Global Disease Index, a novel tool for MTL atrophy quantification

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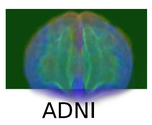
We propose an improvement of the methodology described in Chincarini et al. (2011), [1]. This is a novel automatic analysis technique based on local analysis on structural MRI. Here, 9 volumes of interest (VOI) are selected, extracted from target scan, and filtered with several different intensity and textural filters. Filtered regions are then analyzed with a Random Forest (RF) classifier to prune less relevant features for the discrimination between Cognitively Normal (CN) and Alzheimer's Disease (AD) subjects. Features subset is subsequently processed with a combination of Support Vector Machines (SVM) and Random Forest (RF), to give the final classification index. This value ranges from -1 (AD-like condition) to 1 (normalcy). Other values are to represent intermediate conditions (MCI).

Subjects: TRAIN & TEST

Training dataset consisted in 581 1.5T T1-weighted MR scans; 30 of which provided within CADDementia challenge and the other data coming from ADNI database.
The procedure has been tested on 354 test subjects from CADDementia challenge



ADNI

Cohort	Sample size	Age [y]	Sex [M/F]
CN	190	76.6 ± 5.5	95/95
MCI	195	76.6 ± 7.8	66/79
AD	166	75.5 ± 7.4	71/45

AD cohort includes 50 MCI subjects who converted to clinical dementia after a 2-y follow-up

CADD

Cohort	Sample size	Age [y]	Sex [M/F]
CN	12	62.3 ± 6.2	9/3
MCI	9	68 ± 8.5	5/4
AD	9	66.1 ± 5.2	3/6

Tools

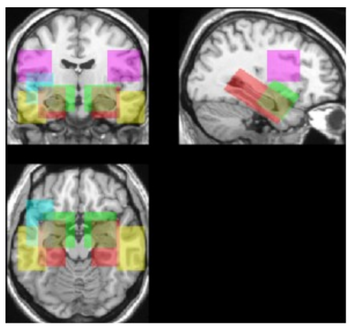
LONI Pipeline

Insight Toolkit

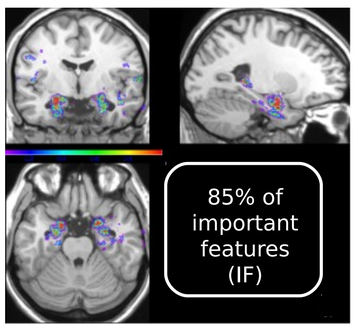
Matlab

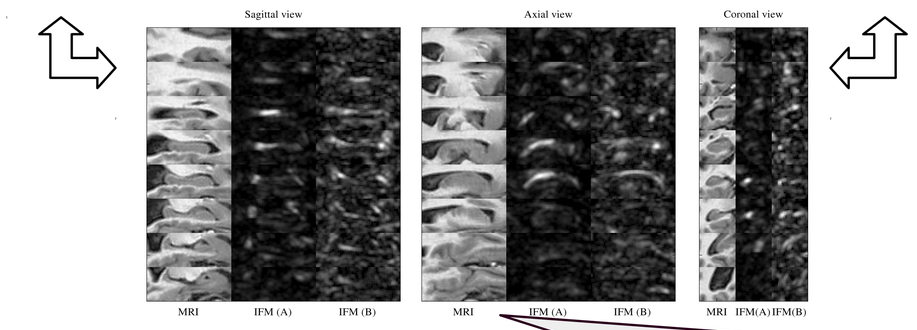
Sun Grid Engine

Feature selection



VOIs are then filtered with 18 filters in order to enhance textural / intensity features. Most relevant features (IF) are selected with Random Forest, that is able to order each feature's weight in CN vs AD discrimination





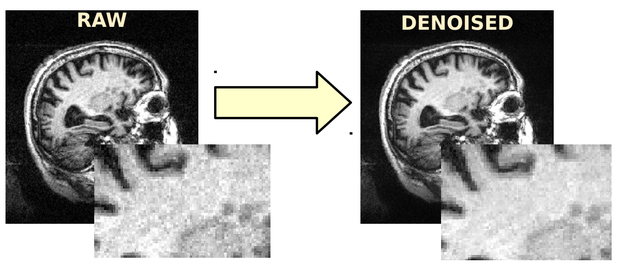
Sagittal / Axial / Coronal view of different employed filters
(Gaussian mean, standard deviation, range, entropy, mexican hat,..)
output computed on an hippoocampal box

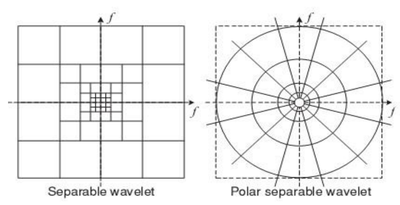
A reduct subset of the Important Features is fed into a Support Vector Machines (SVM) and a Random Forest (RF) classifiers, the two outcomes are combined with a weighted mean providing the final Global Disease Index (GDI) score. Classifiers are trained on 551 ADNI images. The subset of these multiple, highly localized image-based relevant features is found in [1] proved to to be responsible for the overall clinical diagnosis and prognosis.

Preprocessing

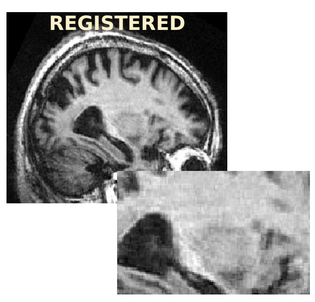
Uniformity across different sites and machineries is achieved by means of a denoise filter in the *Steerable Pyramid* configuration. This filter performs a polar-separable decomposition in the frequency domain, thus allowing independent representation of scale and orientation.
The 3 noise thresholds (one for each image dimension) have been set to an identical value corresponding to the means of the thresholds found for 654 images in a previous study, in which thresholds were calculated as functions of the inflection point of the SSI curve between orignal and denoised image

$$SSIM(x,y) = \frac{(2\mu_x\mu_y + c_1)(2\sigma_{xy} + c_2)}{(\mu_x^2 + \mu_y^2 + c_1)(\sigma_x^2 + \sigma_y^2 + c_2)}$$





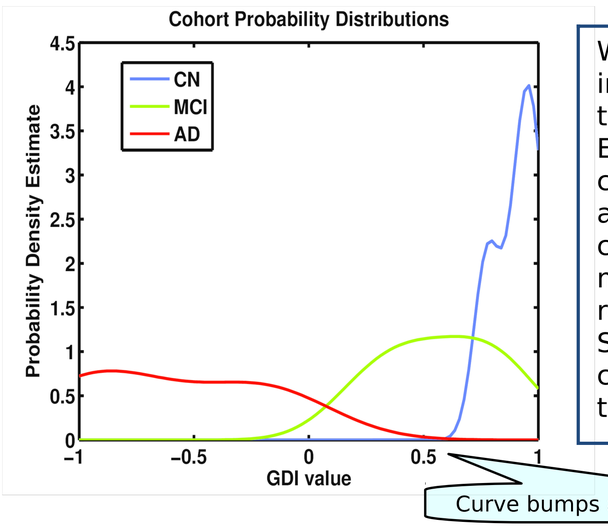
Wavelet-based filters:
- Sparse representation
- Scale & dir dependent



Spatial normalization of denoised images is carried out in 2 steps.
A rigid 7 and a 12 degrees-of-freedom transformations are performed with Insight Toolkit (ITK) in order to map incoming MRIs onto the Montreal Neurological Institute's (MNI) ICBM152 reference. Scans are also resampled with a 1mm^3 isotropic grid.

This procedure yielded a mis-registration rate of approximately 4%

Probability Distribution Estimates

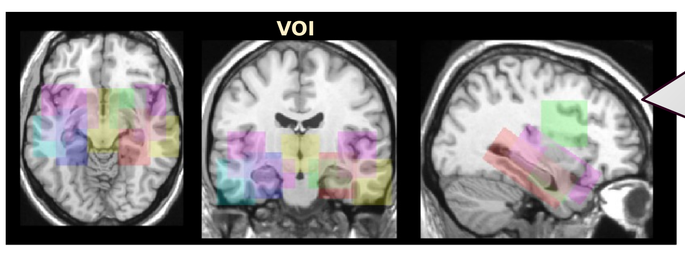


We used CADDementia train images GDI values to create the Probabilty Distribution Estimates of the 3 clinical classes. Projecting the GDI of a test subject on these curves generates the 3 membership probabilities requested for the challenge. Subject final diagnosis corresponds to the largest of these 3 probabilities.

Curve bumps are due to the small # of subjects

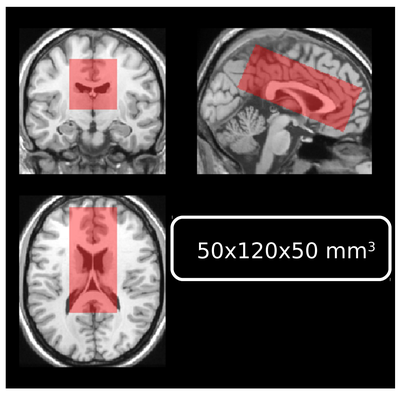
The proposed algorithm is fully automated and requires an average CPU-time (single core) of computation of about 45 minutes per subject.

VOI extraction & normalization



Hippocampus &
entorhinal cortex
Amigdala
Middle & inf temp. gyri
Insula
Rolandic

Parallelepiped-shaped volumes (VOI) are rigidly registered on target normalized scan. 8-10 references for each template VOI are employed to ensure a good registration even in case of severe degeneration.
7 VOI (critical regions in AD onset) and 2 (relatively spared ones) are chosen.

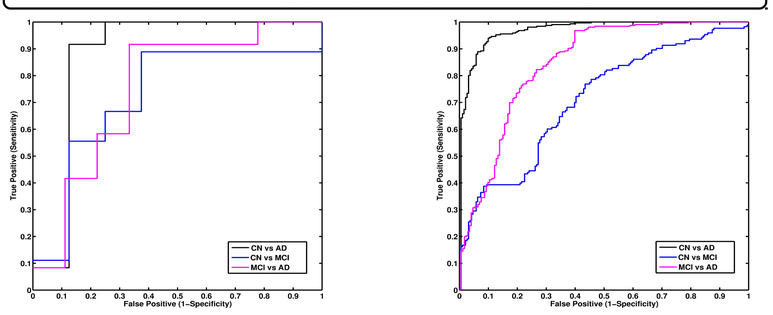


Extracted regions are intensity normalized by means of a region-based algorithm.
A VOI is outlined around ICBM152 template's Corpus Callosum, it is then segmented in CSF/GM/WM, and the 3 cluster means are computed. Target VOI corresponding intensity values are non-linearly matched to the ones of ICBM152. This mapping is extended to intermediate intensities with a smooth piece-wise polynomial curve.

Scans are now well overlapping and content comparable

Results

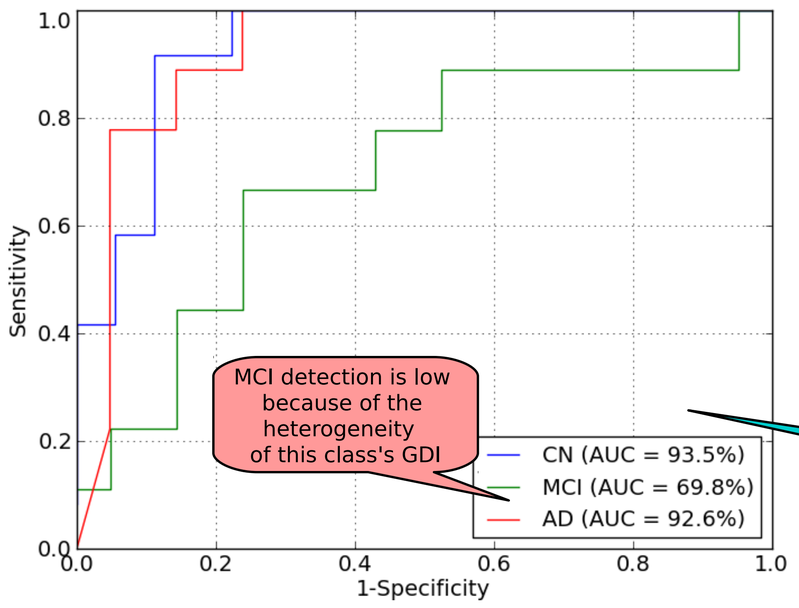
ROC curves for CN vs classification on CADD train data



GDI methodology is able to discriminate on CADDementia train data with:
AUC = 0.93 for CN vs AD
(sensitivity = 0.92 @ specificity = 0.88)
AUC = 0.78 for CN vs MCI
(sensitivity = 0.92 @ specificity = 0.67)
AUC 0.8 for MCI vs AD distinction
(sensitivity = 0.89 @ specificity = 0.62)

Slightly better results are obtained for ADNI data in leave-20-out crossvalidation:
AUC=0.97 for CN vs AD
(sens=0.94 @ spec=0.90)
CN vs MCI: 0.71
(sens = 0.77 @ spec = 0.78)
AD vs MCI: AUC = 0.85
(sensi 0.86 @ spec = 0.64)

ROC curves for one-vs-all classification on CADD train data



GDI blind classification of the test population delivers
146 CN (GDI = 0.85 ± 0.06),
125 MCI (GDI = 0.51 ± 0.16)
83 AD (GDI = −0.31 ± 0.29)

[1] A. Chincarini, P. Bosco, P. Calvini, G. Gemme, M. Esposito, C. Olivieri, L. Rei, S. Squarcia, G. Rodriguez, R. Bellotti, P. Cerello, I. De Mitri, A. Retico, F. Nobili; "*Local MRI analysis approach in the diagnosis of early and prodromal AD*". NeuroImage, 58 (2011) 469-480.