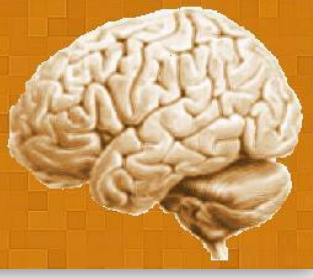
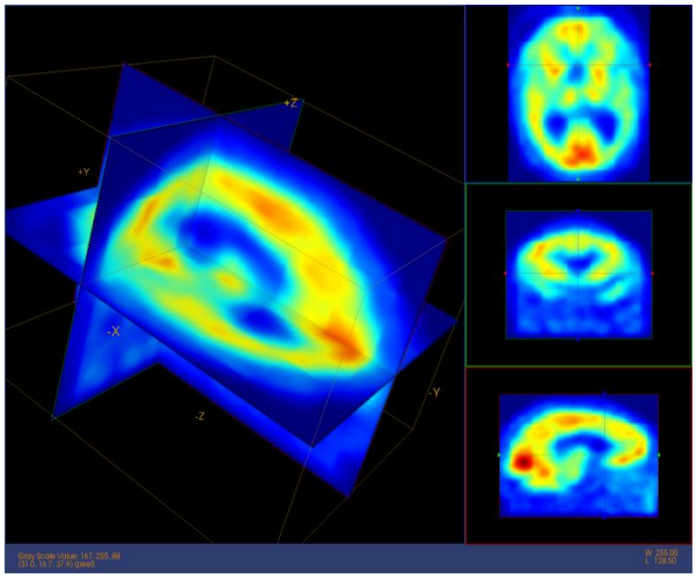
Selecting regions of interest in SPECT images using Wilcoxon Test for the diagnosis of Alzheimer's disease

D. Salas-Gonzalez, J. M. Górriz, J. Ramírez, F. Segovia,
R. Chaves, M. López, I. A. Illán and P. Padilla

Contents

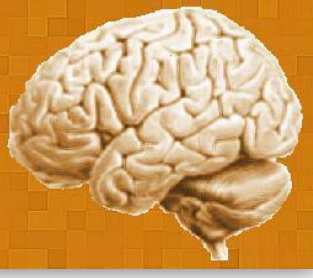


1. Introduction
   - Alzheimer's disease
   - Functional imaging
2. Materials and methods
   - SPECT database
   - Mann-Whitney-Wilconxon Test
   - Support Vector Machines
3. Experiments and results
4. Conclusions

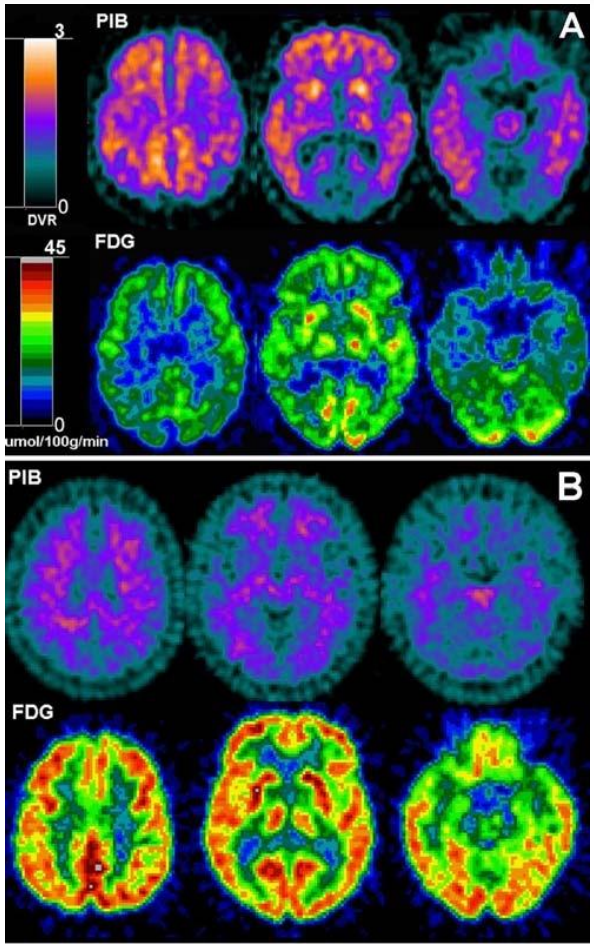


INTRODUCTION

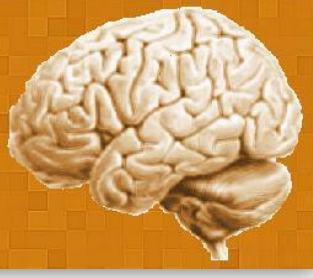
Alzheimer’s disease



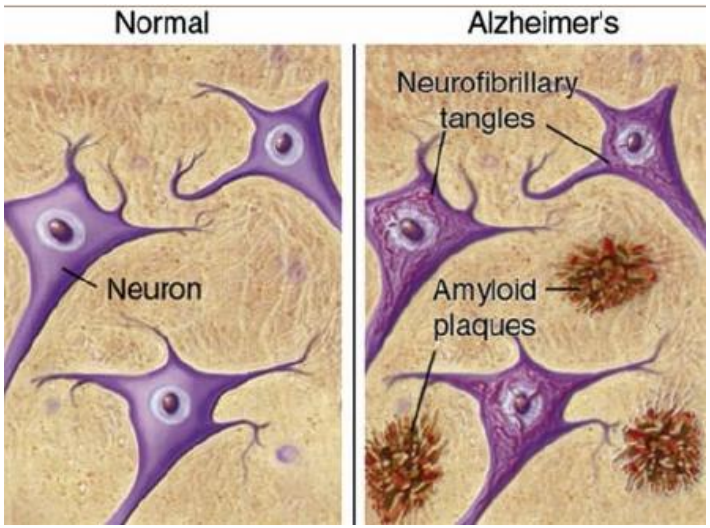
- Alzheimer's disease (AD) is the most common cause of dementia in the elderly and affects 30 million people around the world.
- In Spain, 700,000 people suffer from AD.
- Is expected to triple the number of patients affected in the next 50 years due to aging of the population



Alzheimer's disease



- AD is mainly characterized by:
  - The presence of amyloid plaques and neurofibrillary tangles.
  - Decreased level of neurotransmitters.
  - Loss of nerve cells.



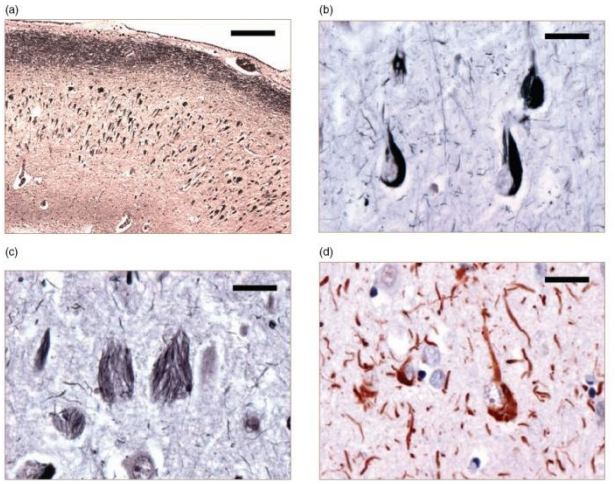


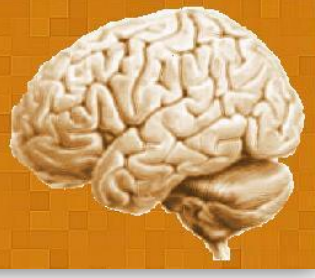
Figure 5.8 Neurofibrillary tangles (NFTs). (a) Numerous NFTs in CA2 region of the hippocampus. (b) Flame-shaped NFTs in pyramidal neurons of hippocampus. (c) Ghost tangles remain after affected neuron has degenerated. (d) NFTs and neuropil threads contain abnormal tau protein. (a–c) Bielschowsky silver stain, (d) immunohistochemistry for hyperphosphorylated tau protein. Scale bar: (a) 500 μm, (b–d) 50 μm.

Diagnosis of Alzheimer's disease

- The diagnosis is made through:
  - Tests of cognitive impairment (memory, language, etc ...).
  - Anatomical diagnostic imaging (CT, MRI) and functional imaging (SPECT, PET).

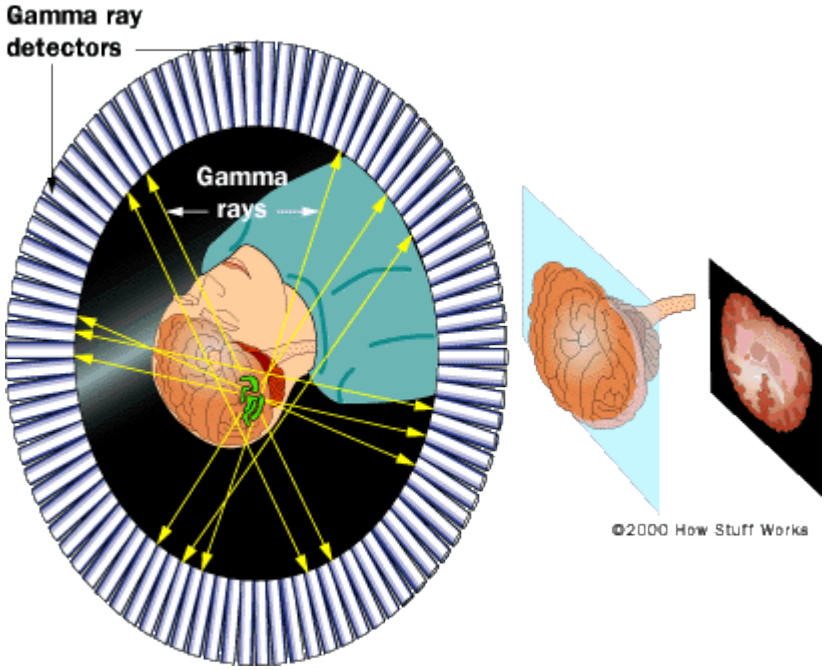
- Accurate diagnosis of AD remains an unsolved problem especially in the early stage which offers the best opportunity to treat their symptoms.

Functional imaging

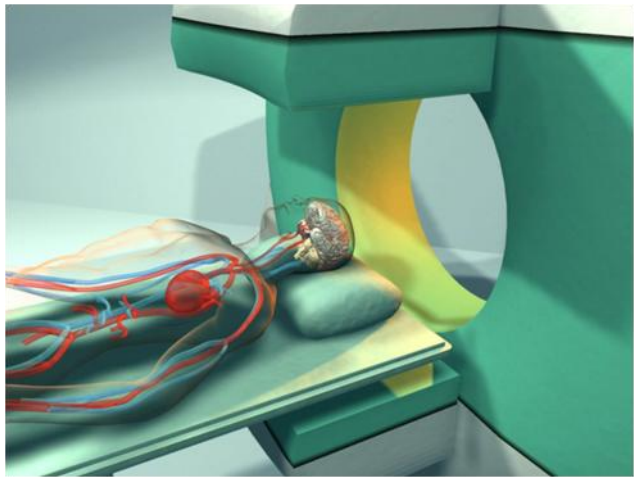


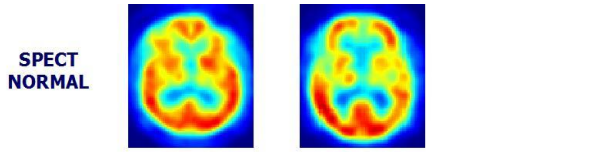
- Emission-Computed Tomography (ECT) is a set of techniques that produce images with maps of the psychological functions.

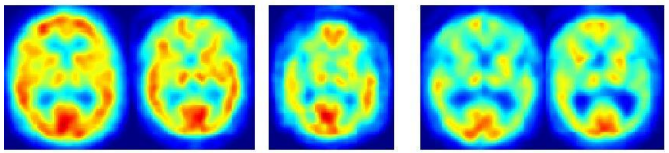
- How it works:
  - Radiopharmaceutical is injected to the patient and when it decays certain particles are emitted.
  - A detector detects those particles and calculate the point they were emitted from.
  - A 3D image is reconstructed by a computer.



SPECT images



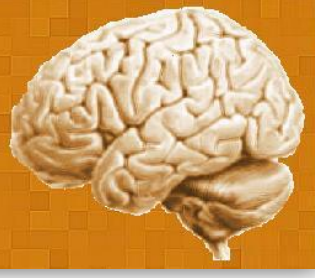




- Single Photon Emission Computerized Tomography (SPECT) is a wide-used ECT technique.
- SPECT images were obtained from gamma ray emitting isotopes such as technetium 99.
- Several captures with different angles of a ray allow the tomographic reconstruction of the image.
- SPECT images provide activation maps that represents the intensity of the regional Cerebral Blood Flow (rCBF).
- In AD patients, temporo-parietal lobe and posterior cingulate show hypoperfusion patterns.

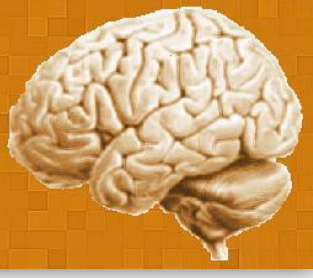
MATERIALS AND METHODS

SPECT database

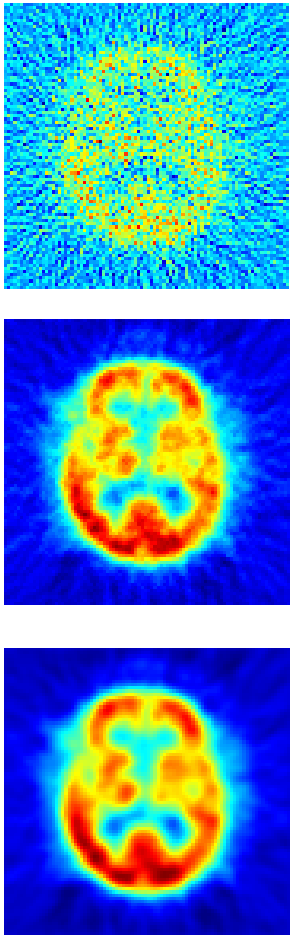


- We have used a database of 78 SPECT images in order to evaluate the proposed system.
- Images were collected during a recent study carried out by the "Virgen de las Nieves" hospital in Granada (Spain).
- The patients were injected with a gamma emitting ^{99m}Tc-ECD radiopharmeceutical.
- SPECT raw data was acquired by a three head gamma camera Picker Prism 3000
- The database consist of:
  - 41 controls images.
  - 37 images from AD patients.
- The images were visually labeled by experts from the hospital.

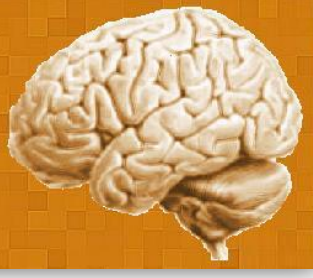
Image reconstruction



- The images of the brain were reconstructed from the projection data using the filtered backprojection (FBP) algorithm in combination with a Butterworth noise removal filter
- FBP algorithm:
  - Removes high frequency noise generated during reconstruction
  - Removes noise in projections (pre-filter)
  - Reduces noise due to the reconstruction (post-filter)

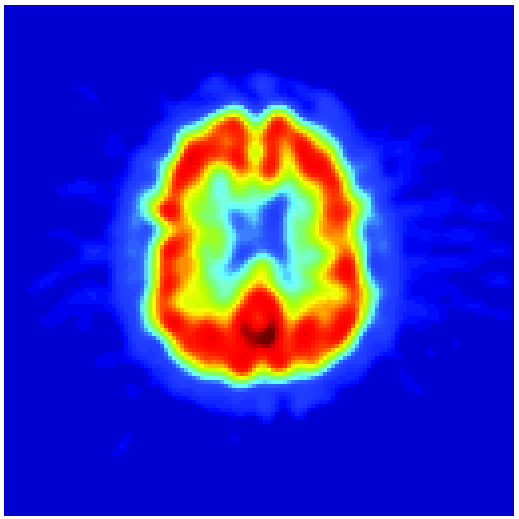


Spatial normalization

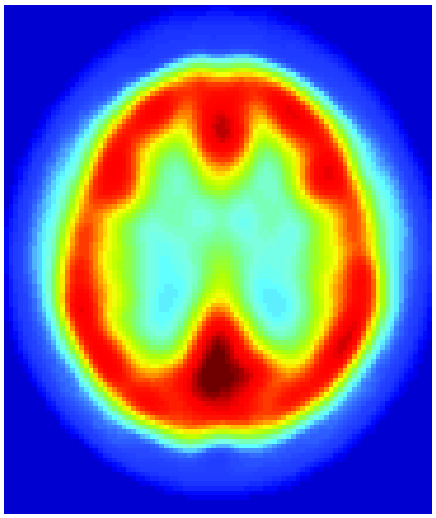


- This step ensures all images have same size and shape by matching them with a template.
- It was made using the SPM software.
- After normalization all images have 95 x 69 x 79 voxels.

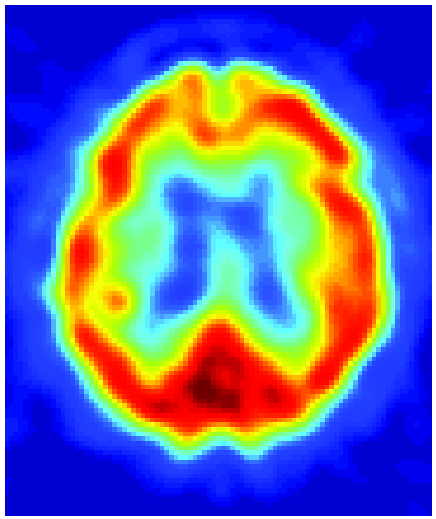
INITIAL IMAGE



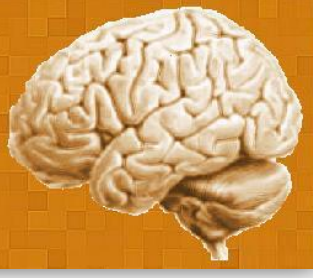
TEMPLATE



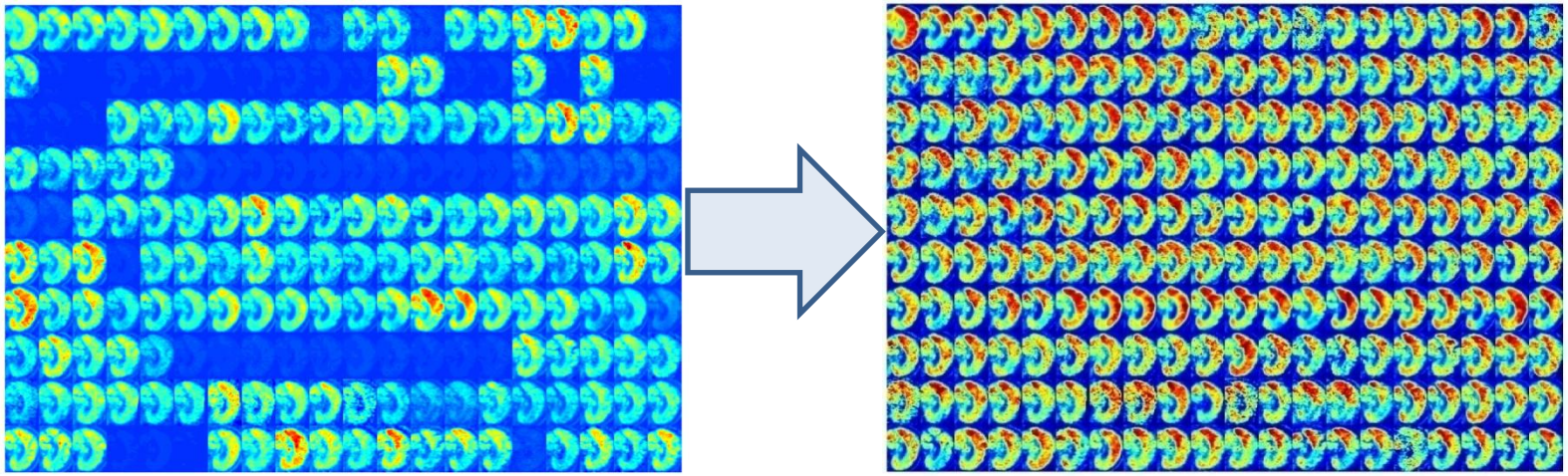
NORMALIZED IMAGE



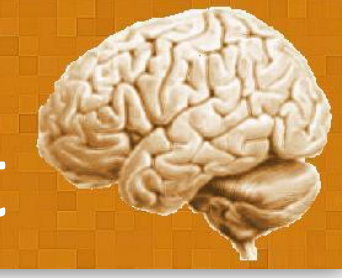
Intensity normalization



- The intensities were also normalized for each image individually.
- In order to avoid the influence of noise, the largest intensity value of an image is obtained by averaging 0.3% higher intensity voxels.

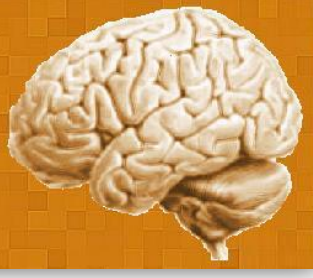


Mann-Whitney-Wilconxon test



- It is a non-parametric test for assessing whether two independent samples of observations have equally large values.
- Proposed by Frank Wilcoxon in 1945 and extended (to arbitrary sample sizes and in other ways) by H. B. Mann and D. R. Whitney in 1947.
- It can be viewed as the nonparametric equivalent of Student's t-test.
- Most robust to outliers in the data than the t-test.
- Usually preferable when the data are not Gaussian.

Mann-Whitney-Wilconxon test



- All the observations are arranged into a single ranked series.
- The rank for the observations which came from sample 1 is computed:

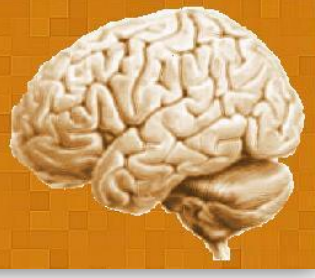
$$U_1 = R_1 - \frac{n_1(n_1+1)}{2}$$

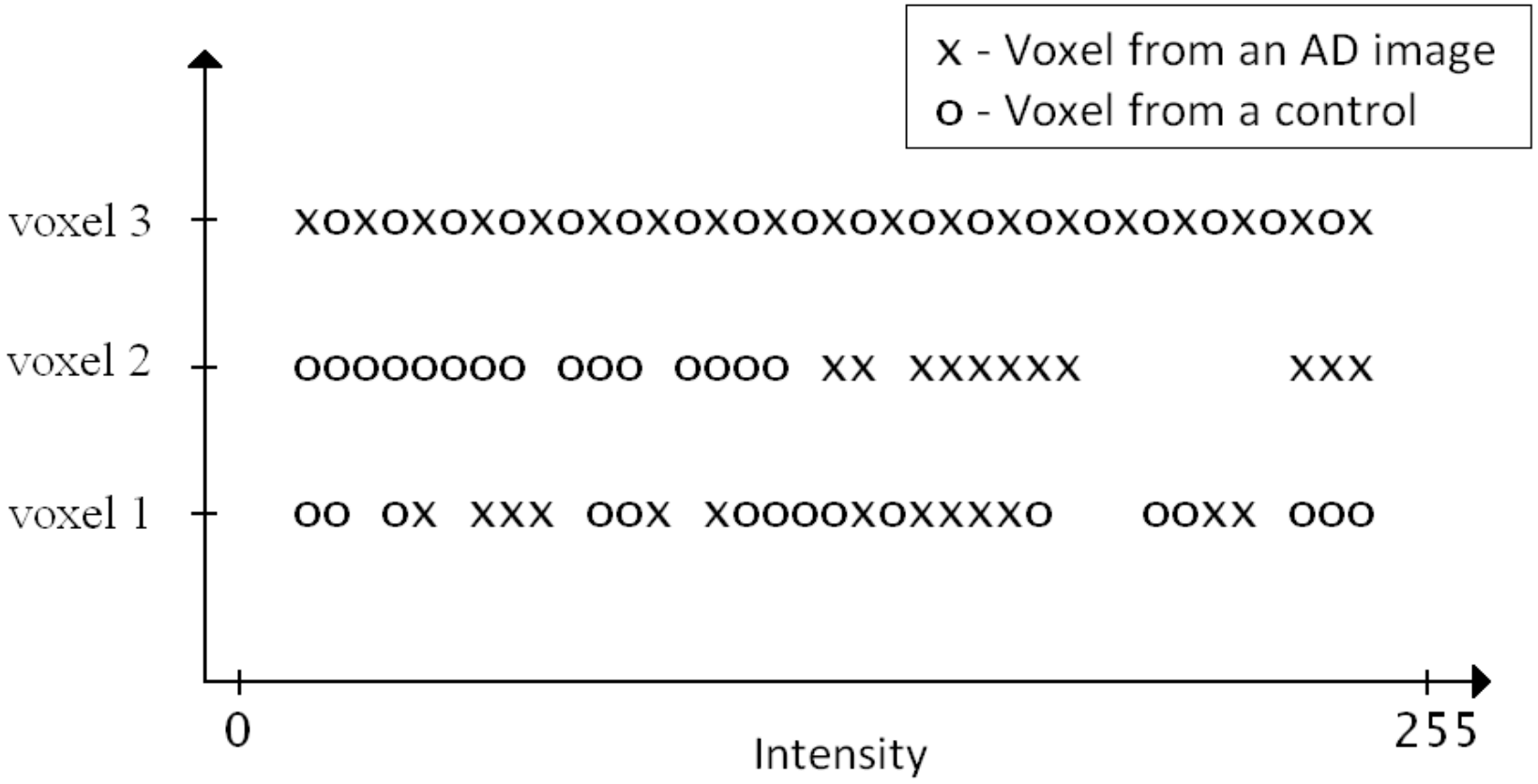
- The same calculation is made for sample 2:

$$U_2 = R_2 - \frac{n_2(n_2+1)}{2}$$

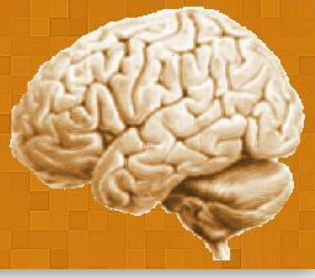
- The distance U given by the test is the smaller value of U_1 and U_2, $U = \min\{U_1, U_2\}$

Mann-Whitney-Wilconxon test





Support Vector Machines



- SVM has attracted recent attention from the pattern recognition community due to a number of theoretical and computational merits derived from the Statistical Learning Theory developed by Vladimir Vapnik at AT&T.

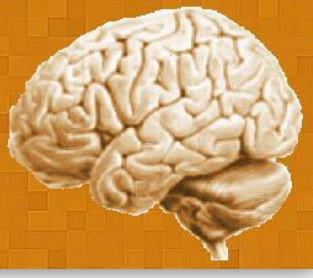
- In SVM-based pattern recognition, the objective is to build a function $f : R^N \rightarrow \pm 1$ using training data, that is, N-dimensional patterns x_i and class labels y_i:

$$(\mathbf{x}_1, y_1), (\mathbf{x}_2, y_2), ..., (\mathbf{x}_\ell, y_\ell) \in (R^N \times \pm 1)$$

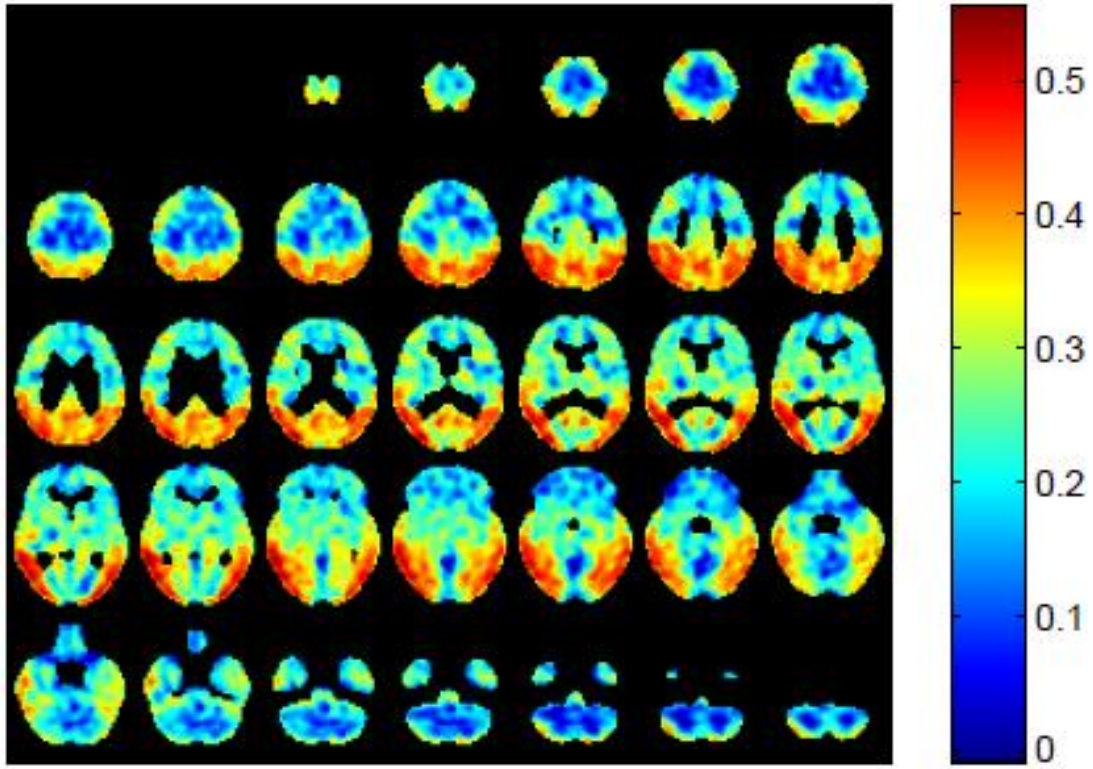
- so that a classifier f is produced which maps an object x_i to its classification label y_i. The classifier f will correctly classify new examples (x,y).

Experiments and results

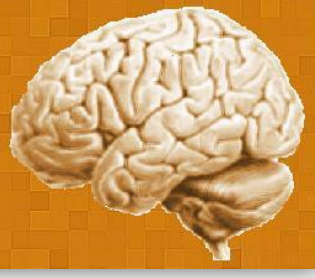
Transaxial U-test brain image



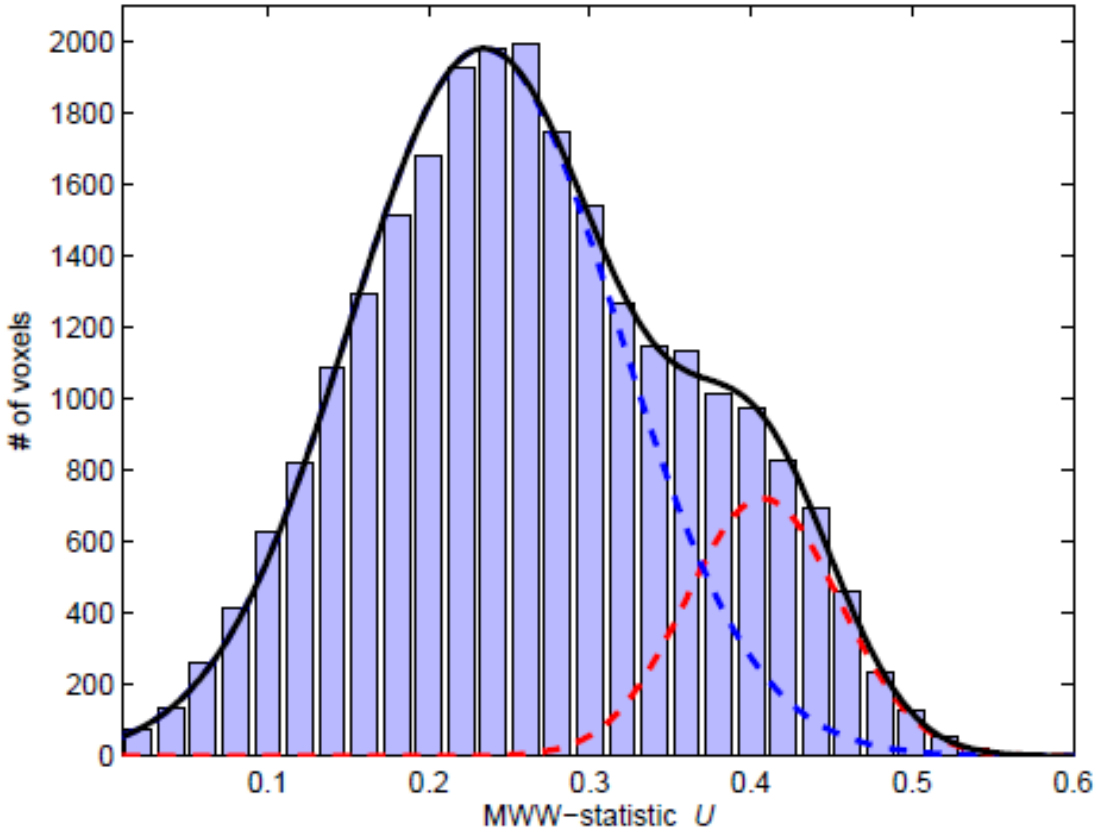
- Higher values denote regions of interests according to the Mann-Whitney-Wilcoxon test.
- The voxels whose intensity is less than 40% of the maximum intensity has not been taken into account



Histogram with U-values

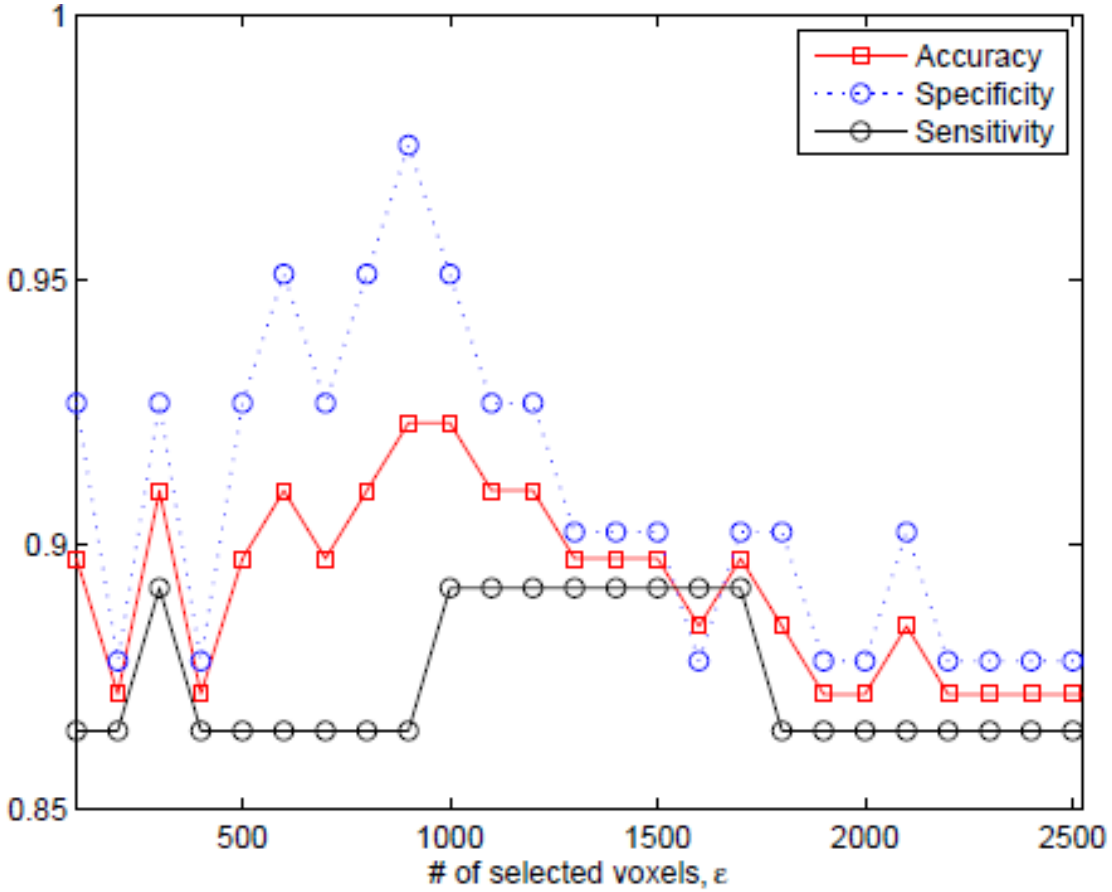


- Two Gaussian components are able to fit the histogram very accurately.
- Voxels which present a U-value greater than 0.4 (mean of the second Gaussian), will be selected as feature vector



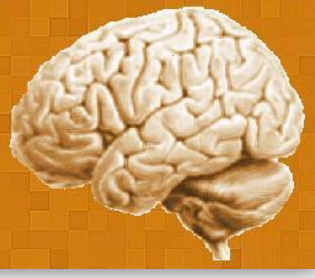
Results

- We choose 25 ε values equally spaced from 100 to 2500.
- A correct rate greater than 90% is obtained for a wide range of ε values and best performance (92,3%) was obtained when ε = 900 and ε = 1000



Conclusions

Conclusions



- A criterion to select a set of relevant voxels for the classification of SPECT brain images is presented.
- This criterion is based the Mann-Whitney-Wilcoxon U-test.
- After normalization of the brain images, the set of voxels which presents higher U-value are selected.
- Selected voxels are used as features to a SVM classifier with linear kernel.
- The proposed methodology reaches an accuracy up to 92% in the classification of controls and AD images.
- The proposed methodology allows us to diagnose AD in an automatic manner, with no prior knowledge about the disease.

Thank you very much for your attention

Contact: fsegovia@ugr.es