Automatic Classification of Alzheimer Disease Based on MRI Volumetric Features

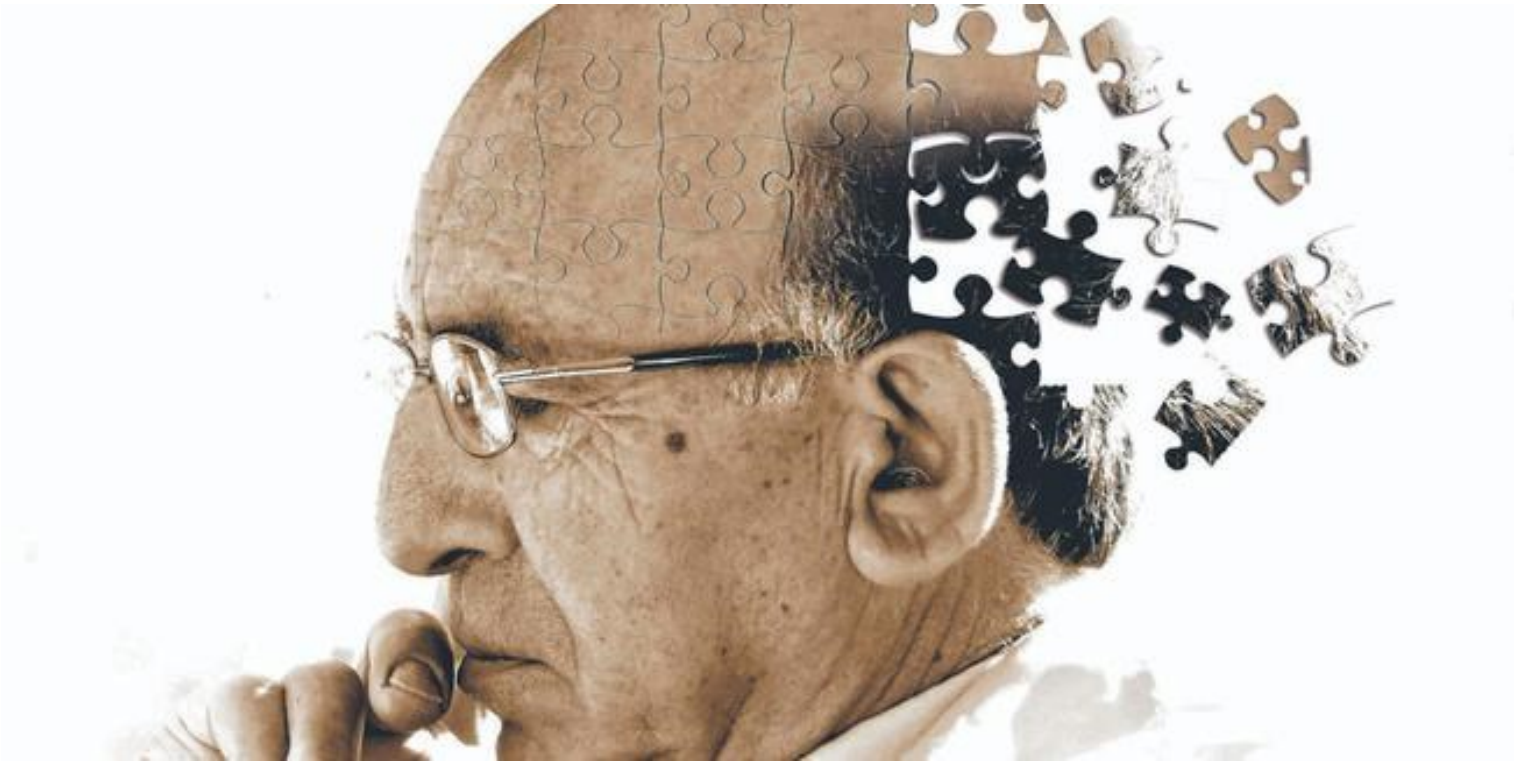
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Alzheimer's Disease

- Alzheimer's disease (AD), the most common dementia, affecting 1 out of 9 people over the age of 65 years.
- AD involves progressive cognitive impairment, commonly associated with **early memory loss**, requiring assistance for activities of self care during advanced stages.



Mild Cognitive Impairment

- An individual is suffering from cognitive impairments, which are greater than the changes associated with the normal aging process.
- MCI is confusing because
  - it overlaps with both normal-age related cognitive impairments and the onset of AD.

Important!

- Not everyone who suffers from MCI will develop AD,
- But those who are eventually diagnosed with AD first suffer from MCI.

Alzheimer's Disease & Mild Cognitive Impairment

- For those that truly suffer from MCI and not the onset of AD, they will not experience the same progressive symptoms. In fact, many individuals will not experience worsening symptoms and in some cases, recover.
- Of course, those with AD, they will continually get worse until they reach the late stages of their disease.

Biomarkers Needed

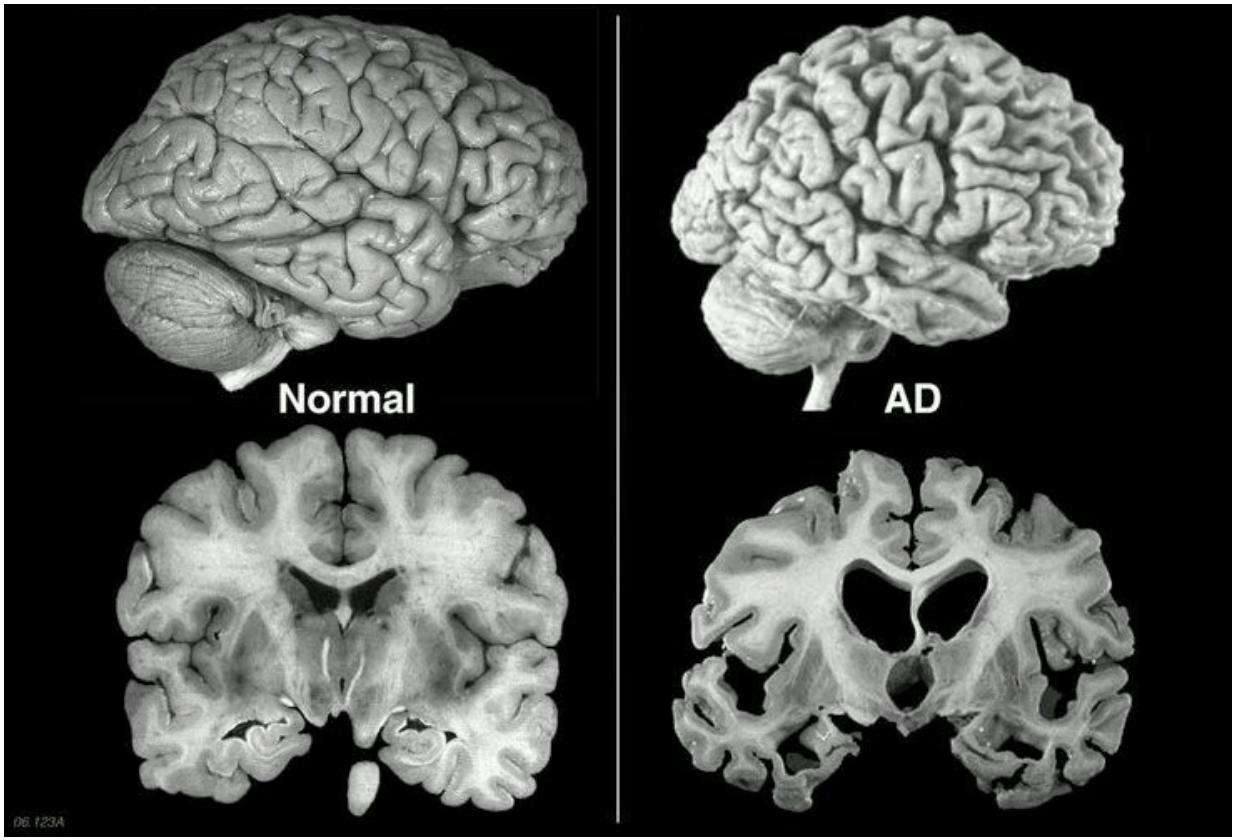
- There is an urgent need to develop biomarkers that can identify the changes in a living brain due to the pathophysiology of AD.

Neuroimaging Modalities for Biomarkers

- Neuroimaging modalities such as MRI and FDG-PET have been previously used to develop such biomarkers for diagnosis of AD.

Structural MRI

- Structural MRI provides measures of brain gray matter, white matter and CSF compartments enabling the quantification of volumes, cortical thickness and shape of various brain regions.



Goal of Our Study

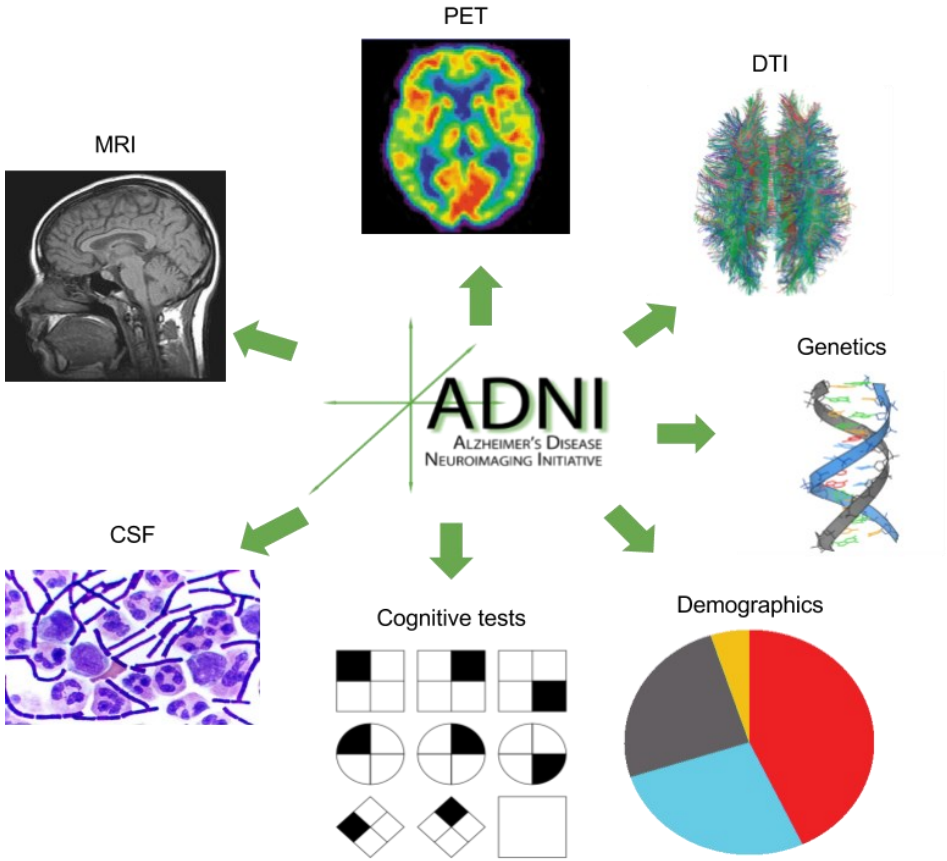
Perform automatic classification of

- healthy, MCI and AD patients

using volumetric features extracted from structural MR images.

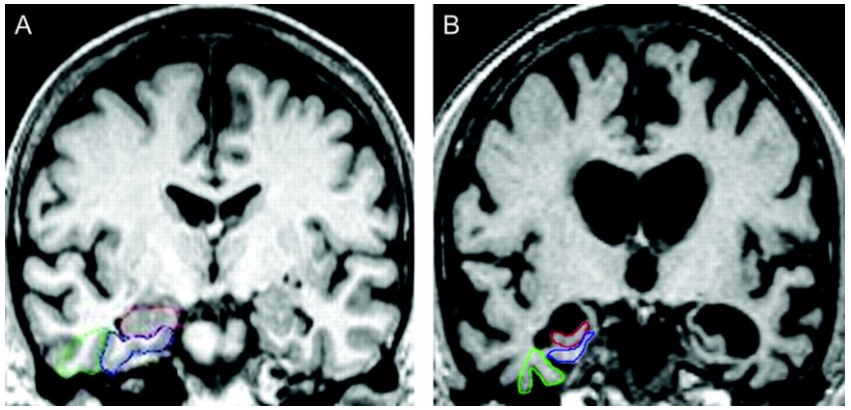
Alzheimer's Disease Neuroimaging Initiative (ADNI)

- The ADNI was established in 2004 as a public-private partnership, led by Dr. Michael W. Weiner from UCSF.
- Since then a total 9665 scans from 2384 people.
- 1.5T and 3T MRI
- FDG-PET
- Genetic data
- Cognitive test results



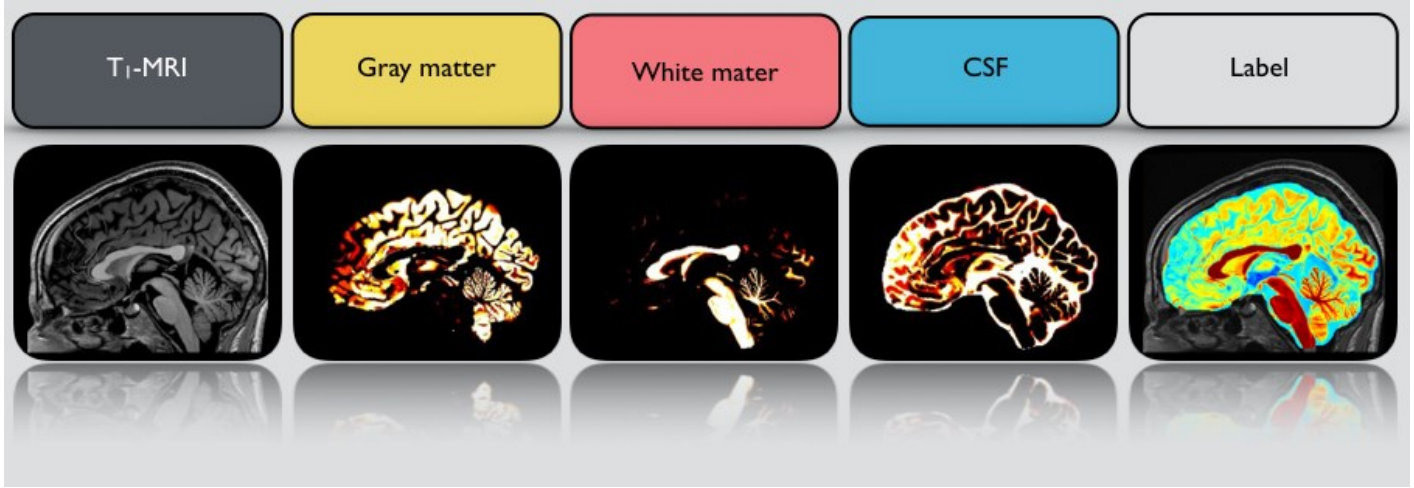
Dataset

- A subset of ADNI database was used in this study
- a total of 351 MRI scans (3T) from:
  - 22 healthy subjects (129 scans),
  - 20 MCI patients (145 scans),
  - 18 AD patients (77 scans).
- Every 6 months a scan was performed on each patient and the patients were monitored for three years.



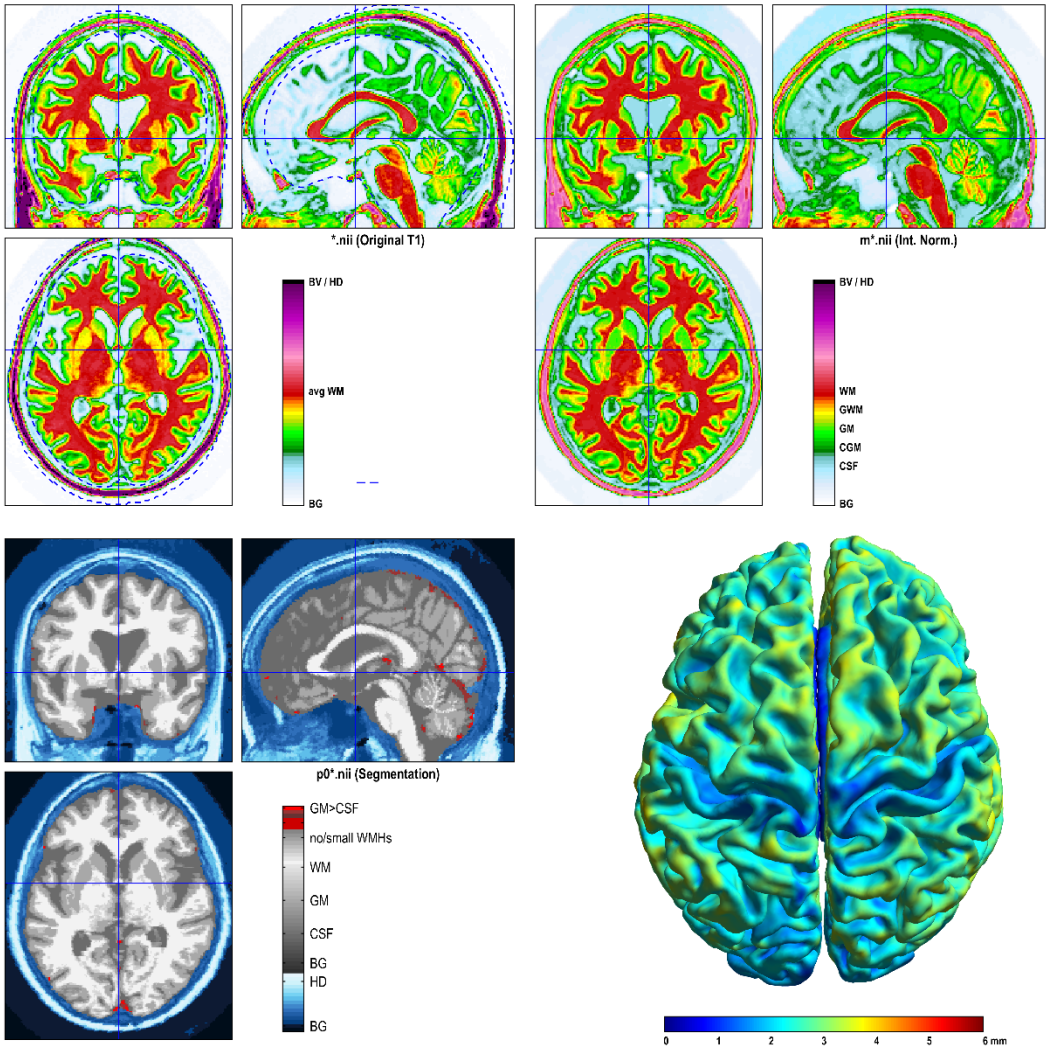
Computational Anatomy Toolbox (CAT) for SPM

- CAT is a an extension to SPM to provide computational anatomy. This covers diverse morphometric methods such as voxel-based morphometry (VBM).
- VBM provides the voxel-wise estimation of the local amount or volume of a specific tissue compartment (Ashburner 2005). It is most often applied to investigate the local distribution of grey matter, but can also be used to examine white matter.
- The concept of VBM incorporates different preprocessing steps:
- (1) spatial registration to a reference brain (template)
- (2) tissue classification (segmentation) into grey and white matter and CSF
- (3) bias correction of intensity non-uniformities
- Finally, segmentations are modulated by scaling with the amount of volume changes due to spatial registration, so that the total amount of grey matter in the modulated image remains the same as it would be in the original image.



Segmentation using SPM

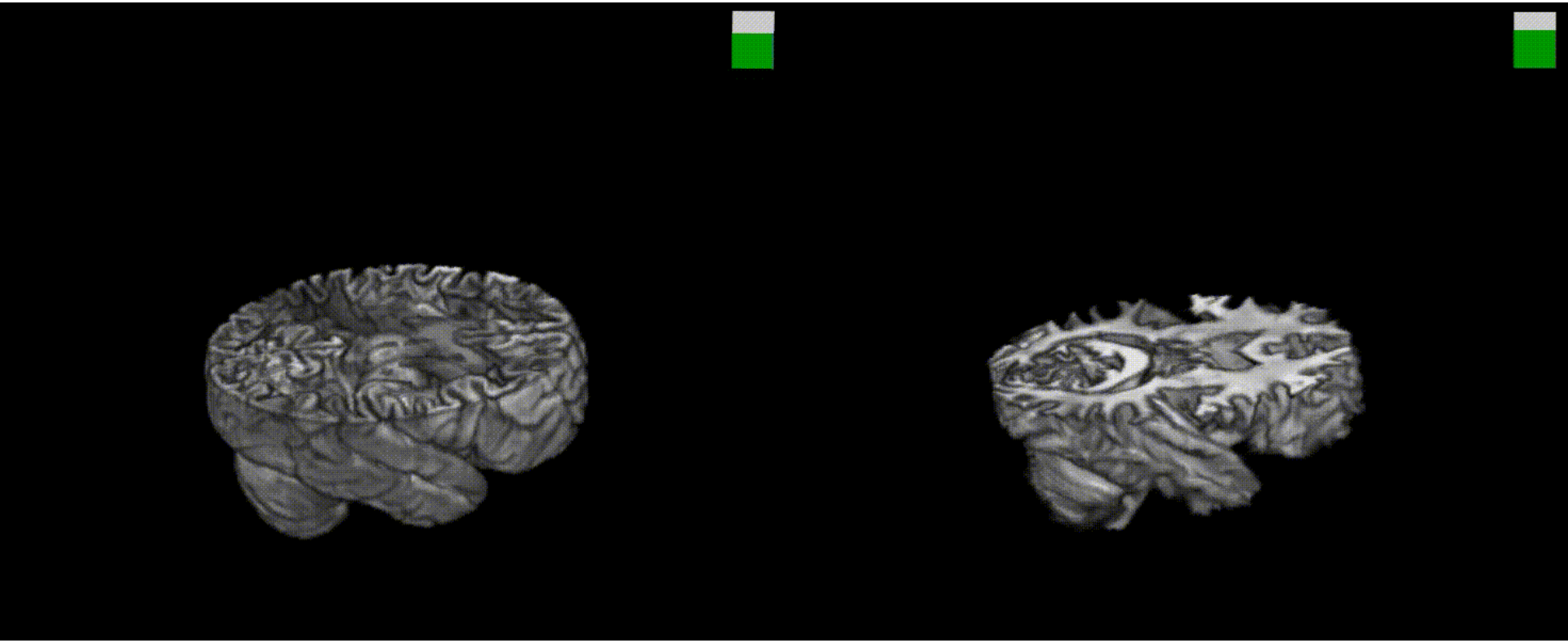
- The slices from MRI scans were segmented using CAT12 toolbox in Statistical Parametric Mapping (SPM) software implemented in MATLAB.
- One scan took almost 2 hours in a desktop with i7 processor (4.2 GHz) and 16 GB RAM
- Images were normalized using Montreal Neurological Institute (MNI) template



Segmentation Outputs

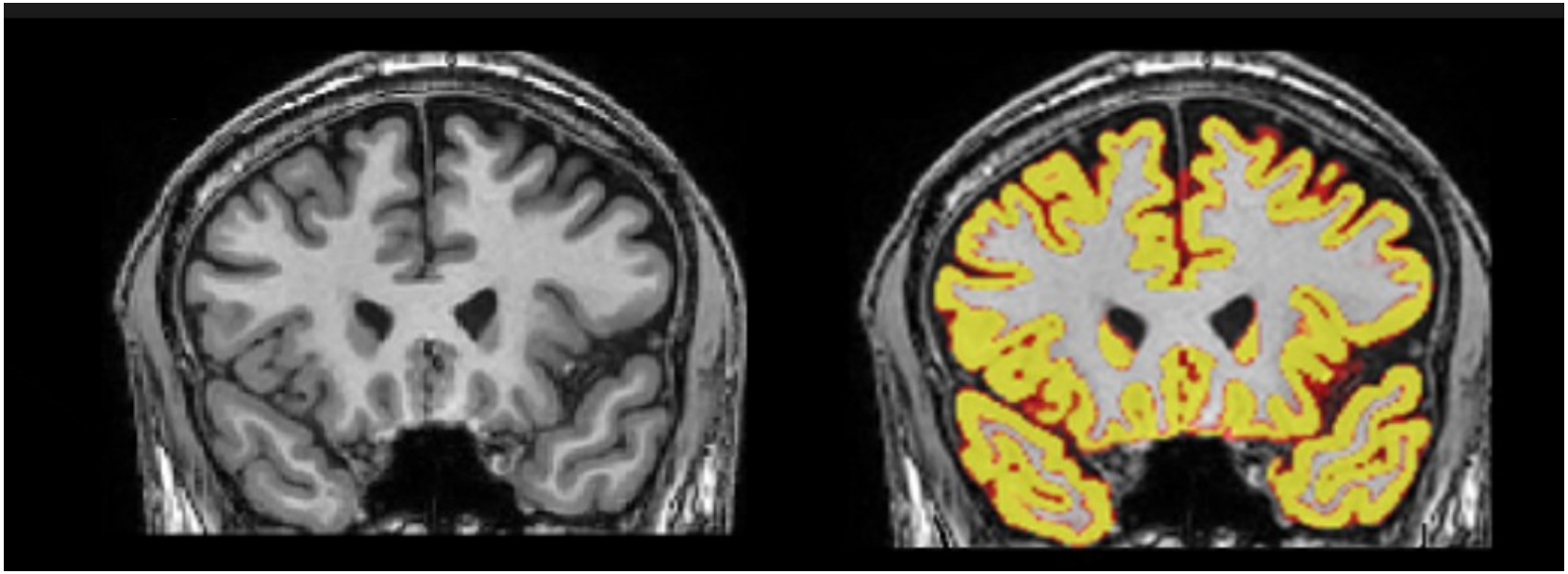
GM

WM



MRI Volumetric Features

- SPM provided us white matter (WM), grey matter (GM), cerebrospinal fluid (CSF), total intracranial volume (TIV) and cortical thickness (CT) values.



- Age and gender information were included as additional features (inputs to the classifiers)

Classifiers

- k-Nearest Neighbors (*k*NN)
- Random Forest
- Naïve Bayes
- Support Vector Machines
- Decision tree (J48)

- WEKA for classification

Results

Classification Methods:	kNN			Random Forest			Naive Bayes			Support Vector Machines			J48		
Correctly Classified Instances (out of 351):	321 (91.5%)			306 (87.2%)			213 (60.7%)			205 (58.4%)			274 (78.1%)		
Kappa statistic:	0.87			0.8			0.39			0.34			0.66		
Mean absolute error:	0.06			0.19			0.31			0.34			0.16		
RMS error:	0.24			0.27			0.42			0.44			0.36		
Relative absolute error:	14.1%			44.2%			71.2%			79.6%			36.0%		
Root relative squared error:	51.2%			58.37%			91.4%			95.14%			77.0%		
Classified as →	CN	AD	MCI	CN	AD	MCI	CN	AD	MCI	CN	AD	MCI	CN	AD	MCI
CN (out of 129):	116	4	9	112	2	15	107	1	21	74	4	51	109	7	13
AD (out of 77):	3	71	3	5	63	9	16	32	29	24	21	32	13	55	9
MCI (out of 145):	10	1	134	11	3	131	39	32	74	17	18	110	22	13	110

Results

Healthy vs. MCI vs. AD

Classification Approach	Accuracy %	Kappa Statistic
k-Nearest Neighbors	91.5	0.87
Random Forest	87.2	0.80
Decision trees (J48)	78.1	0.66
Naïve Bayes	60.7	0.39
Support Vector Machines	58.4	0.34

10-fold cross-validation

Conclusion

- This study showed that volumetric features obtained using SPM have a great potential in automatic classification of healthy, MCI and AD patients.
- A simple approach like *k*NN might be used as the method of choice.

Future Plans

- Using MR images, investigation of changes in volumetric parameters with respect to time.
- MR and PET images will be used together to determine novel and effective biomarkers for characterizing MCI and AD.
- More scans from ADNI
- Deep learning for classification

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