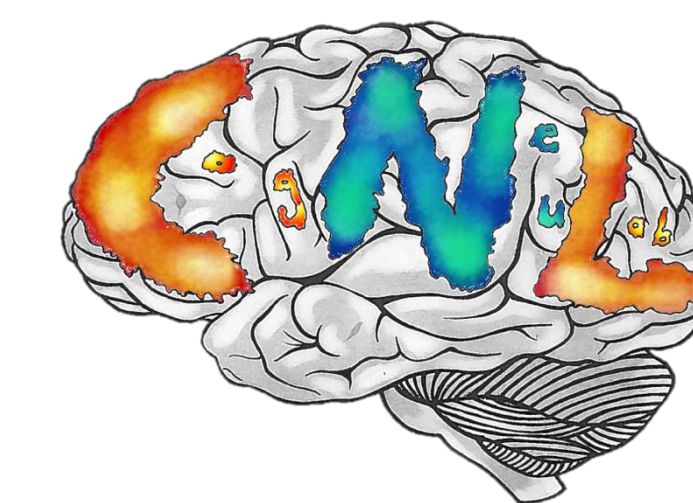




Multi-Feature Voxelwise Anomaly Mapping of Alzheimer's Disease

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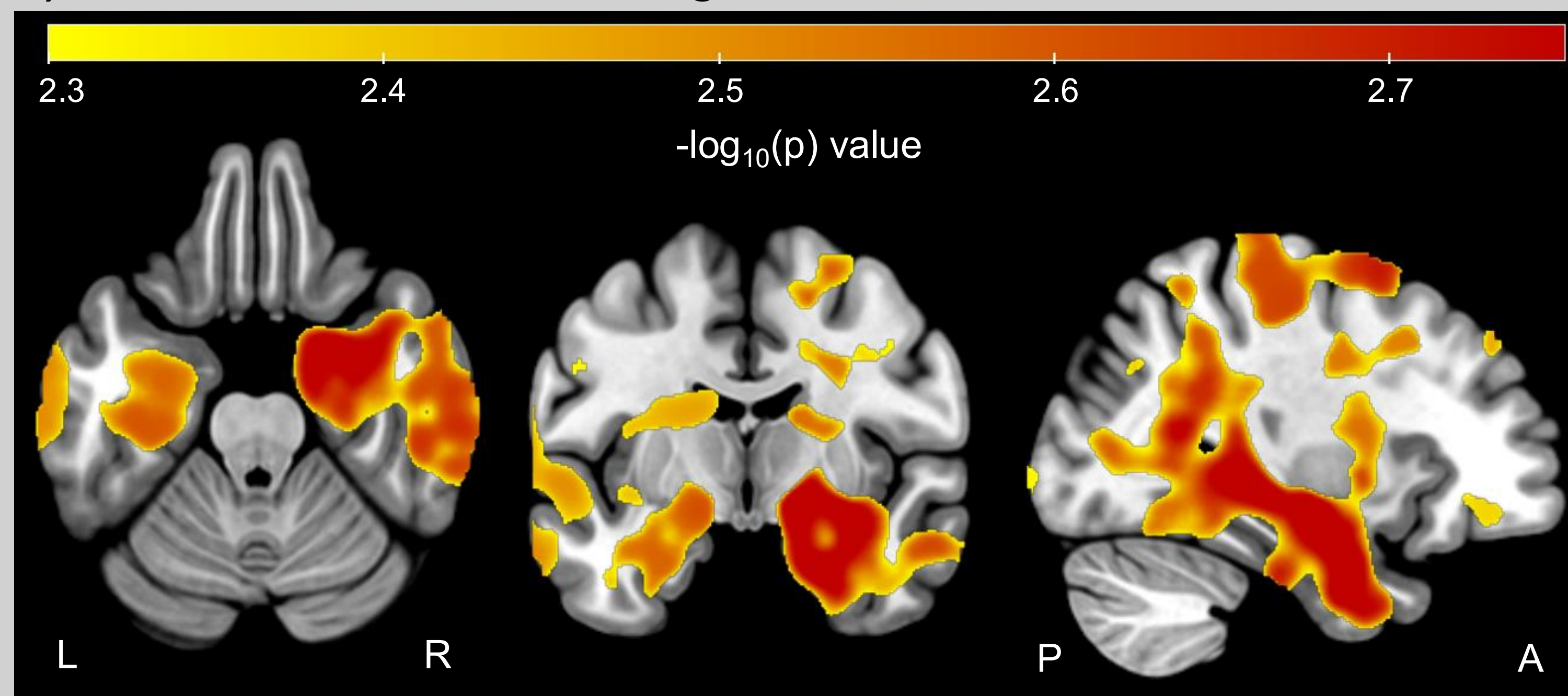
BACKGROUND

- Currently, most anomaly detection pipelines include unimodal MRI data, but incorporating multimodal MRI can greatly increase the sensitivity and specificity
- We created a voxelwise anomaly detection method that can be adapted for multimodal MRI input
- This study validated our voxelwise anomaly detection method using multiple features of structural MRI, and tested differences between controls, mild cognitive impairment (MCI), and Alzheimer's disease (AD)

METHODS

- We utilized two separate datasets including in-house data from our lab (ADDF dataset), as well as data from the Alzheimer's Disease Neuroimaging Initiative (ADNI dataset) as an external validation dataset
- Normative populations for comparison were comprised of healthy subjects from other large, publicly available datasets including HCPa, HABS, NACC, and IXI
- All subjects underwent T1w MRI scans on a 3T scanner, and six voxelwise feature maps such as grey matter concentration were calculated from these MR images using the CAT12 toolbox (MATLAB)
- Control and normative subjects were selected to best match each test group on age, sex, and intracranial volume
- Anomaly index at each voxel location was calculated from feature maps as Mahalanobis distance between all features measured in a subject versus the normative group
- Group analyses were conducted on the resulting voxelwise anomaly maps using a two-way t-test with threshold free cluster enhancement (TFCE, 5000 permutations) and family-wise error (FWE) correction (SPM25)

a) ADDF Dataset: Anomalous regions in AD/MCI versus Controls



b) ADNI Dataset: Anomalous regions in AD versus Controls

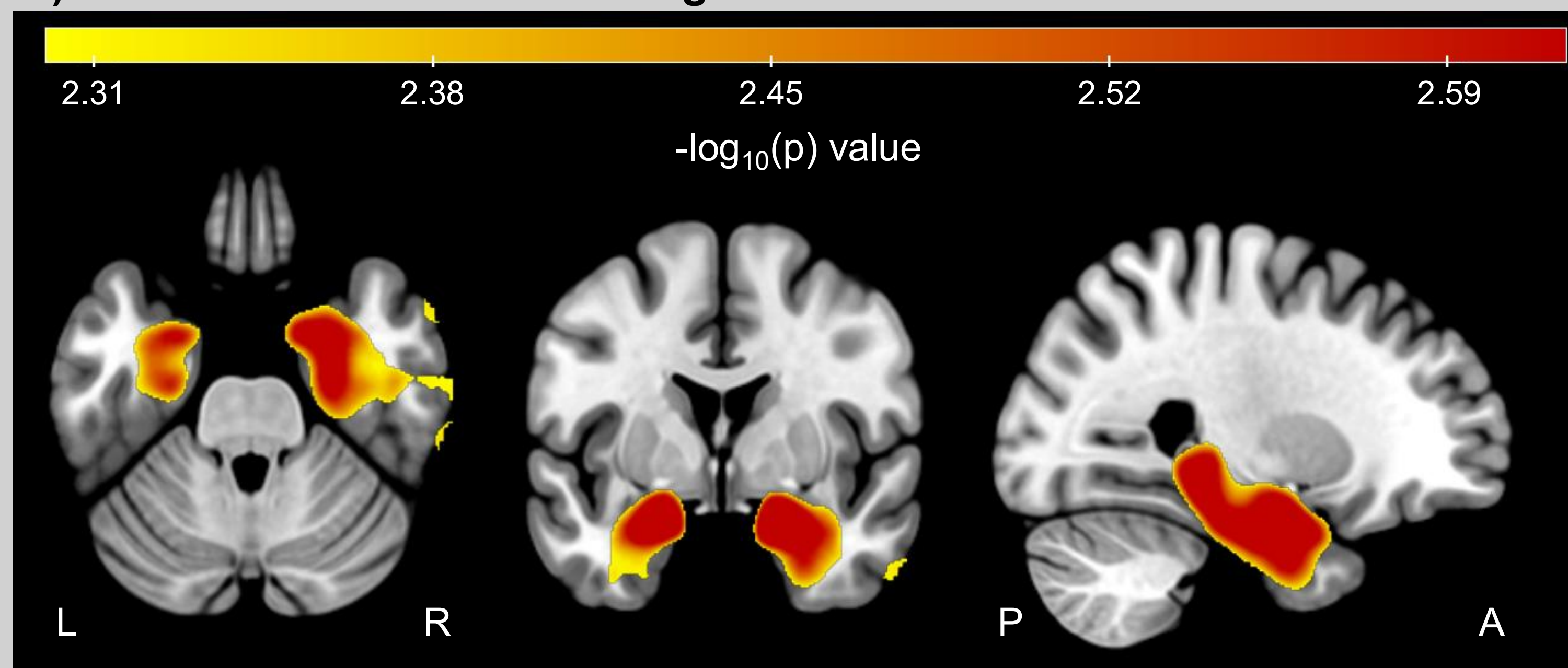


Figure 1. Regions of highest anomaly index in a) people with AD (n=15) or MCI (n=12) compared to matched controls (n=27), with a normative sample from other datasets (n=613); and b) people with AD (n=87) compared to matched controls (n=82), with a normative sample from other datasets (n=474). Statistical maps are shown for data smoothed with 6mm FWHM Gaussian kernel. Results are shown following threshold-free cluster enhancement (TFCE) and family-wise error correction (FWE). Significant regions include the bilateral medial temporal lobe ($p_{FWE} < 0.005$) with the peak value in a) the right parahippocampal gyrus (MNI coordinates: [22.5, -1.5, -31.5], $p_{FWE} = 0.0012$), and b) right amygdala (MNI coordinates: [19.5, 3.0, -19.5], $p_{FWE} = 0.0008$).

Participant Demographics:

		Controls	AD (+ MCI ¹)	Normative	p-value
ADDF	n	27	27	613	
	Age (y)	69.0 (5.6)	72.7 (7.6)	70.8 (8.9)	0.30
	Sex (F)	12 (44.4%)	10 (37.0)	251 (40.1%)	0.86
	TIV (cm ³)	1521.0 (162.7)	1530.8 (198.2)	1524.3 (142.4)	0.97
ADNI	n	82	87	474	
	Age (y)	71.6 (5.6)	71.8 (6.3)	71.6 (8.8)	0.98
	Sex (F)	30 (36.6%)	32 (36.8%)	176 (37.1%)	0.99
	TIV (cm ³)	1483.6 (152.5)	1443.9 (144.4)	1463.8 (159.2)	0.26

Table 1. Demographic information about all included subjects from ADDF, ADNI, and other public datasets used in normative group, reported as M (SD) for age and TIV, and count (%) for sex assigned at birth. Group differences were tested with an ANOVA or chi-squared. ¹MCI and AD groups were combined for the ADDF dataset only.

RESULTS

- Group comparisons for both datasets showed patterns of increased anomaly index across the bilateral medial temporal lobes (MTL):
 - Increased anomaly in AD/MCI versus controls in the ADDF dataset (Fig 1a; $p_{FWE} < 0.005$)
 - Increased anomaly in AD versus controls in the ADNI dataset (Fig 1b; $p_{FWE} < 0.005$)

CONCLUSIONS

- For both analyses, there were consistent patterns of anomaly centered in the MTL
- These regions of largest group difference are in accordance with well-characterized regions of disease progression, validating our technique
- Importantly, this pipeline can be modified in future work to incorporate other MRI modalities including dMRI and fMRI

ADDITIONAL INFORMATION

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Public Datasets Used:

ADNI: Alzheimer's Disease Neuroimaging Initiative

HABS: Harvard Aging Brain Study

HCPa: Human Connectome Project Aging

NACC: National Alzheimer's Coordinating Center

IXI: Information eXtraction from Images

