Results of an Adaboost approach on Alzheimer's Disease detection on MRI

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Alzheimer's Disease

- Neurodegenerative disorder and one of the most common cause of dementia in old people.
- Incurable, degenerative and terminal.
- Definitive diagnosis can only be made after a postmortem study of the brain tissue.
- T1 weighted MRI scans of the brain may detect changes on the AD patient's brain years before the first clinical signs of dementia.

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Motivation

Objective

- Detection of patients with very mild to mild Alzheimer's disease.

- Using sMRI and standard classifiers
  - Feature extraction based on VBM analysis
  - Classification using AdaBoost and Support Vector Machines (SVM) as weaklearners.

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Differential features of our work

- This issue has been addressed in many other works.

The differences here are:

- Freely available database with good quality images and well-documented.
- The number of subjects selected for this study is relatively high.

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Voxel-based Morphometry

- Morphometry analyses allow a measurement of structural differences within or across groups throughout the entire brain.
- VBM measures differences in local concentrations of brain tissue, through a voxel-wise comparison of multiple brain images.

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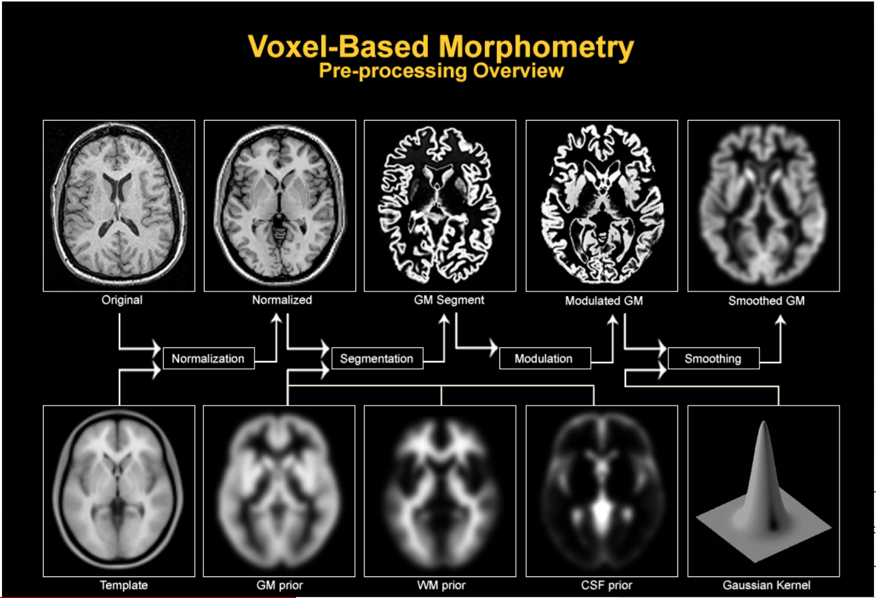
VBM Preprocessing Pipeline



VBM and the General Linear Model (GLM)

- After preprocessing we fit a linear statistical model to the data, each grey matter voxel independently.
- Use the estimated model parameter values to look for a specific effect we are interested in.
    - Identifying and characterizing structural differences among populations.

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VBM and GLM

- The GLM equation expresses the observed response variable in terms of a linear combination of regressors.

$$Y = X\beta + \varepsilon$$

- Y: observation vector (Mx1)
- X: design matrix (MxL). Each column corresponds to an effect that the user has built into the experiment or that may confound the results.
- β: regressor or covariate vector (Lx1). Unknown parameters
- ε: vector of error terms (Mx1)

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VBM (Statistical Inference)

- On the results of GLM a t-test is computed at each voxel.
- The t-test values constitute a Statistical Parametric Map (SPM).
- The decision threshold for the test is set using Random Field Theory to account for spatial dependencies.

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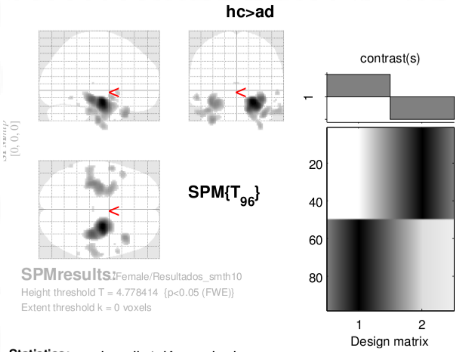
SPM Example



Statistics: ***p–values adjusted for search volume***

set-level p	set-level c	cluster-level $p_{corrected}$	cluster-level k_E	cluster-level $p_{uncorrected}$	voxel-level $p_{FWE-corr}$	voxel-level $p_{FDR-corr}$	voxel-level T	voxel-level $(Z_{\equiv})$	voxel-level $p_{uncorrected}$	mm	mm	mm
0.000	12	0.000	1764	0.000	0.000	0.000	7.59	6.70	0.000	24	-8	-16
					0.000	0.000	6.43	5.85	0.000	34	-24	-12
					0.007	0.000	5.33	4.98	0.000	34	-8	-48
		0.000	1355	0.000	0.001	0.000	5.91	5.44	0.000	-34	-20	-16
					0.001	0.000	5.87	5.41	0.000	-30	-12	-18
					0.002	0.000	5.71	5.29	0.000	-34	-14	-40
		0.000	161	0.004	0.002	0.000	5.68	5.26	0.000	40	24	-30
		0.000	195	0.002	0.006	0.000	5.36	5.00	0.000	58	-20	-28
					0.018	0.000	5.07	4.76	0.000	62	-10	-22
		0.005	42	0.106	0.007	0.000	5.33	4.98	0.000	-56	4	-8
		0.003	60	0.058	0.011	0.000	5.21	4.88	0.000	-48	20	-32
		0.018	13	0.358	0.015	0.000	5.12	4.80	0.000	58	12	-2
		0.024	8	0.475	0.030	0.000	4.93	4.64	0.000	-58	-54	-10
		0.034	3	0.679	0.038	0.000	4.86	4.58	0.000	56	10	-12
		0.027	6	0.541	0.041	0.000	4.84	4.57	0.000	62	-44	-18
		0.034	3	0.679	0.043	0.000	4.82	4.55	0.000	0	-22	10
		0.042	1	0.830	0.049	0.000	4.79	4.52	0.000	48	8	-40

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Subjects

- The set of subjects used consists in 98 women selected from the Open Access Series of Imaging Studies (OASIS) database

	Very mild to mild AD	Normal
No. of subjects	49	49
Age	78.08 (66-96)	77.77 (65-94)
Education	2.63 (1-5)	2.87 (1-5)
Socioeconomic status	2.94 (1-5)	2.88 (1-5)
CDR (0.5 / 1 / 2)	31 / 17 / 1	0
MMSE	24 (15-30)	28.96 (26-30)

- We find many subjects with high MMSE and low CDR.

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Feature Extraction

- The clusters (regions) detected as result of VBM were used as a mask on the grey matter (GM) segmentation images to select the potentially most discriminant voxels.

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Adaptive Boosting (AdaBoost)

- Meta-algorithm for machine learning that can be used in conjunction with many other learning algorithms to improve their performance.
- Adaptive in the sense that subsequent classifiers built are adjusted in favor of those instances misclassified by previous classifiers.
- Sensitive to noisy data and outliers. Otherwise, less susceptible to over-fitting.

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Support Vector Machines (SVM)

- Standard SVM to perform classification of patients with mild AD vs. control subjects.
- Algorithm included in the libSVM software package.
- Two kernels: linear and radial basis function (RBF) kernel.

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Experiments

- Three different AdaBoost classifier were created:
  1. Independent SVM classifiers for each VBM detected cluster and the combination of their responses by a simple majority voting.
  2. Independent SVM classifiers for each VBM detected cluster and the combination of their responses by taking into account a given weight based on their training errors.
  3. Using all the voxels within the SPM; we trained SVM with different RBF kernel sigma values, weighted them taking into account its training error and then, selected the classifiers with highest diversity based on its weight.

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Features extracted

1. Mean and standard deviation of grey matter probability voxels within each cluster
2. All grey matter voxels within clusters in a vector

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Showing the results

- All the results were extracted from the VBM detected clusters.
- We performed 10 times a 10-fold cross-validation for each experiment.
- For each experiment we show:
    - Size of feature vector
    - Classification accuracy
    - Sensitivity (controls correctly classified)
    - Specificity (AD patients correctly classified)

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Results of SVM and global feature vectors

- Using all voxels within all clusters and only one SVM.

Feature extracted	Features	Accuracy (lk/nlk)	Sensitivity (lk/nlk)	Specificity (lk/nlk)
Mean & StDev	24	78.57 / 80.61	0.72 / 0.75	0.88 / 0.89
Voxel intensities	3611	73.47 / 76.53	0.72 / 0.77	0.75 / 0.76

Table: Classification results with a linear kernel (lk) and a non-linear RBF kernel (nlk). The values of $\gamma = (2\sigma^2)^{-1}$ for non linear kernel were 0.5, 0.031, 0.0078 for each feature extraction process, respectively.

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Results of AdaBoost and majority voting

- Using one SVM for each voxel cluster and majority voting to final decision.

Feature extracted	Features	Accuracy (lk/nlk)	Sensitivity (lk/nlk)	Specificity (lk/nlk)
Mean & StDev	24	74% / 75%	0.51 / 0.56	0.97 / 0.95
Voxel intensities	3611	77% / 78%	0.74 / 0.76	0.80 / 0.82

Table: Majority voting classification results with linear kernel (lk) and non-linear kernel (nlk) SVM built independently for each VBM cluster.

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Results of AdaBoost and weighted classifiers

- Using one SVM for each voxel cluster and classifying based on the weight of each classifier.

Feature extracted	Features	Accuracy (lk/nlk)	Sensitivity (lk/nlk)	Specificity (lk/nlk)
Mean & StDev	24	71% / 79%	0.54 / 0.78	0.88 / 0.80
Voxel intensities	3611	73% / 86%	0.76 / 0.80	0.70 / 0.92

Table: Weighted individual SVM per cluster classification results. The value of the RBF kernels for the nonlinear (nlk) classifiers were searched for the best fit to the training set.

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Results of Diverse AdaBoost

- Using many SVM classifiers trained with different RBF variance values (σ) and using weights to decide.

Feature extracted	Features	Accuracy	Sensitivity	Specificity
Mean & StDev	24	85%	0.78	0.92
Voxel intensities	3611	78%	0.71	0.85

Table: Diverse AdaBoostSVM classification results.

- The σ_{min} is set as 0.1, the σ_{ini} is set as 100 and σ_{step} is set as 0.1.

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Conclusions

- We performed feature extraction processes based on VBM analysis to classify MRI volumes of AD patients and normal subjects.
- We used the basic GLM design without any covariate to detect subtle changes between AD patients and controls.
- As we don't have post-mortem confirmation of AD subjects, the very mild demented subjects could be false positives.

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Further work

- Using other morphometry methods such as Deformation-based morphometry.
- Try these methods with real clinical subjects and different types of dementia like MD1 and FTD.

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Questions?

Thank you for your attention.

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