Visualizing Convolutional Networks for MRI-based Diagnosis of Alzheimer's Disease

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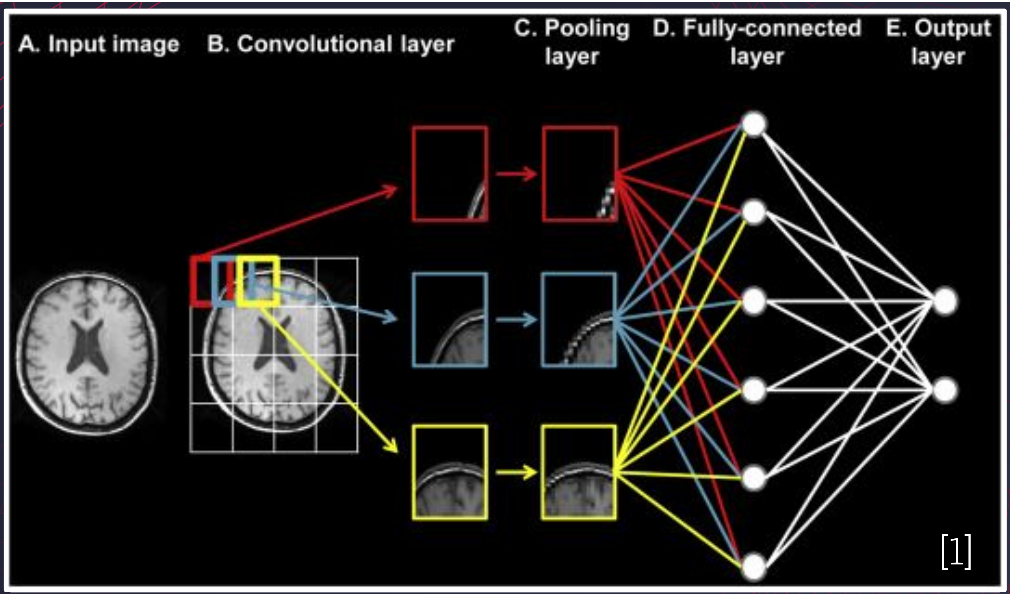
Introduction

“Alzheimer’s caregivers ride the world’s biggest, fastest, scariest, emotional roller coaster every day.”

—Bob DeMarco, Founder of the Alzheimer's Reading Room

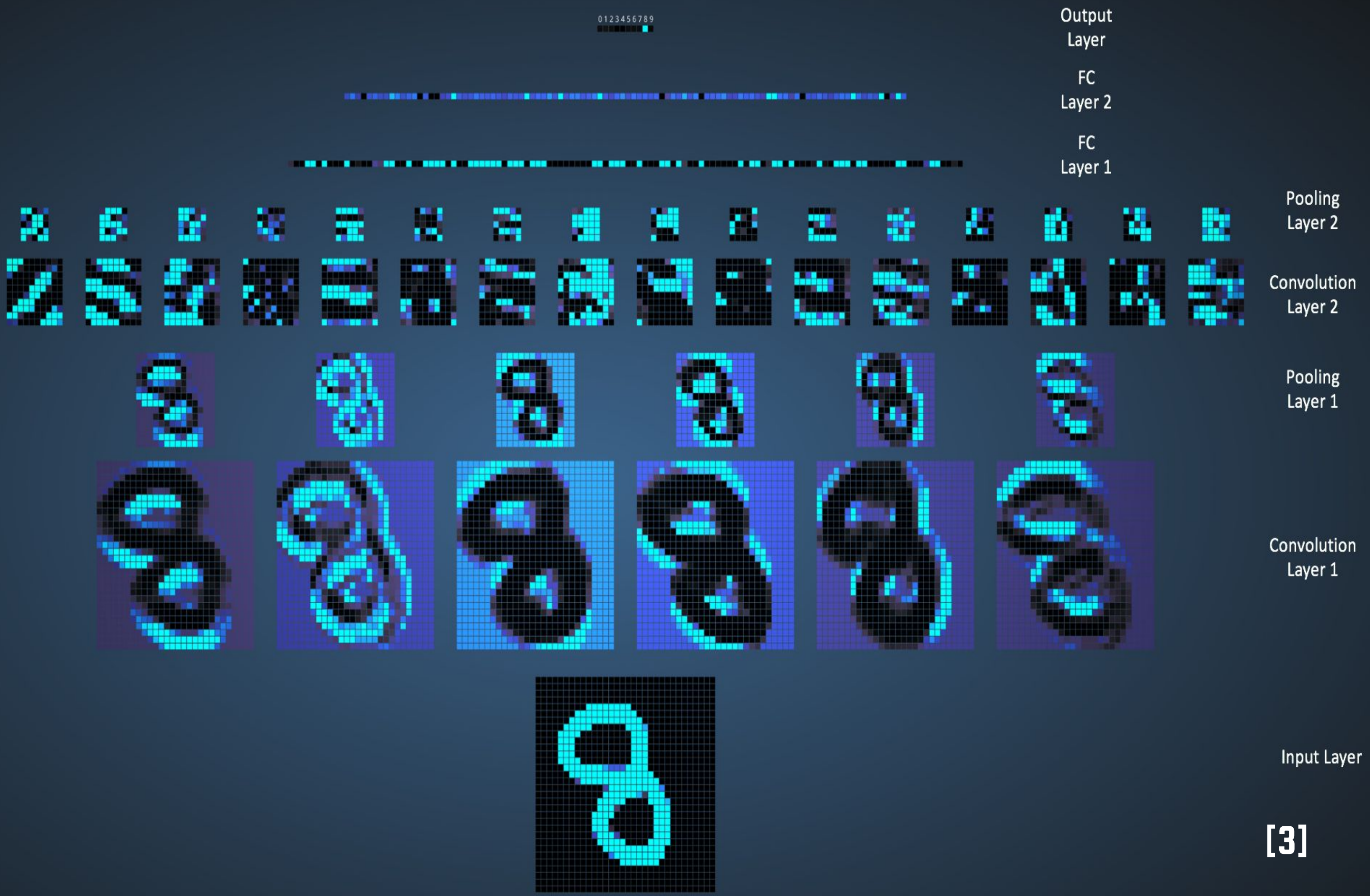
Alzheimer Classification with Convolutional Neural Networks



Authors	Methodology	Modalities	Content	Data (size)	Accuracy (AD/NC)
Ahmed et al.	Feature-based	sMRI	2 ROIs	ADNI (509)	0.838
Ebadi et al.	Feature-based	DTI	Full brain	custom (34)	0.8
LeI et al.	Feature-based	sMRI+PET	Full brain	ADNI (398)	0.969
Ahmed et al.	Feature-based	sMRI+DTI	1 ROI	ADNI (203)	0.902
Sarraf et al.	NN-based	sMRI+ fMRI	Full brain	ADNI (302)	0.988
Suk et al.	NN-based	sMRI	93 ROIs	ADNI (805)	0.903
Li et al.	NN-based	sMRI	1 ROI	ADNI (1776)	0.965

[2]

Visualization methods

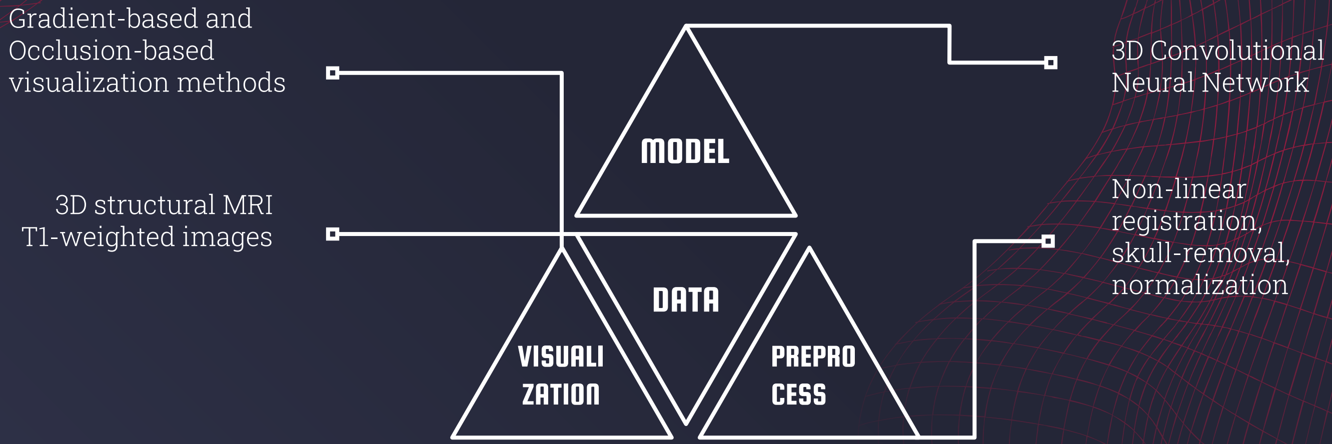


[3]

02

Methods

Classification System Overview



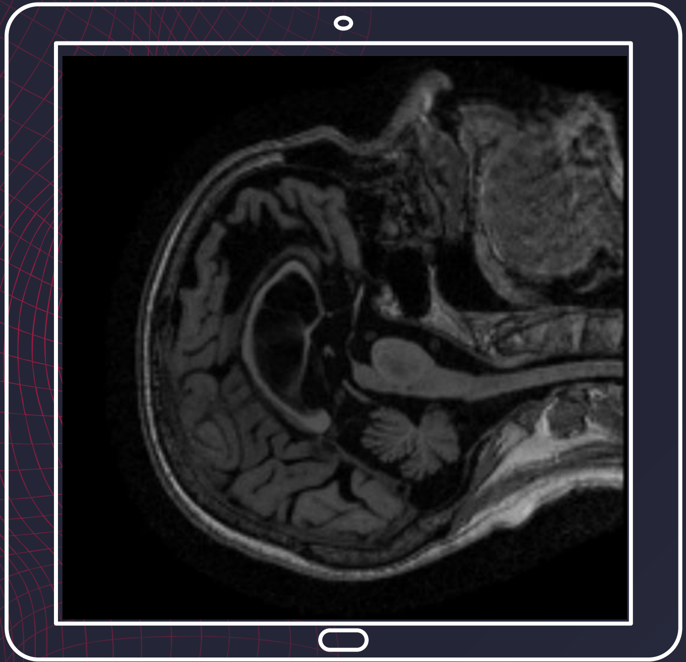
Alzheimer's Disease Neuroimaging Initiative

New participants were recruited across North America during each phase of the study and agreed to complete a variety of imaging and clinical assessments.

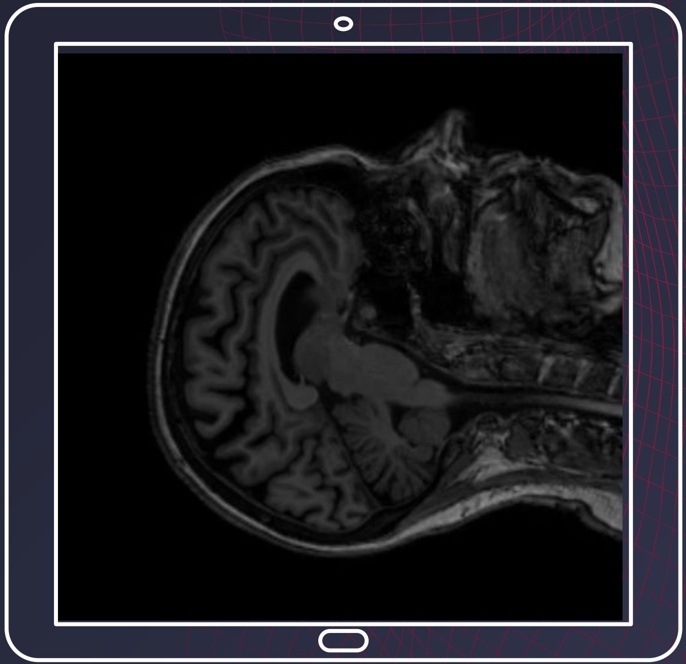
ADNI began in 2004, funded by 20 companies and two foundations.It has been extended by 10 years, with each phase lasting about 5 years.

Counts thousands of researchers contributing to the project.

3D MRI T1-weighted image 1.5T



3D MRI T1-weighted image 3T



CSV table from ADNI

PTID	Exam Date	Image ID	Visit	Month	Diagnosis
011_S_0003	2005-09-12	32237	Screening	0	AD
011_S_0003	2006-09-12	35576	Month 12	11.9672	AD
011_S_0005	2005-09-07	32246	Screening	0	NC
011_S_0005	2007-09-07	200385	Month 24	23.9344	NC

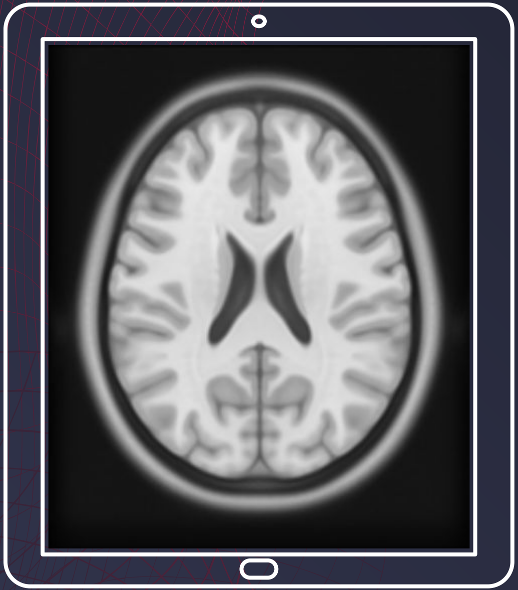
Preprocessing

Linear Registration

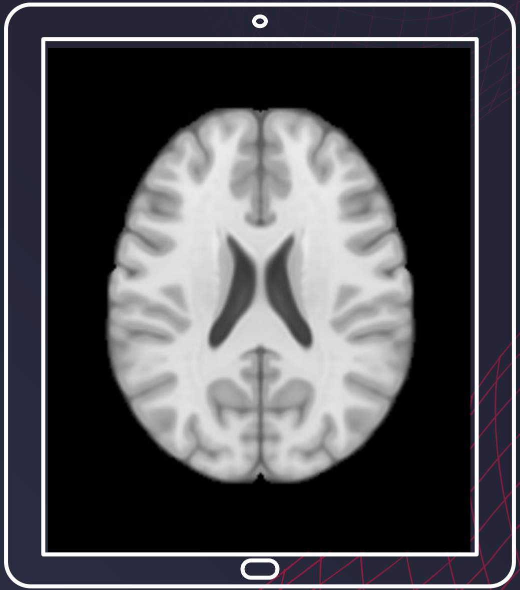
Normalization

Skull Removal

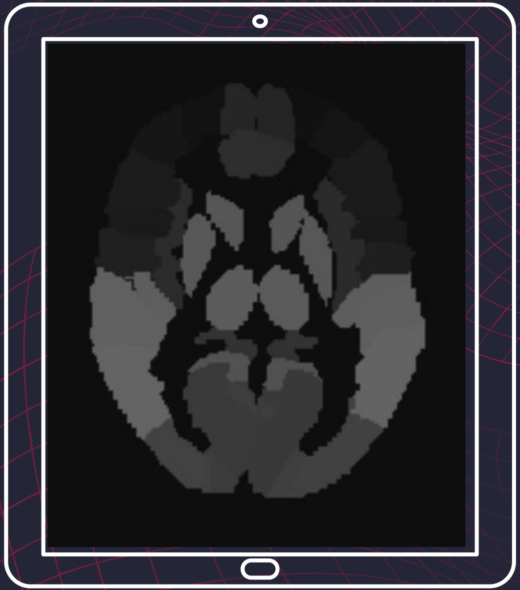
MRI image template



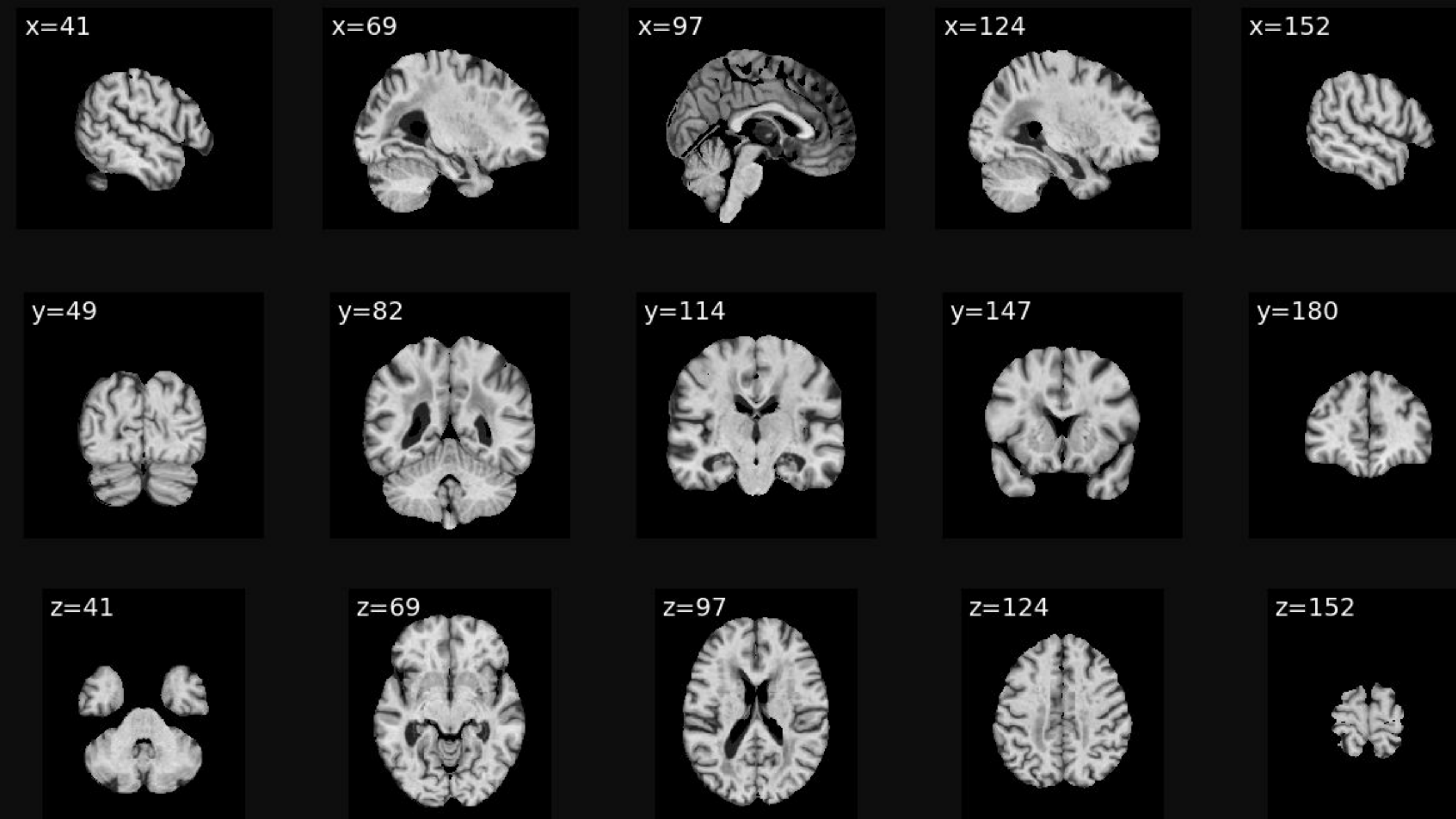
Skull-free MRI image



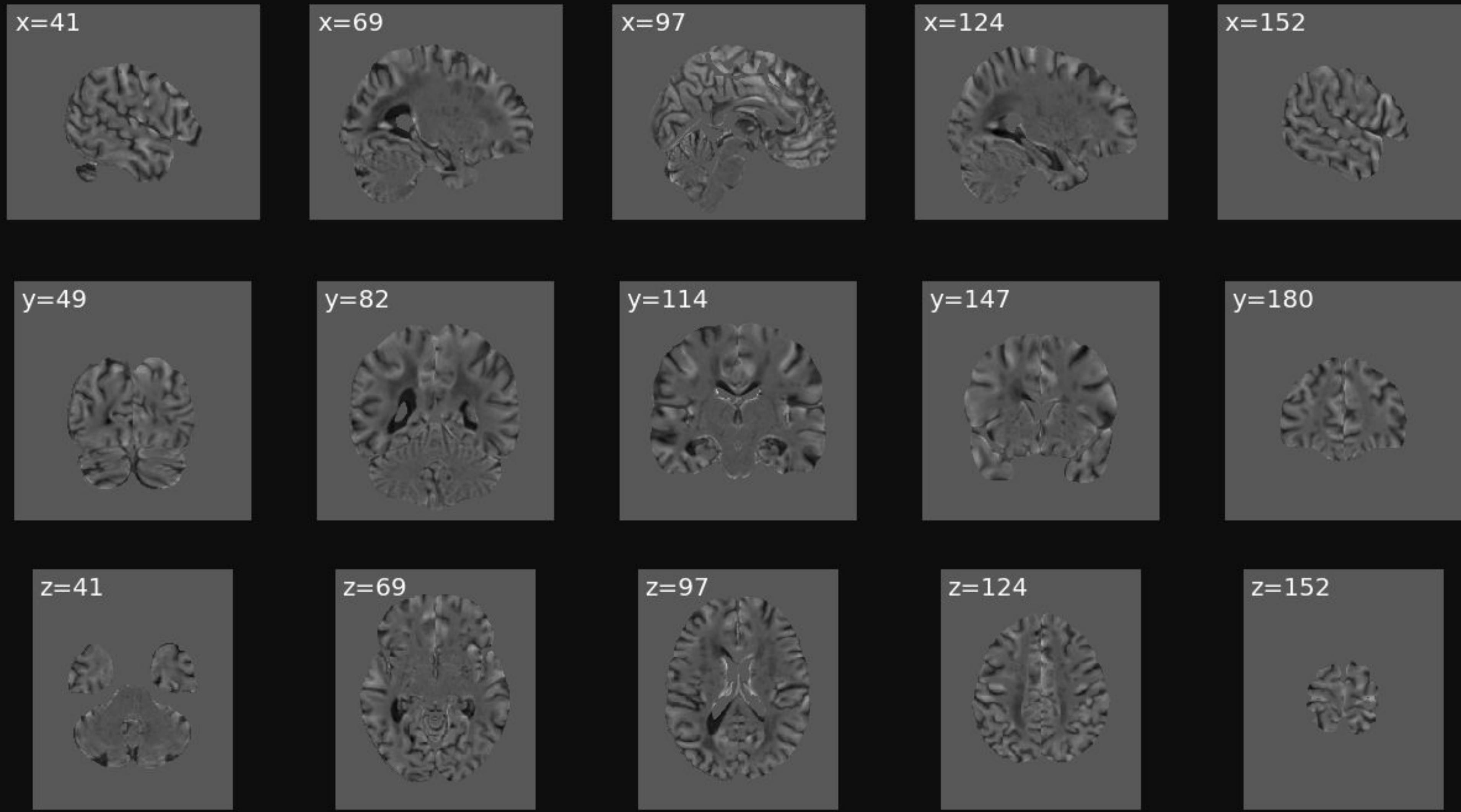
Automated Anatomical Labeling Atlas



The final preprocessed images look like this...


x=41
x=69
x=97
x=124
x=152
y=49
y=82
y=114
y=147
y=180
z=41
z=69
z=97
z=124
z=152

and this is how the network sees them (normalized) ...


x=41
x=69
x=97
x=124
x=152
y=49
y=82
y=114
y=147
y=180
z=41
z=69
z=97
z=124
z=152

The Tools

Aliza Medical Imaging & DICOM Viewer

Advanced Normalization Tools

FMRIB Software Library

Model

- 4 convolutional layers with filter size 3x3x3 and 8/16/32/64 feature maps
- ReLU activation function
- 2 fully connected layers with 128/64 neurons
- Batch normalization and pooling after each convolution
- Dropout of 0.8 before the 1st FC layer
- 2 output neurons with softmax activation
- Cross-entropy loss function
- Adam optimizer for training with learning rate 0.0001 and batch size 5
- Training lasts 20 epochs
- 5-fold cross validation

PyTorch implementation with torchsample for high-level training

```
class ClassificationModel3D(nn.Module):
    """The model we use in the paper."""

    def __init__(self, dropout=0, dropout2=0):
        nn.Module.__init__(self)
        self.Conv_1 = nn.Conv3d(1, 8, 3)
        self.Conv_1_bn = nn.BatchNorm3d(8)
        self.Conv_2 = nn.Conv3d(8, 16, 3)
        self.Conv_2_bn = nn.BatchNorm3d(16)
        self.Conv_3 = nn.Conv3d(16, 32, 3)
        self.Conv_3_bn = nn.BatchNorm3d(32)
        self.Conv_4 = nn.Conv3d(32, 64, 3)
        self.Conv_4_bn = nn.BatchNorm3d(64)
        self.dense_1 = nn.Linear(5120, 128)
        self.dense_2 = nn.Linear(128, 64)
        self.dense_3 = nn.Linear(64, 2)  #1
        self.relu = nn.ReLU()
        self.dropout = nn.Dropout(dropout)
        self.dropout2 = nn.Dropout(dropout2)
```

Data statistics for 3T images

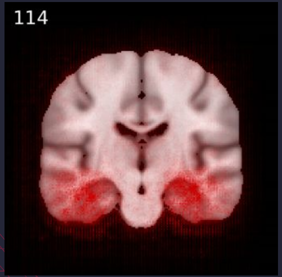
	Images	AD	CN	Patients	AD	CN
All	180	88	92	65	37	28
Train	73	48	25	25	17	8
Validation	107	40	67	40	20	20

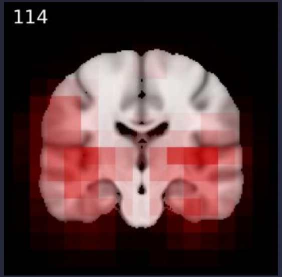
Data statistics for 1.5T images

	Images	AD	CN	Patients	AD	CN
All	969	475	494	344	193	151
Train	794	399	395	284	163	121
Validation	175	76	99	60	30	30

Visualization Methods

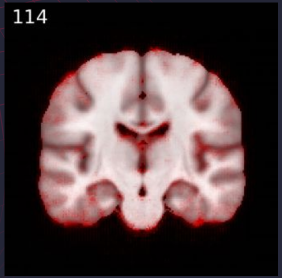
Sensitivity Analysis (Backpropagation)

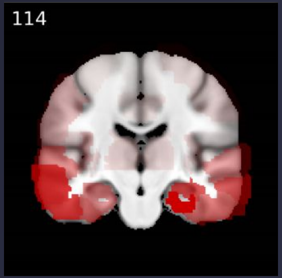




Occlusion

Guided Backpropagation





Brain Area Occlusion

03

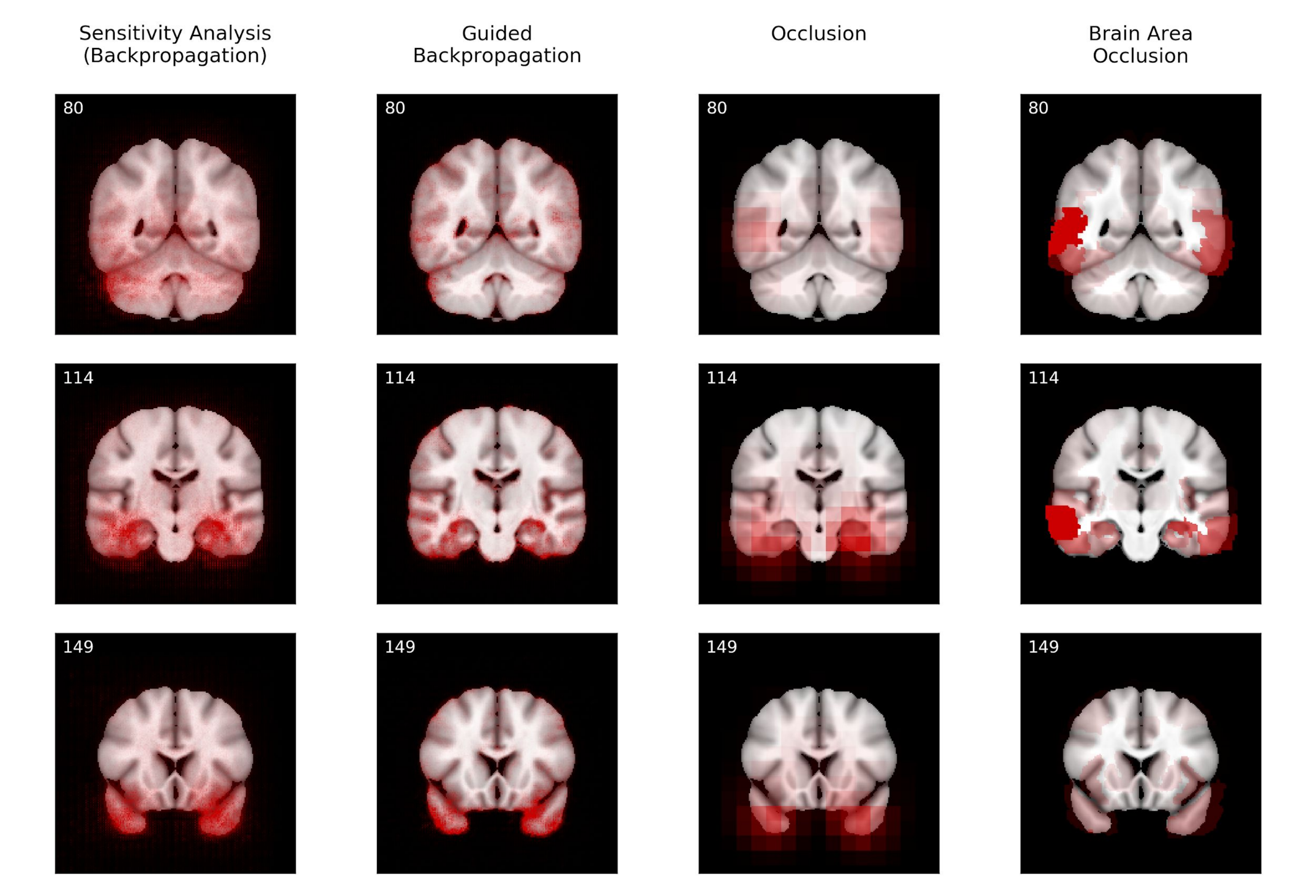
Results

Classification

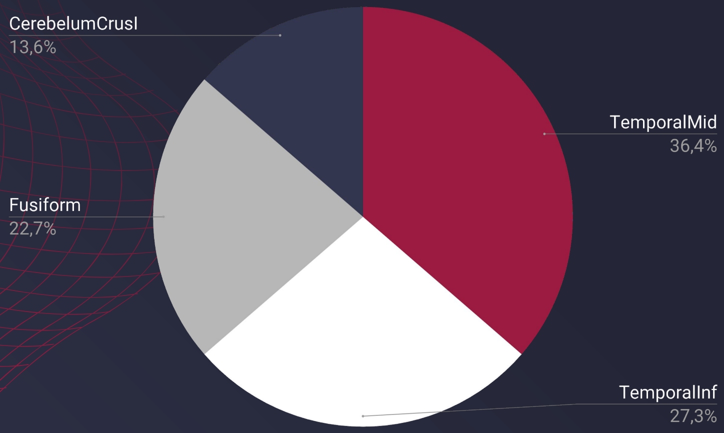
0.77 ± 0.06 — 1.5T

0.69 ± 0.05 — 3T

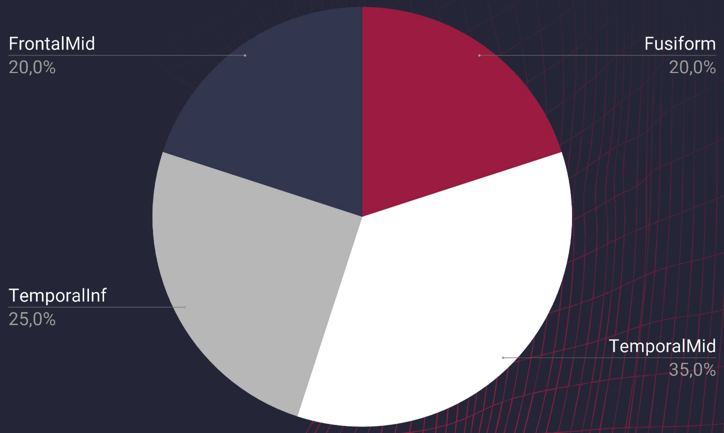
Relevance Heatmaps
(averaged over all AD samples in the test set)


Sensitivity Analysis (Backpropagation)
Guided Backpropagation
Occlusion
Brain Area Occlusion
80
114
149

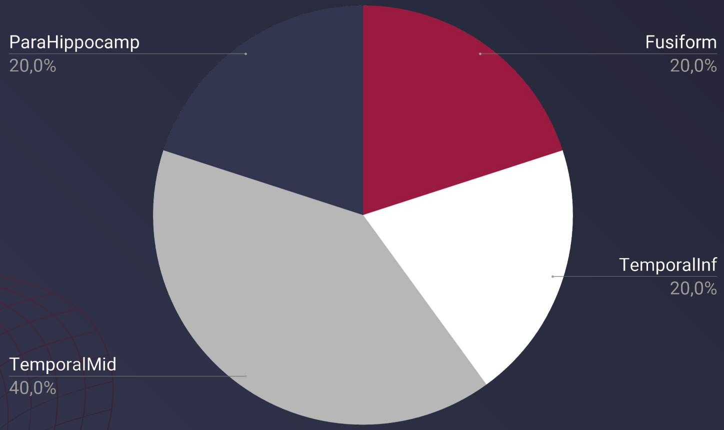
Sensitivity Analysis (Backpropagation)



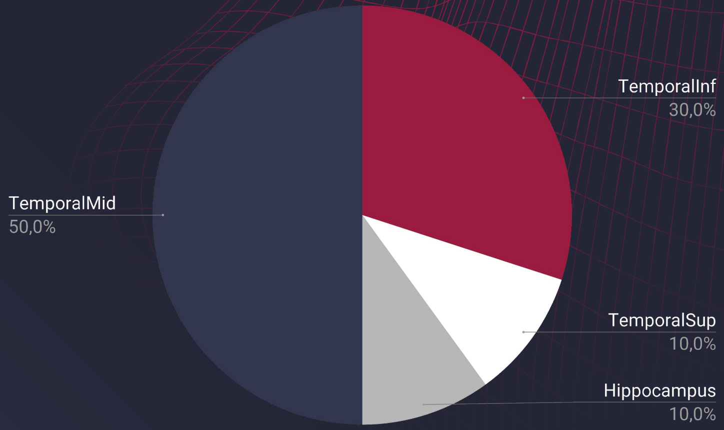
Guided Backpropagation



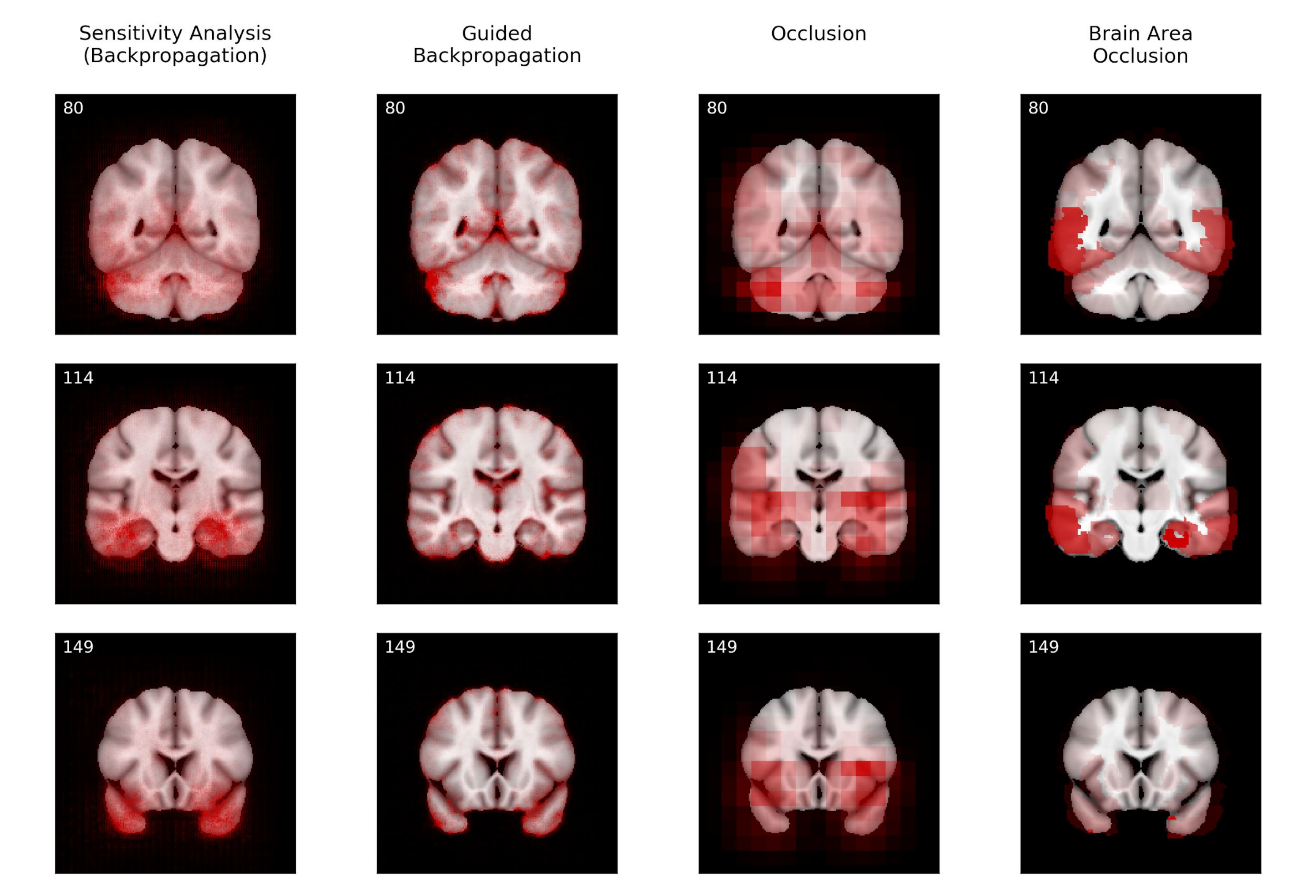
Occlusion



Brain Area Occlusion

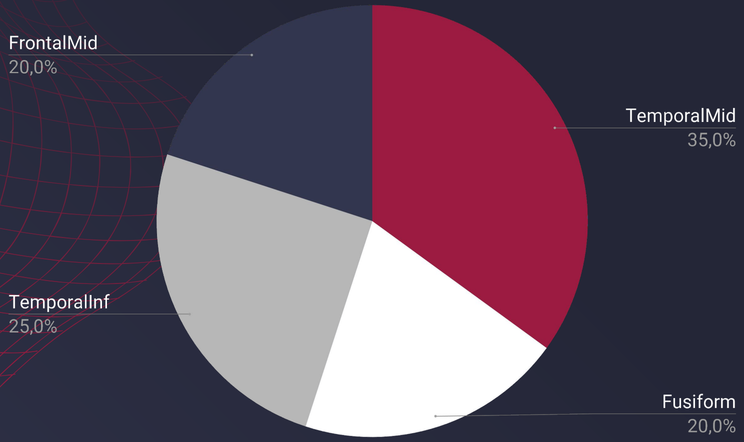


Relevance Heatmaps
(averaged over all CN samples in the test set)

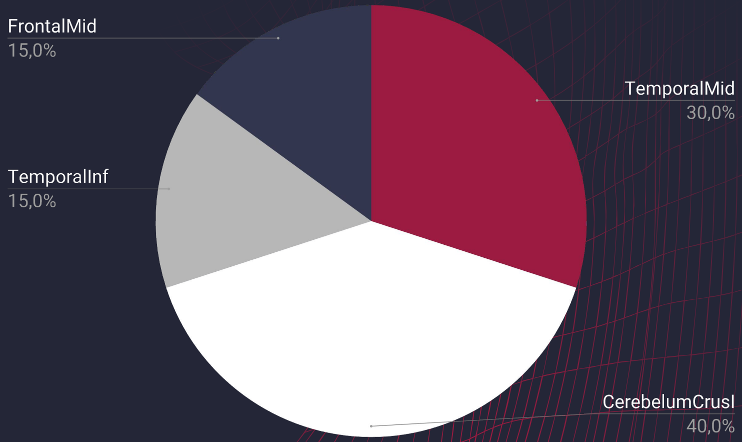


Sensitivity Analysis (Backpropagation)
Guided Backpropagation
Occlusion
Brain Area Occlusion
80
80
80
80
114
114
114
114
149
149
149
149

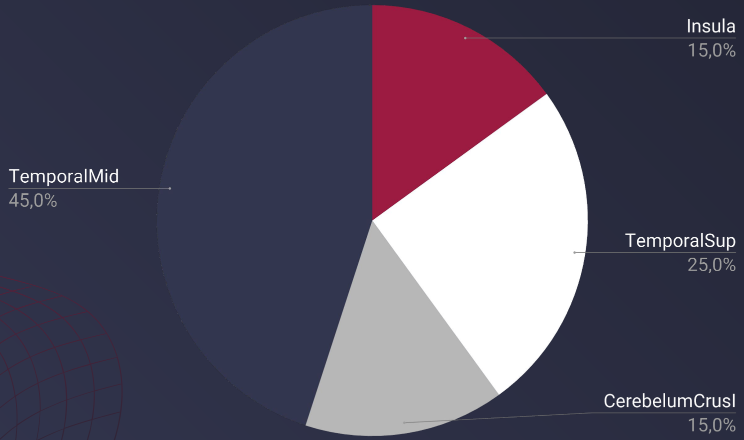
Sensitivity Analysis (Backpropagation)



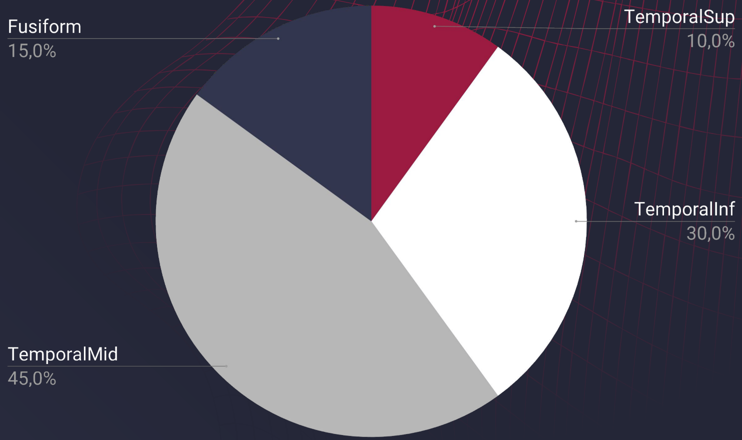
Guided Backpropagation



Occlusion



Brain Area Occlusion



Relevant Brain Areas

- For both AD and NC patients, we can see that the main focus of the network is on the temporal lobe, especially its medial part, which has been empirically linked to AD **[4]**.

- We observe some relevance on the hippocampus, but usually the whole area around it is crucial for the network's decision. The hippocampus itself is usually one of the earliest areas affected by AD **[5]**. This may be explained by the fact that our samples contain only advanced forms of the disease.

- In addition to temporal regions, we observe some relevance attributed to other areas across the brain. We find that the distribution of relevance varies between patients: Some brains have strong relevance in the temporal lobe, while in others, the cortex plays a crucial role.

- Lastly, we note that the heatmaps for AD and NC samples are quite similar. This makes sense, given that the network should focus on the same regions to detect presence or absence of the disease.

Future Research

Prognostic Prediction

More Visualization methods

Ground Truth for the relevance heatmaps

04

References

[1] Basaia et al. *Automated classification of Alzheimer's disease and mild cognitive impairment using a single MRI and deep neural networks*. NeuroImage: Clinical 21 (2019).

[2] Khvostikov et al. *3D CNN-based classification using sMRI and MD-DTI images for Alzheimer disease studies*. arXiv preprint (2018).

[3] Simonyan et al. *Deep Inside Convolutional Networks: Visualising Image Classification Models and Saliency Maps*. arXiv preprint (2014).

[4] Frisoni et al. *The clinical use of structural MRI in Alzheimer disease*. Nature Reviews Neurology 6 (2010).

[5] Mu et al. *Adult hippocampal neurogenesis and its role in Alzheimer's disease*. Molecular Neurodegeneration 6 (2011).

Use visualizations on your own PyTorch model:

```
from interpretation import sensitivity_analysis
from utils import plot_slices

cnn = load_model()
mri_scan = load_scan()

heatmap = sensitivity_analysis(cnn, mri_scan, cuda=True)
plot_slices(mri_scan, overlay=heatmap)
```

THANKS!

Report + Code available!

github.com/iliaspan/cnn-adni

slidesgo