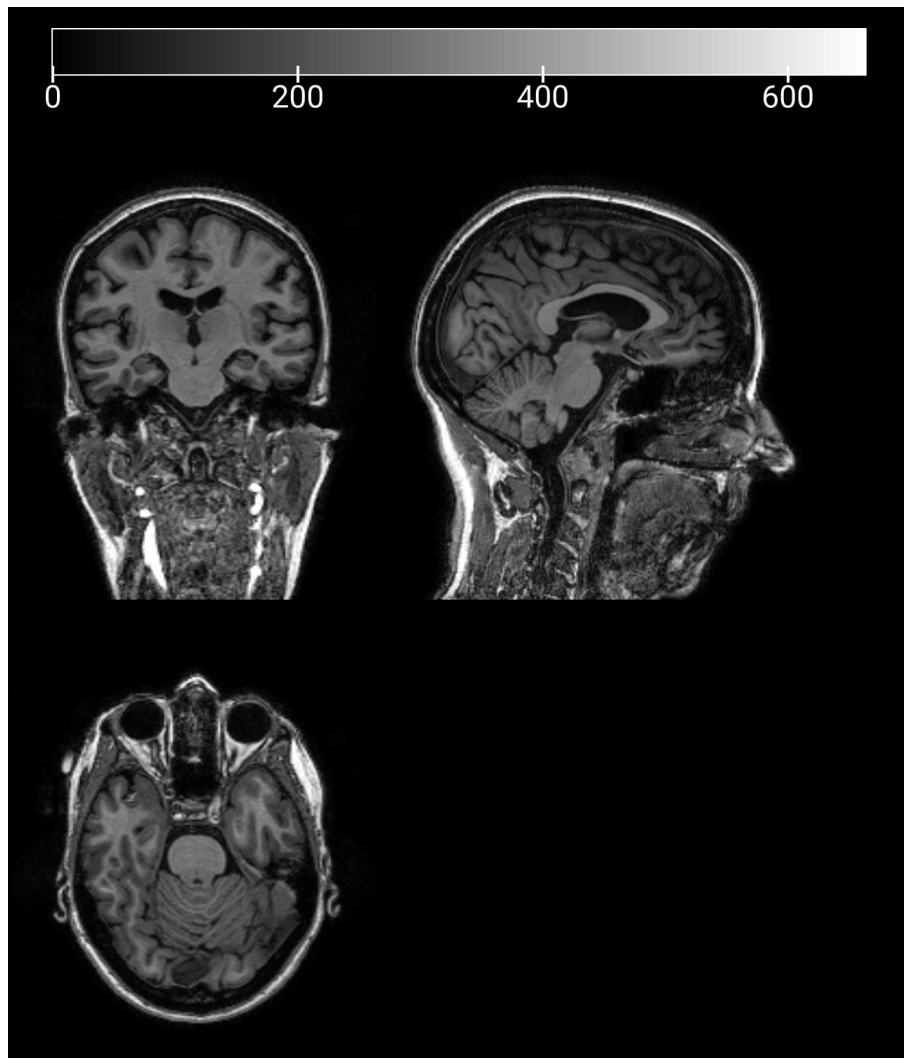
2. Registration: `registration.py`

– [FSL] `fs1reorient2std`

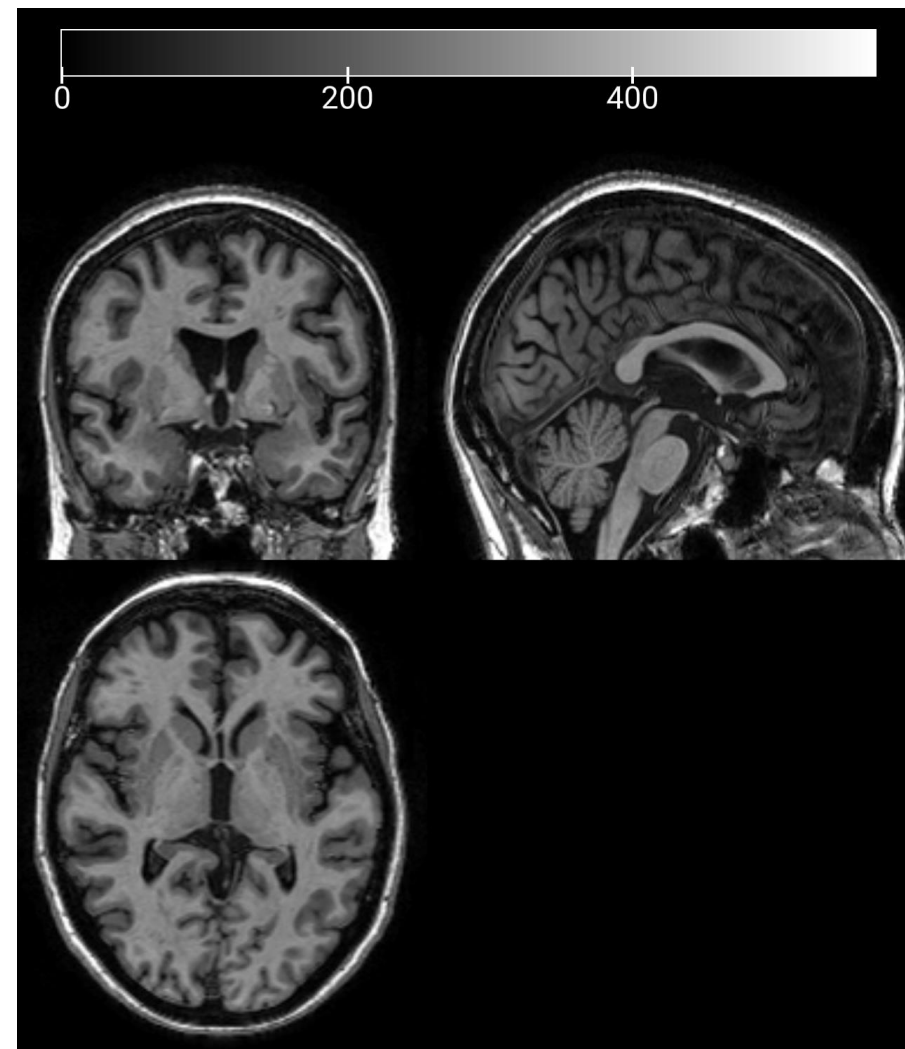
- Tool for reorienting an image to match the approximate orientation of the standard template image (MNI152) by only applying 0, 90, 180 or 270 degree rotations
- `$ fs1reorient2std input_image output_image`

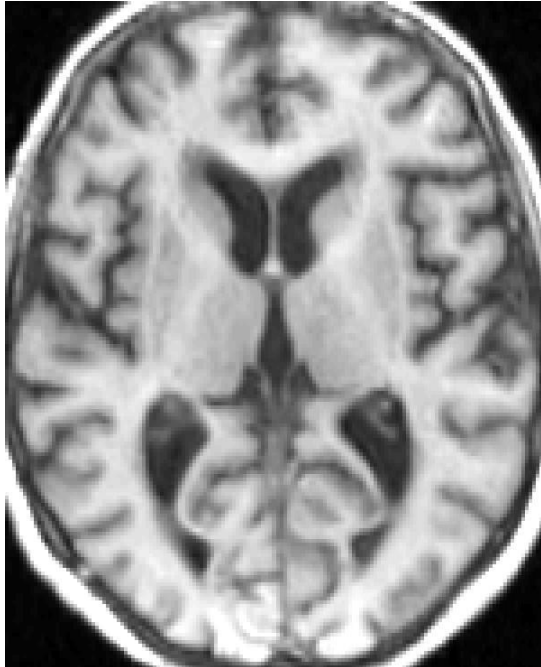
– [FSL] `flirt`

- FMRI's Linear Image Registration Tool
- Tool for linear (affine) intra- and inter-modal brain image registration
- `$ flirt -in input_image -ref MNI152_T1_1mm_brain.nii.gz -out output_image -bins 256 -cost corratio -searchrx 0 0 -searchry 0 0 -searchrz 0 0 -dof 12 -interp spline`

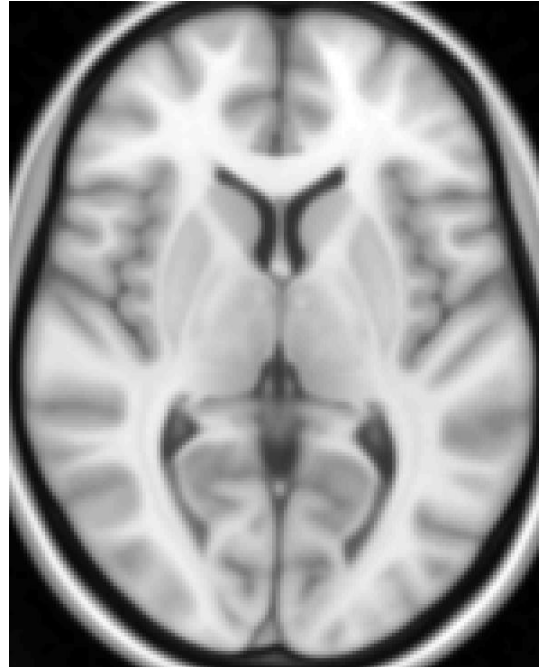


MNI152 T1

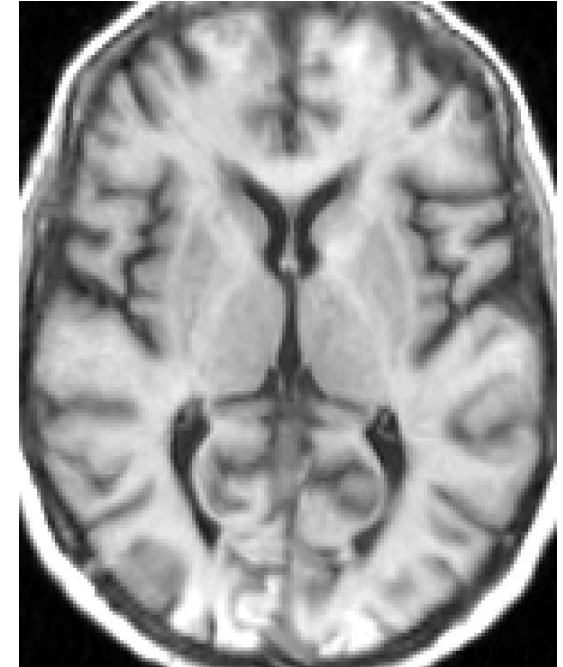




Registration by **flirt**



MNI152 T1



Registration by **fnirt**

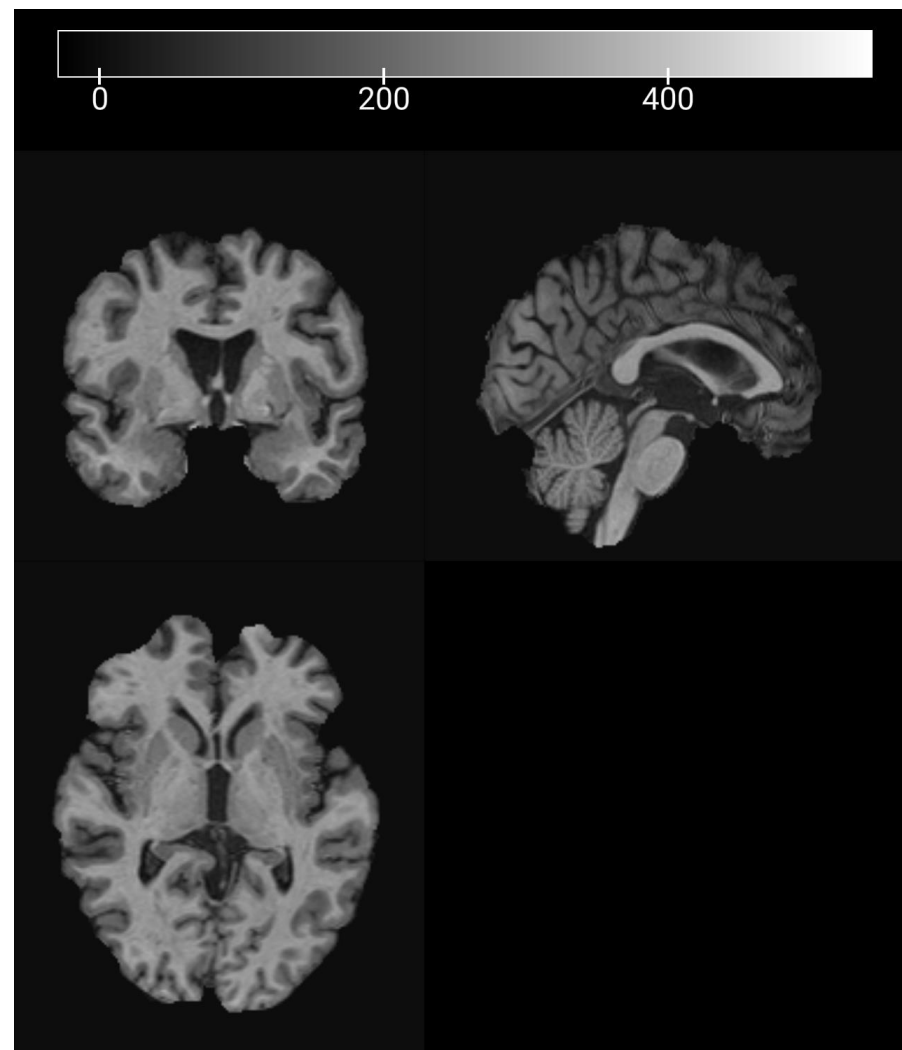
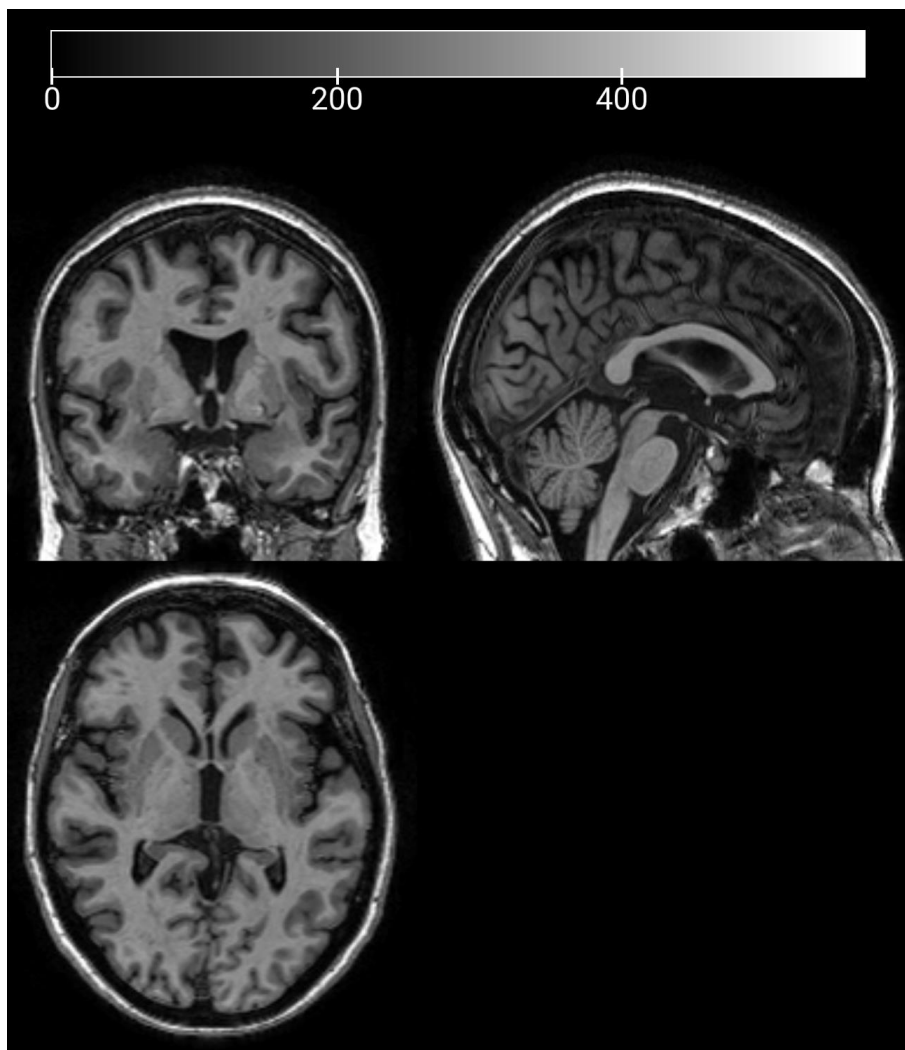
[\[https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FNIRT\]](https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FNIRT)

Comparisons of registration between linear and non-linear methods

3. Skull-stripping: `skull_stripping.py`

– [FSL] `bet`

- Brain Extraction Tool
- Command-line script which makes calling `bet2` for simple brain extraction
- `$ bet input_image output_image -R -f 0.4 -g 0`

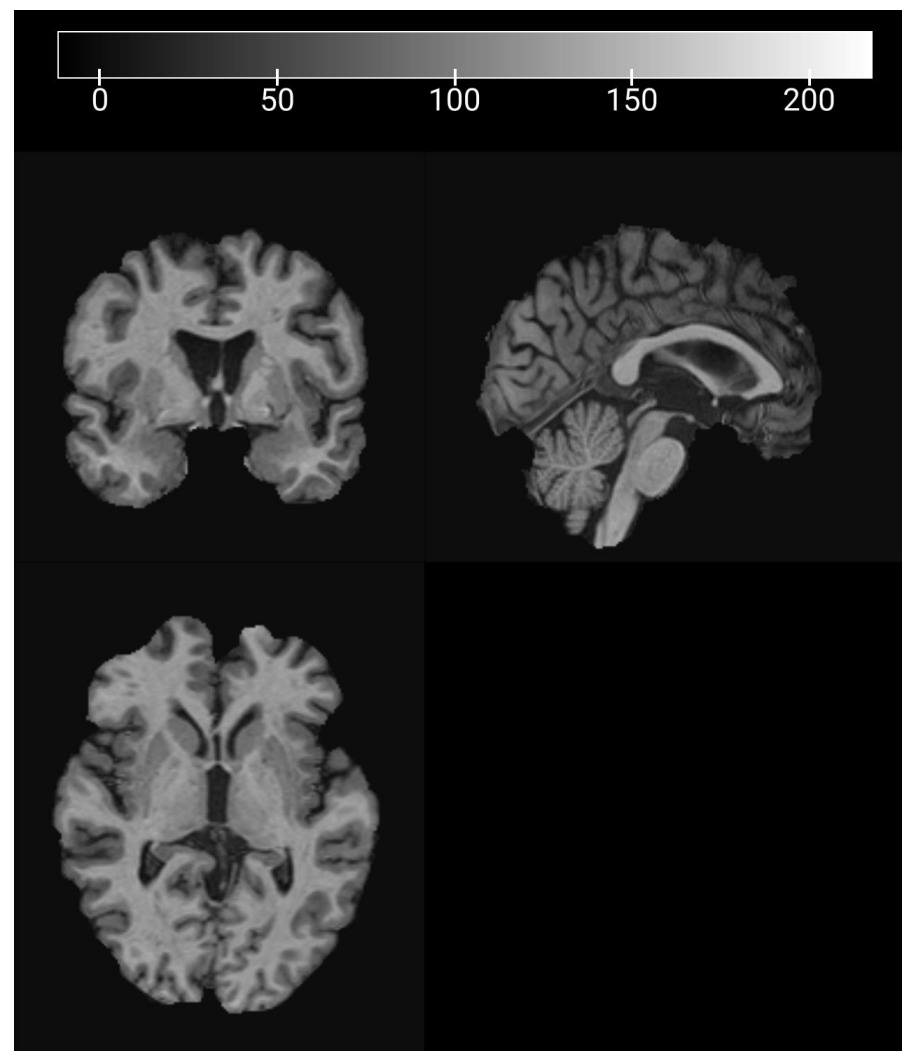
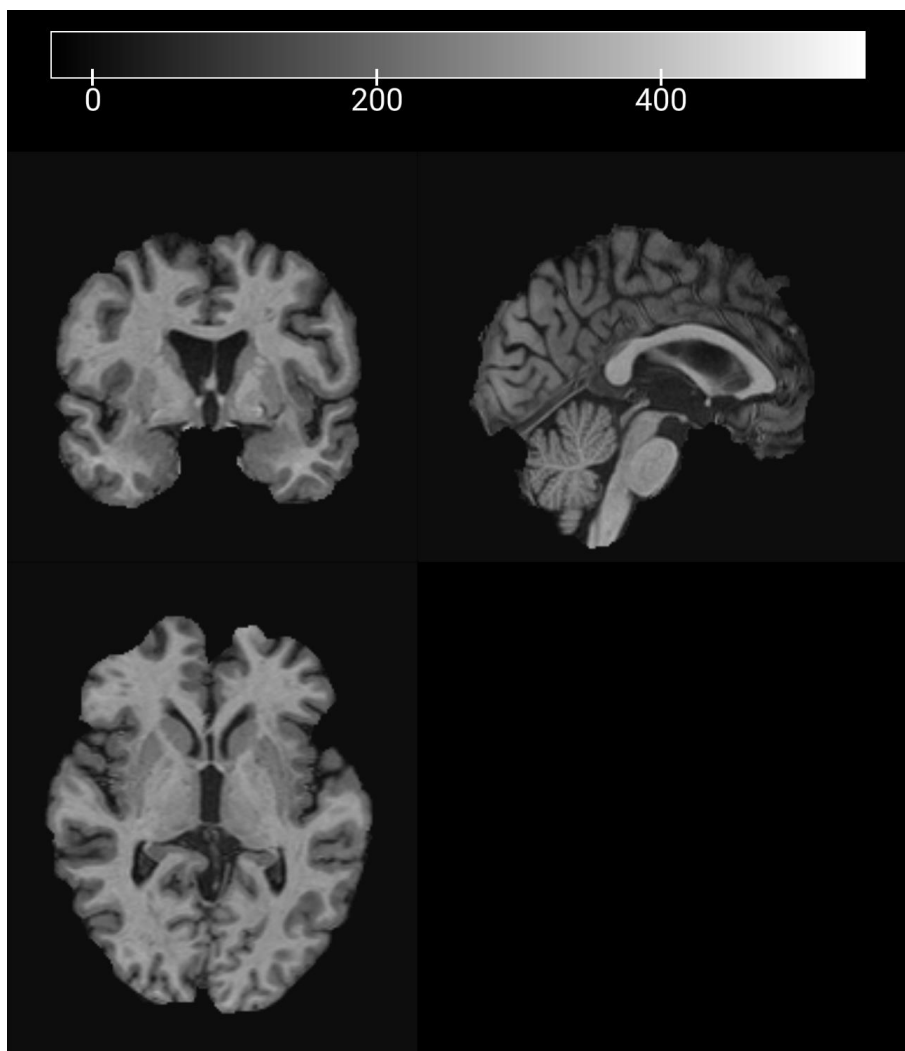


4. Bias field correction: `bias_correction.py`

– [ANTs through `nipy.interfaces ants.segmentation`]

`N4BiasFieldCorrection`

- Tool for bias field correction based on the assumption that the corruption of the low frequency bias field can be modeled as a convolution of the intensity histogram by a Gaussian
- `$ N4BiasFieldCorrection --bspline-fitting [300] --image-dimensionality 3 --input-image input_image --convergence [100x100x60x40, 0.0001] --output output_image --shrink-factor 3`



5. Enhancement: `enhancement.py`

– [scipy.signal] `medfilt`

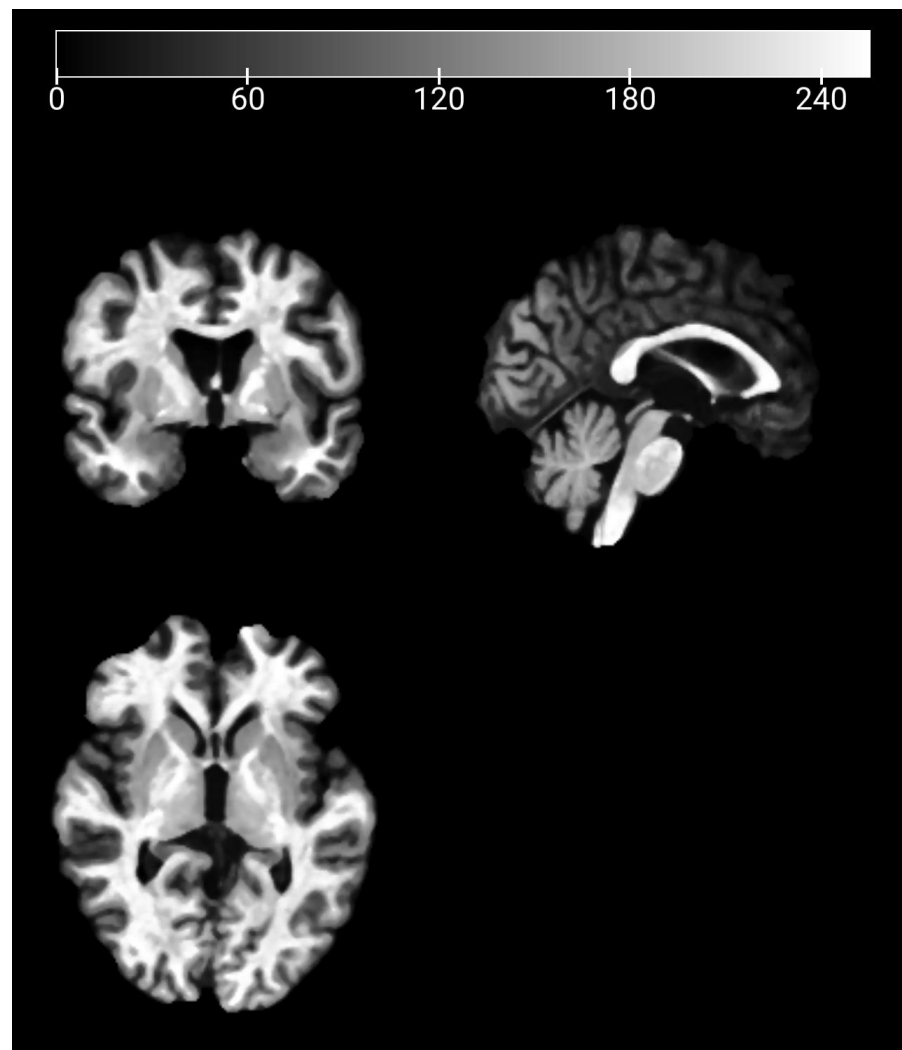
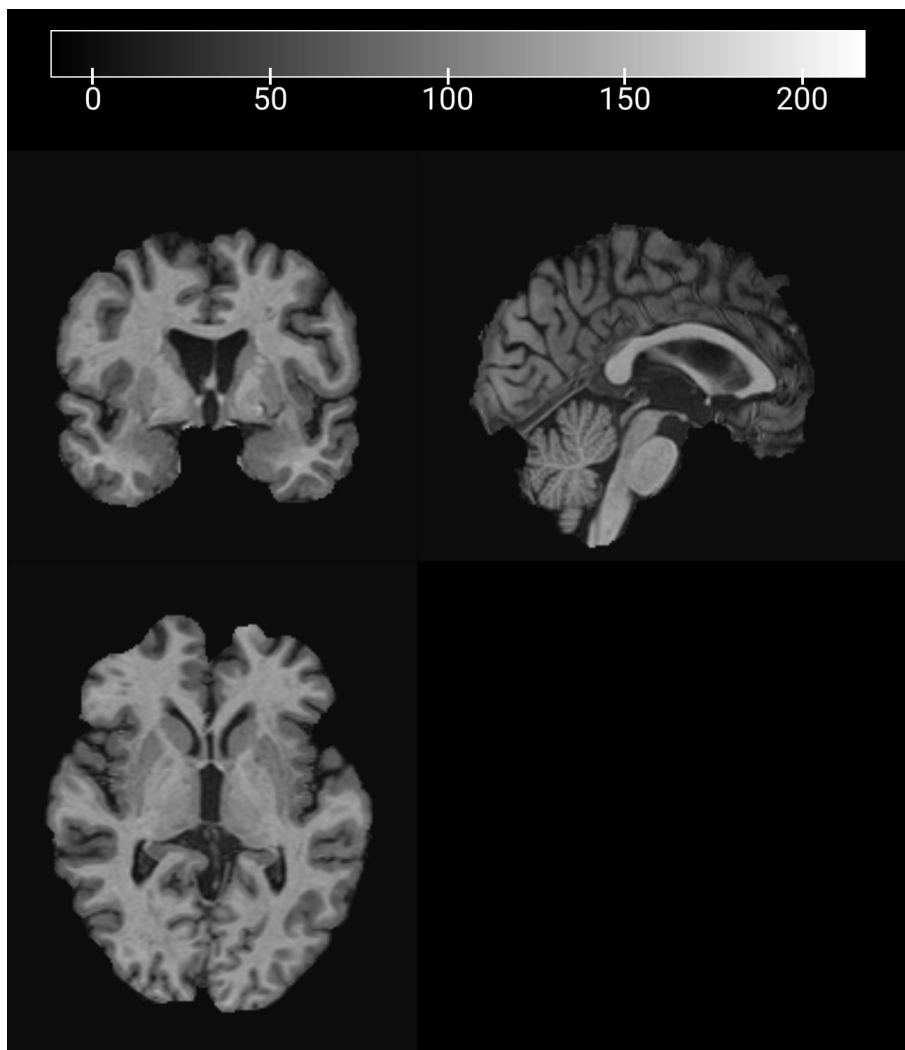
- Applies a median filter using a local window-size given by *kernel_size*
- `>>> medfilt(input_image, kernel_size=3)`

– [in-house] `rescale_intensity`

- Normalises intensity and assigns it to one of bins
- `>>> rescale_intensity(input_image, percentils=[0.5, 99.5], bins_num=256)`

– [in-house] `equalize_hist`

- Adjusts intensity by histogram values
- `>>> equalize_hist(input_image, bins_num=256)`



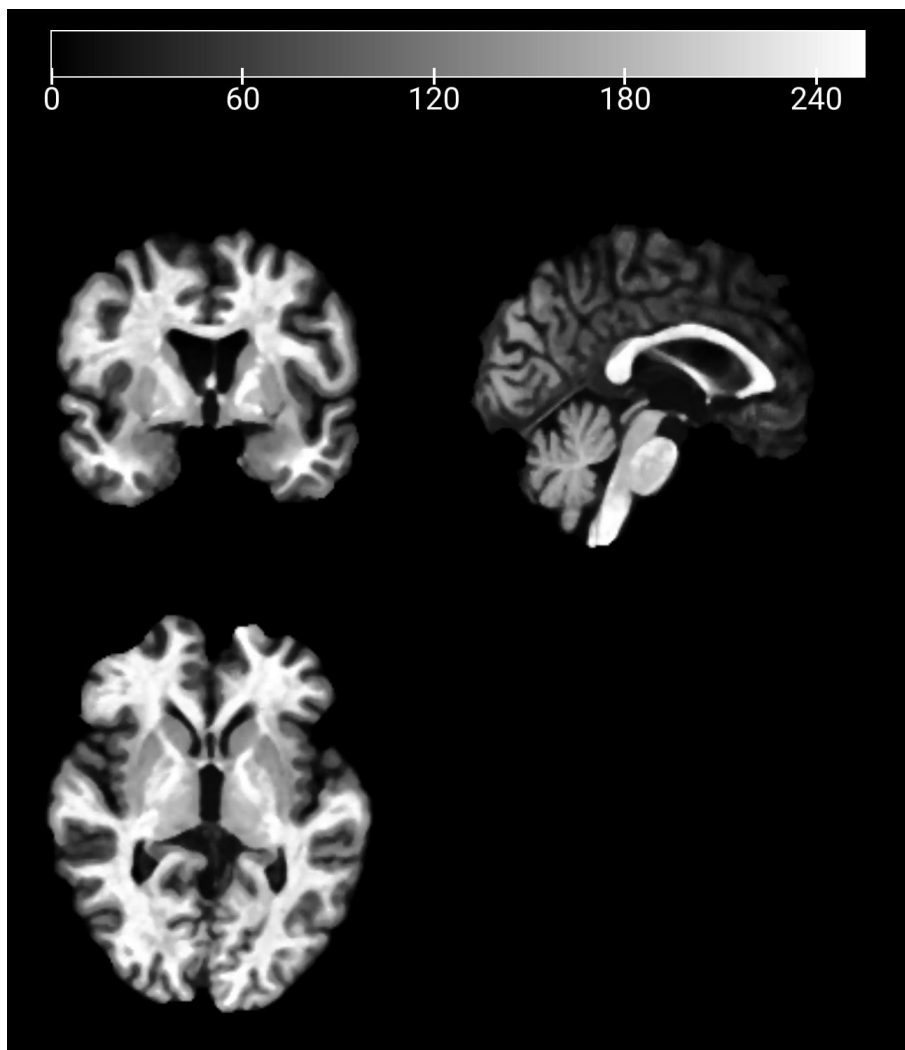
6. Tissue segmentation (1): `segment.py`

– Method 1: `[sklearn.cluster] KMeans`

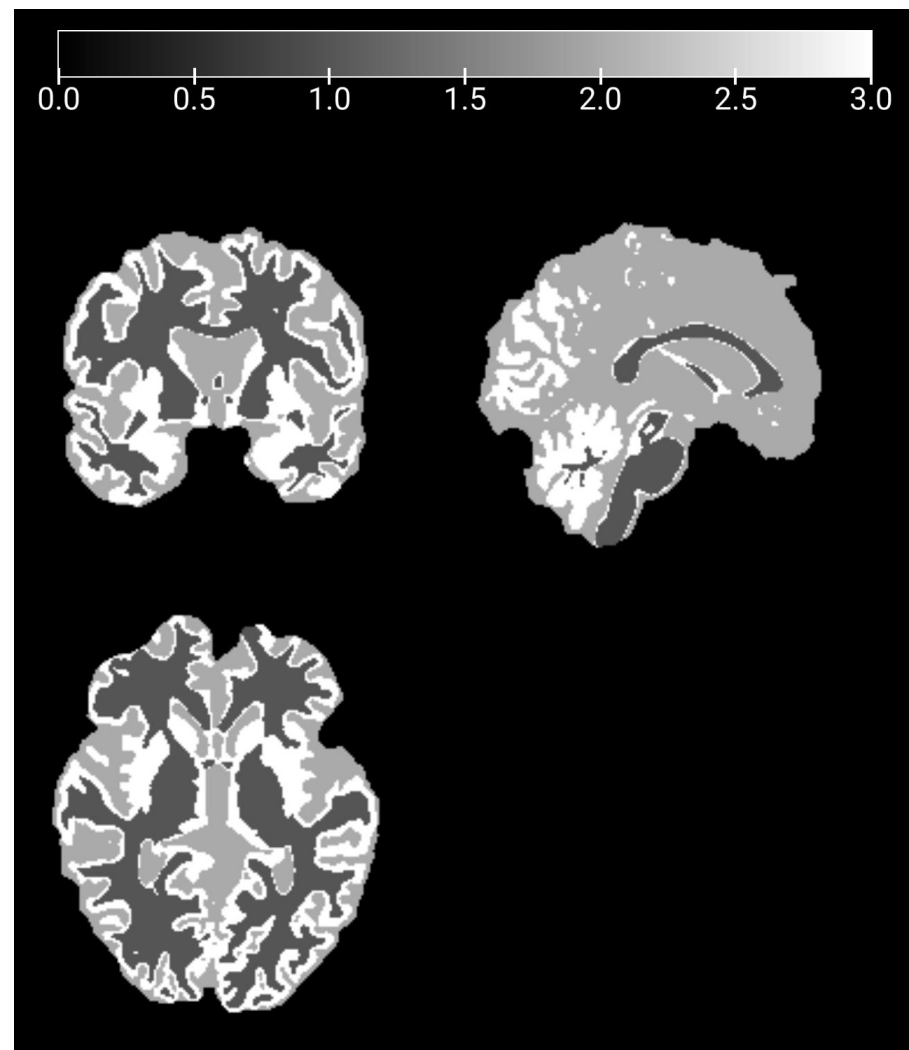
- Performs K-means clustering
- ```
>>> KMeans(n_clusters=3, init="k-means++", verbose=0,
 random_state=7, n_init="auto", max_iter=1000, tol=1e-6,
 algorithm="lloyd").fit(intensities)
```

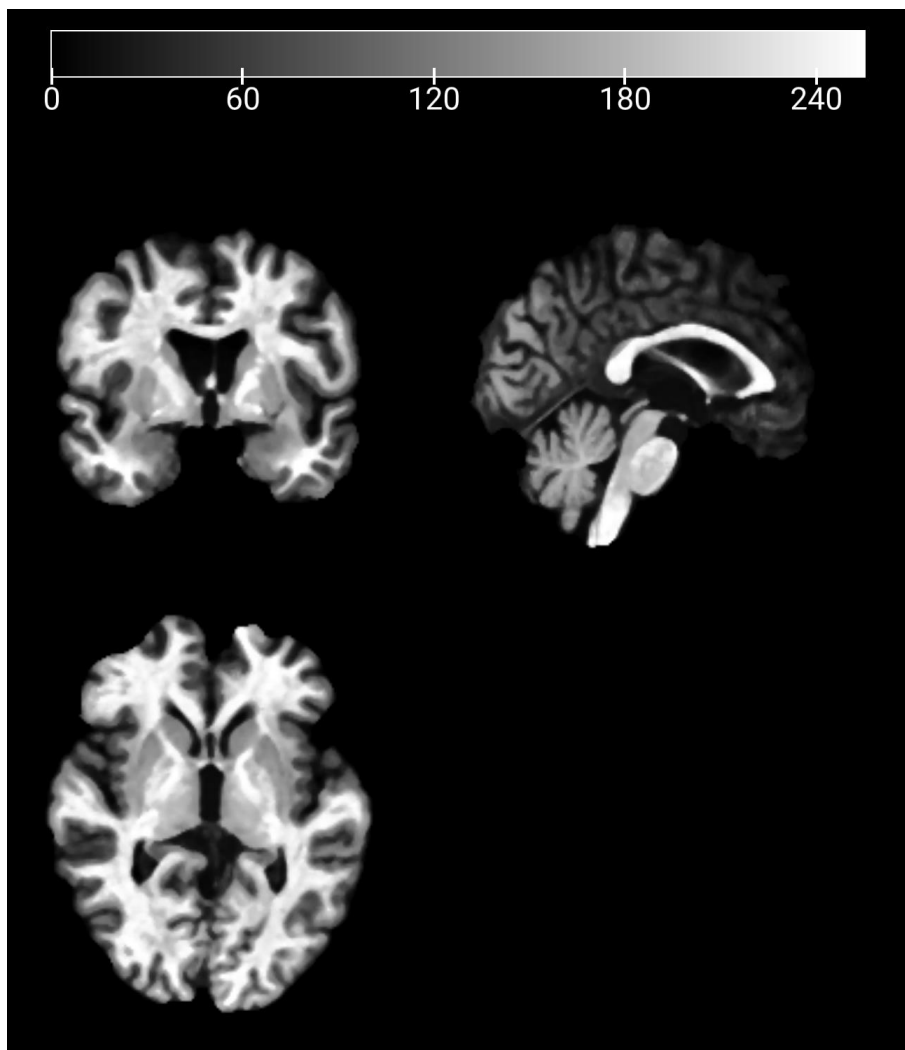
### – Method 2: `[skfuzzy.cluster] cmeans`

- Performs fuzzy C-means clustering
- ```
>>> cmeans(intensities, c=3, m=2, error=1e-6,  
            maxiter=1000, init=None, seed=7)
```

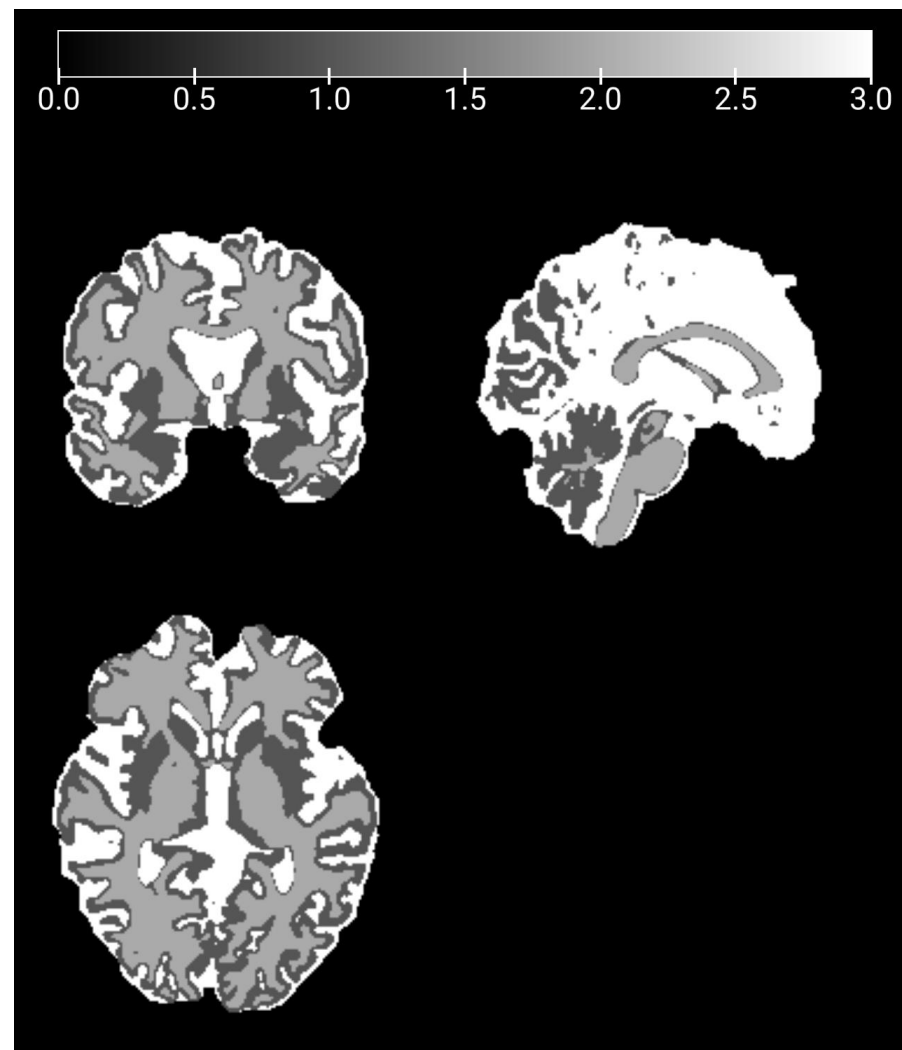



K-means





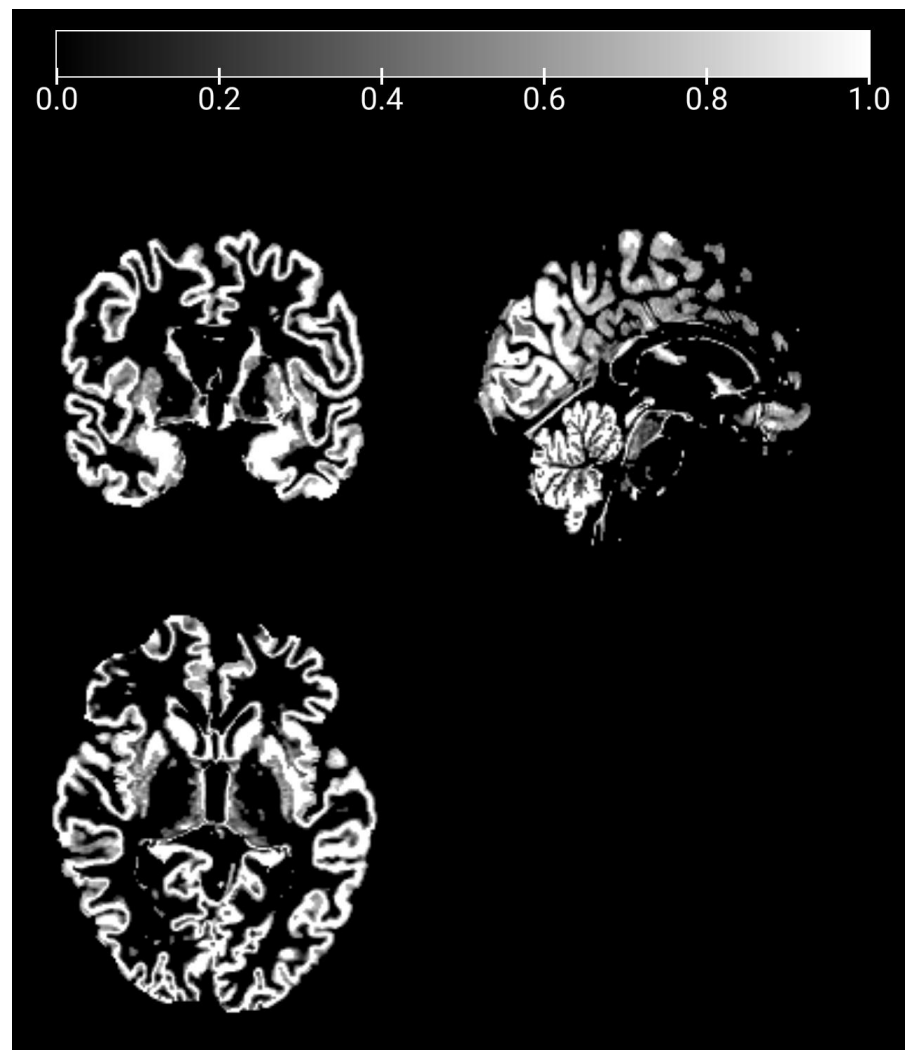
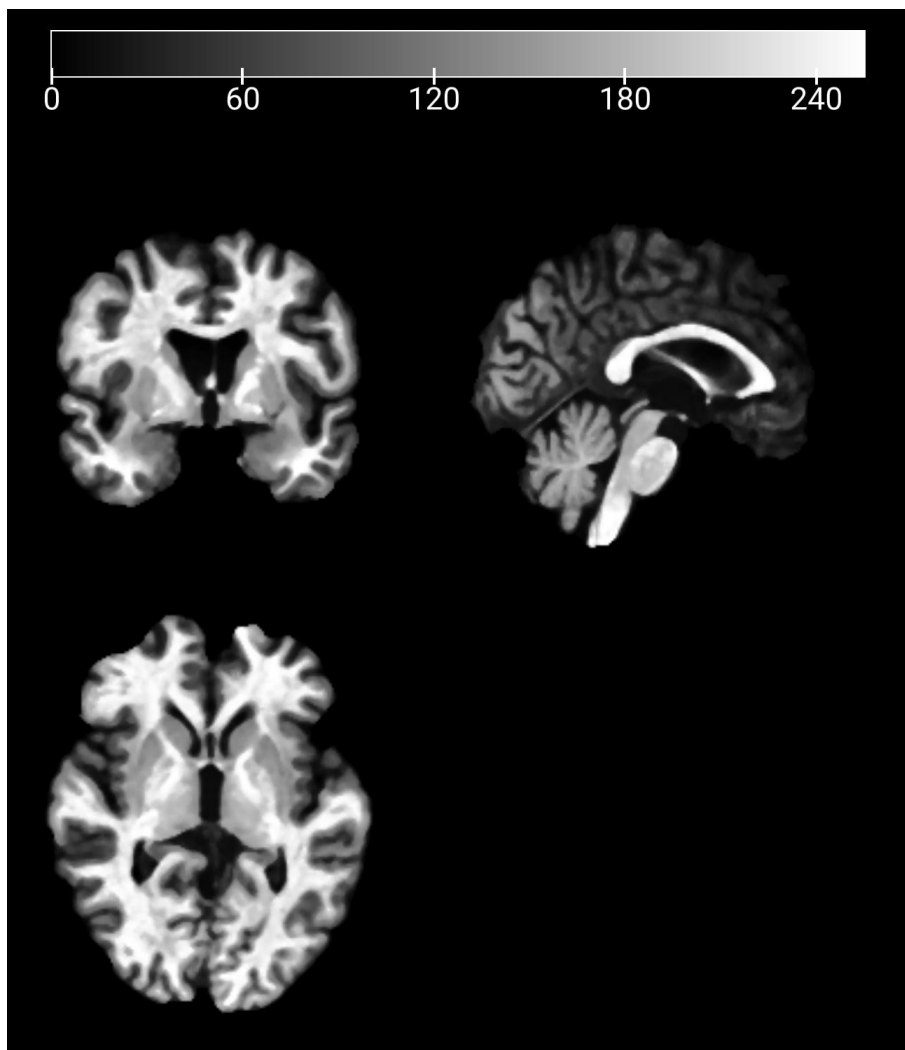
Fuzzy
C-means



6. Tissue segmentation (2): `fast_segment.py`

– [FSL] `fast`

- FMRIB's Automated Segmentation Tool
- Segments a three-dimensional image of the brain into different tissue types (grey matter, white matter, cerebrospinal fluid, etc.) based on a hidden Markov random field model and an associated Expectation-Maximization algorithm
- `$ fast --type=1 --class=3 --Hyper=0.1 --iter=1 --lowpass=20.0 --out=output_basename input_image`





K-means clustering



Fuzzy C-means clustering

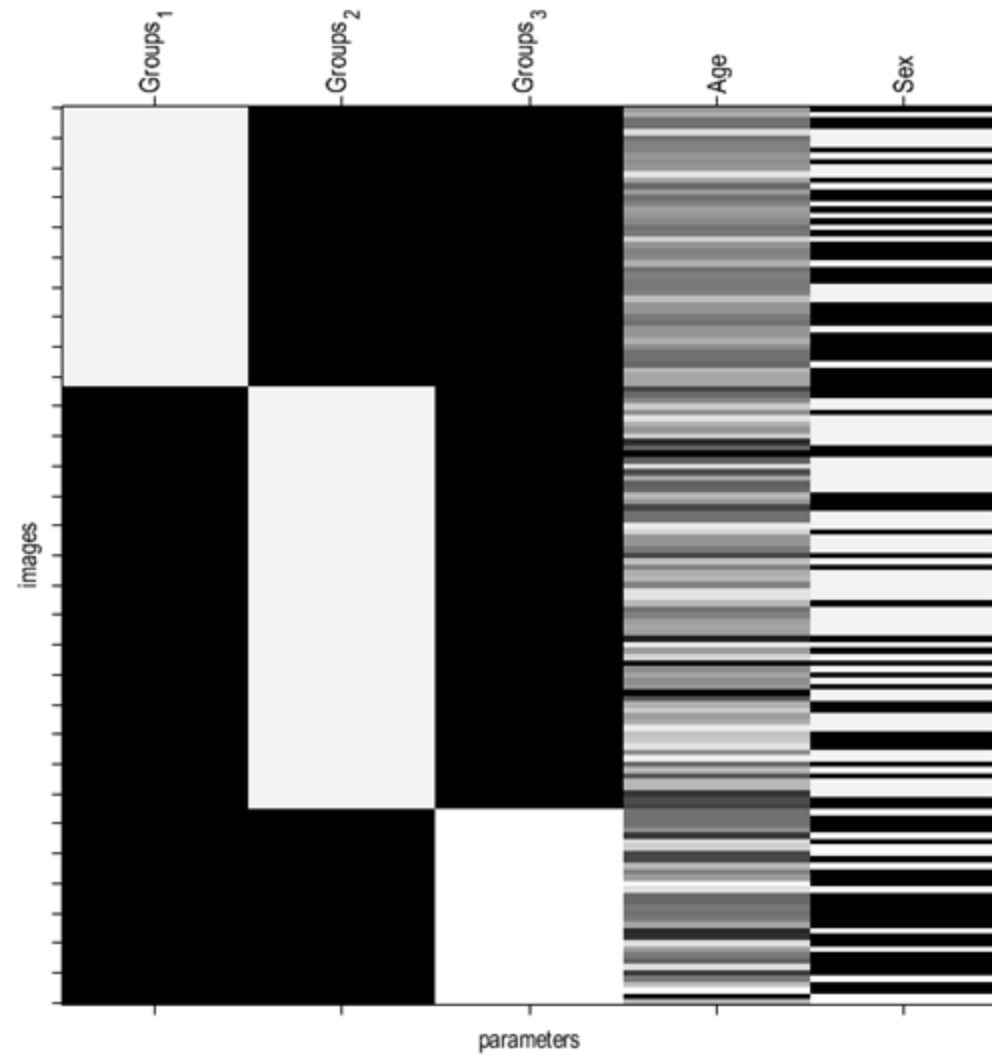


FAST

Comparison of segmented grey matter

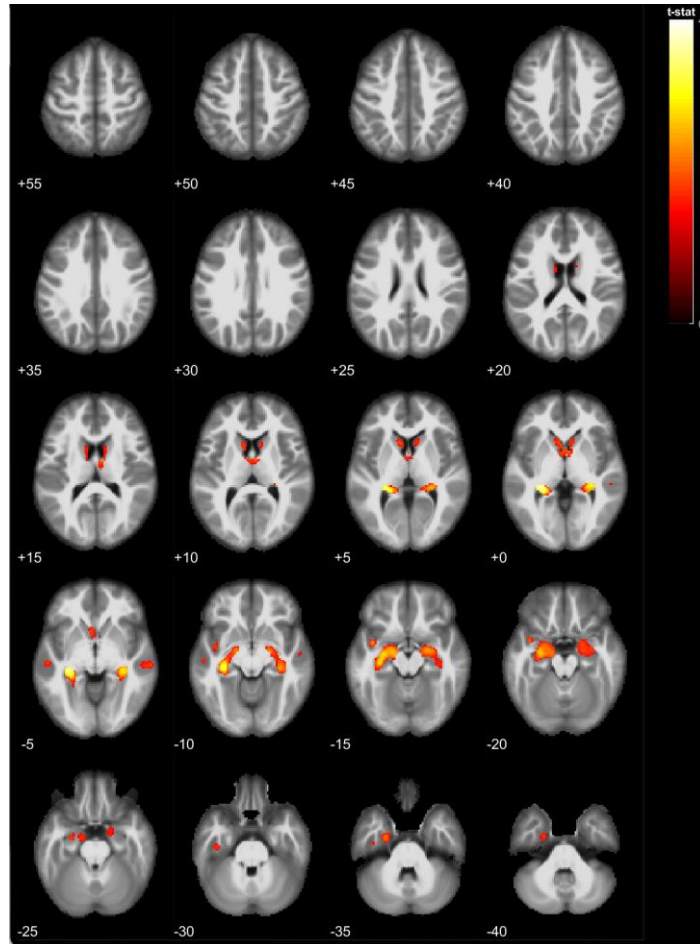
Statistical Inferences on Processed Maps

- Comparison of grey matter/white matter volume
 - Voxel-wise one-way ANOVA
 - CN vs. MCI vs. AD

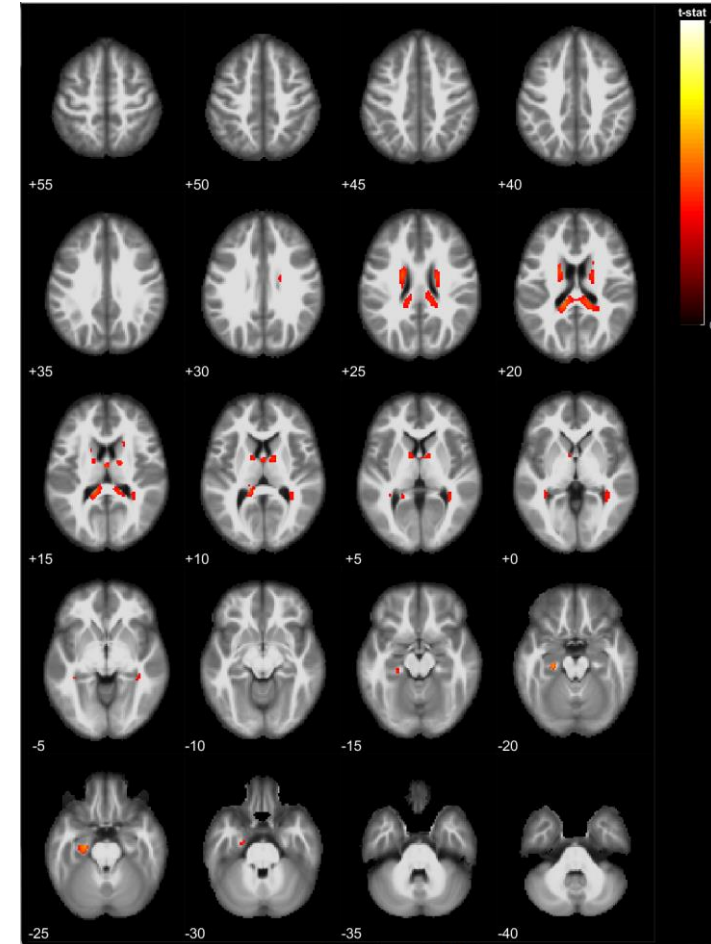


Design matrix for one-way ANOVA

One-way ANOVA: CN vs. MCI vs. AD

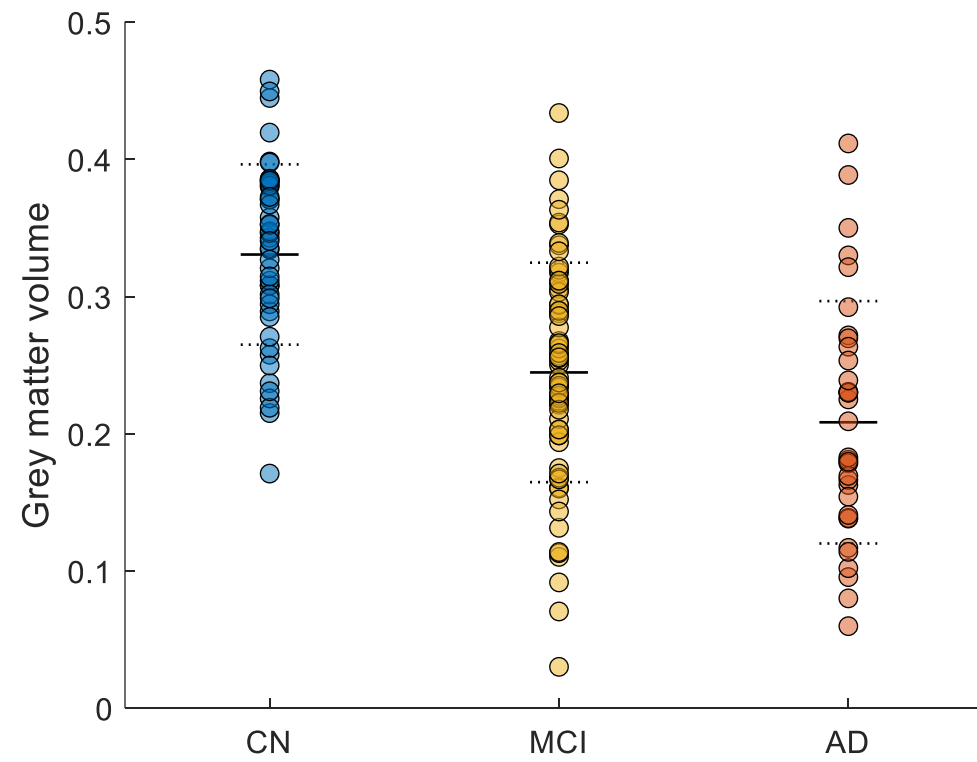


Grey matter volume

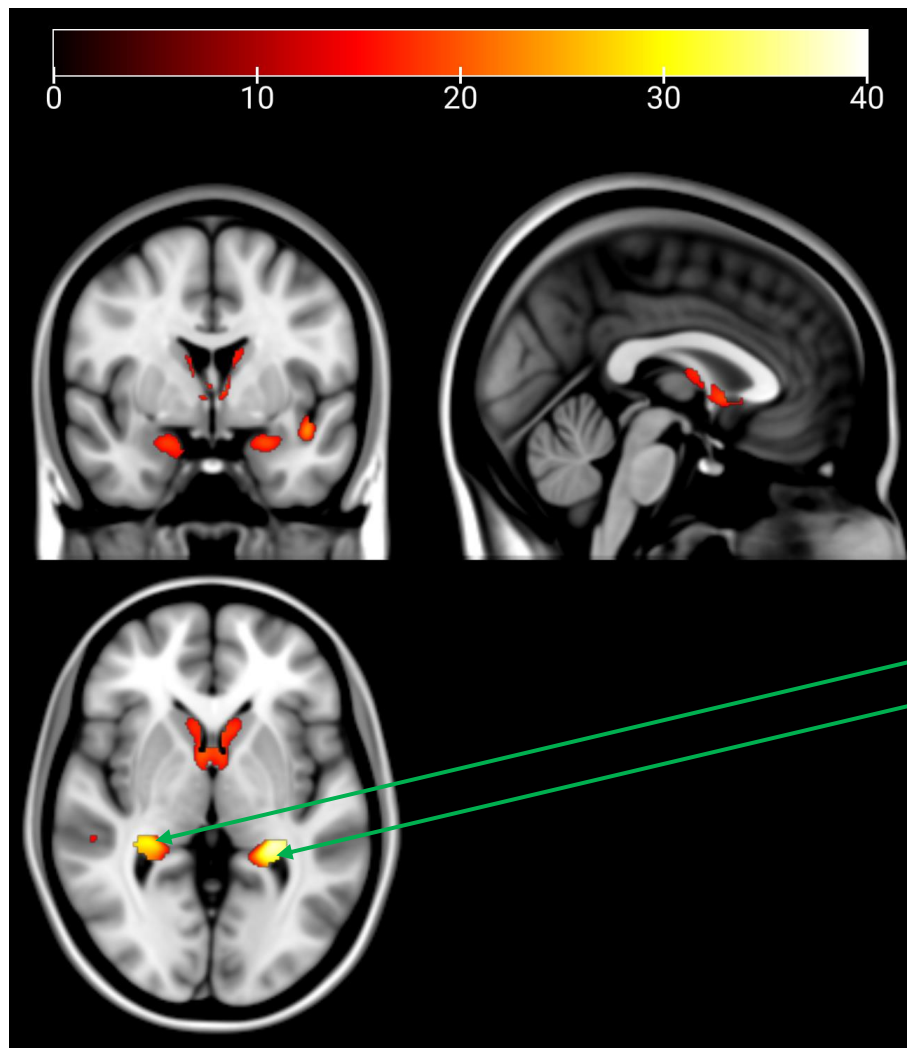


White matter volume

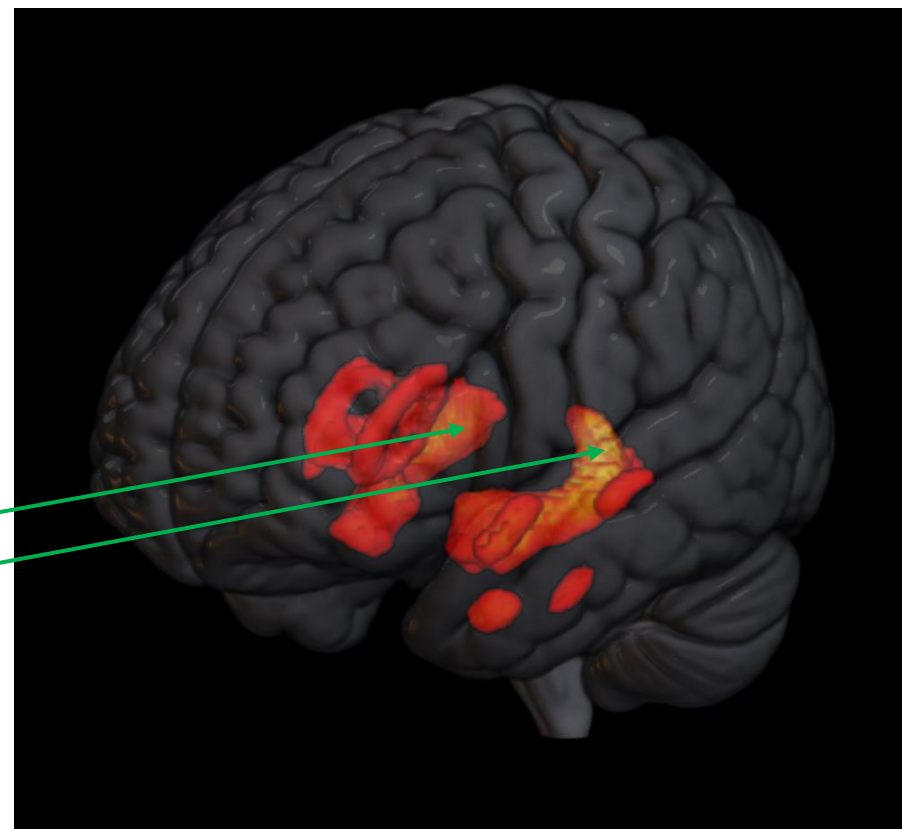
Thresholded at FDR corrected $p = 0.05$ at the cluster level and FWE corrected $p = 0.05$ at the voxel level



Maximum statistic at $x = -26$ mm, $y = -36$ mm, $z = 1$ mm



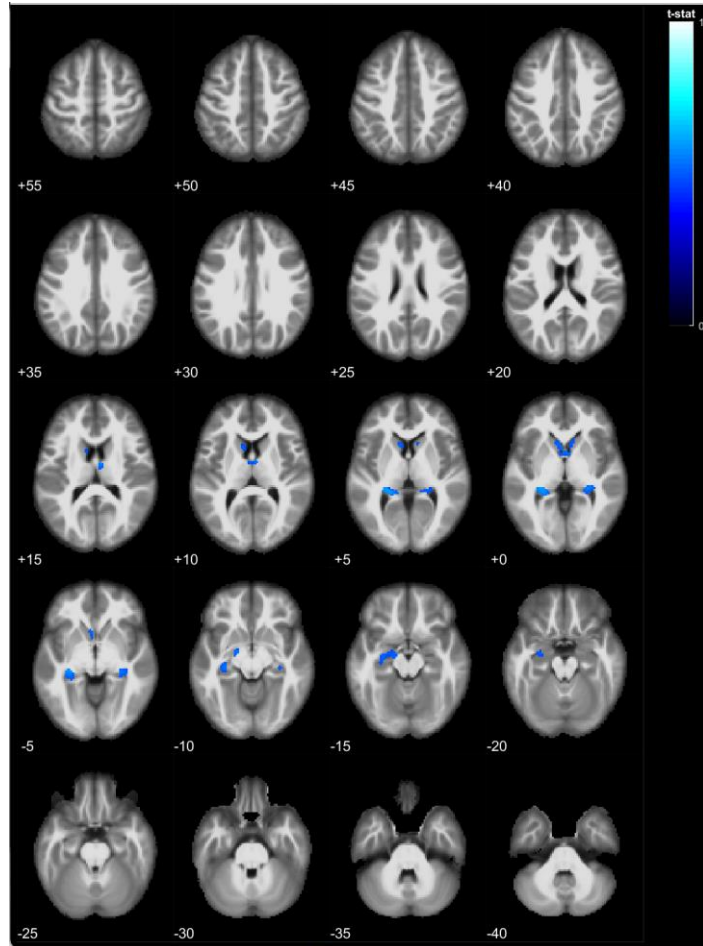
Hippocampus



– Voxel-wise two sample t -test

- CN vs. MCI
- CN vs. AD
- MCI vs. AD

Two-sample t -test: CN > MCI

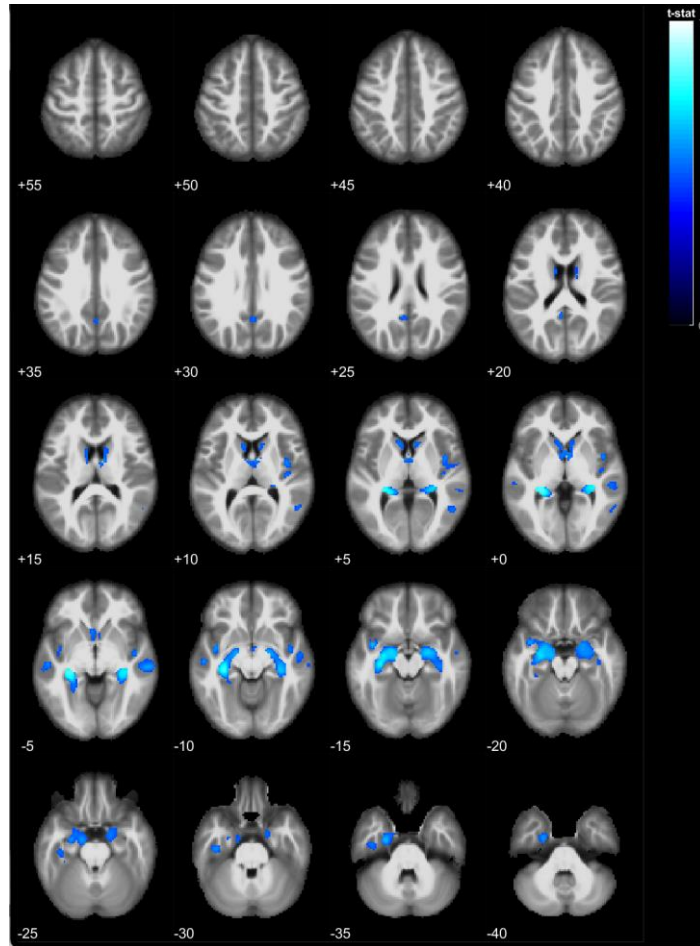


Grey matter volume

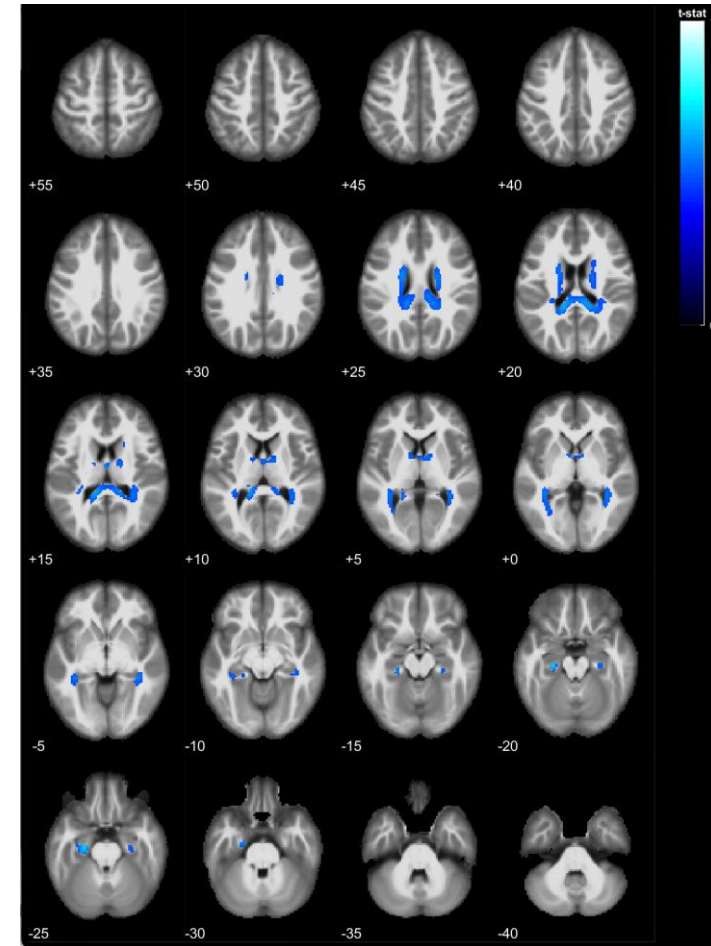
White matter volume

Thresholded at FDR corrected $p = 0.05$ at the cluster level and FWE corrected $p = 0.05$ at the voxel level

Two-sample t -test: CN > AD



Grey matter volume



White matter volume

Thresholded at FDR corrected $p = 0.05$ at the cluster level and FWE corrected $p = 0.05$ at the voxel level