Computer Assisted Radiology and Surgery. H Lemke et al eds. Elsevier Science 1999 (*pp139-143*)

Increased Sensitivity and Position Accuracy in the Detection of Brain Activation by fMRI using Multiscale Analysis

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Introduction

Functional Magnetic Resonance Images (fMRI) are traditionally analyzed by applying statistical tests to each and every voxel in the dataset. This results in maps (Statistical Parametric Maps, SPM) showing the voxels that significantly change between different brain states, usually two (rest-activation).

These conventional SPM methods do not exploit the neighborhood information (activation regions usually span over several voxels) to increase the statistical power of the tests. At most, this information is sometimes used in a post-processing step to enhance the shape of the detected activation areas [1][2].

In this paper we present an analysis method that makes full use of that neighborhood information. It processes the images at different scales by using multiresolution decomposition based on a wavelet transform. The statistical tests are then applied in the wavelet domain taking benefit from the possible existing spatial correlation.

Another remarkable problem in this type of studies is the lack of a 'gold standard' to validate the results, as the exact size and position of activation areas is never known in real patient studies.

In this work, sensitivity, specificity and spatial resolution of the multiscale results have been assessed with a realistic computer-simulated phantom that resembles fMRI studies where activation areas are known *a priori*.

Material And Methods

Algorithm

Functional images have been analyzed through wavelet decomposition up to the sixth level. At each level, the null-hypothesis was tested (z-test) at a given p-value and the inverse transform computed using only the significant coefficients which passed the test. In this way,

This work has been partially supported by grants FIS 97/270 and Comunidad de Madrid 8.1/49/1998

information from voxels with a high spatial correlation is concentrated into a few wavelet coefficients.

Software phantoms

In order to validate the proposed method and to assess the performance of the different wavelet families and orders, fMRI computer-simulated phantoms were designed. As in these phantoms the activation regions are known, they make it possible to evaluate the performance of the multiscale methods under different conditions of activation and noise levels.

A set of phantom images has been built starting from a 2D baseline image with a uniform intensity level in a “brain-like” shape. On this image, four activation regions with irregular shape have been created (figure 1) with intensity levels that are 4 %, 3 %, 2 % and 1 % higher than the surrounding area (actual brain activation is in the order of 1 to 4%).

To simulate a real acquisition, all the images have been smoothed by a gaussian filter and white gaussian noise (5%, 3%, 2%) has been added.

Each phantom study contained four simulated fMRI scans (64x64x64) with two epochs in six activation-rest cycles.

Evaluation

Several wavelet basis functions have been tested: Haar, Daubechies, Spline, maxflat, Lemarie and symlets with 2, 4, 8, 16 coefficients, and Gabor (11 coefficients) [3,4].

The results of the standard z-test statistical parametric mapping (SPM) were used as a standard for the comparison. Tests were performed at three significance levels ($p<0.05$, $p<0.01$, $p<0.001$).

For each study, sensitivity (percentage of pixels activated in the phantom that have been properly detected as activated) and specificity (percentage of pixels correctly detected as not activated) have been measured.

RESULTS

Figure 2 presents the result of the standard statistical parametric mapping.

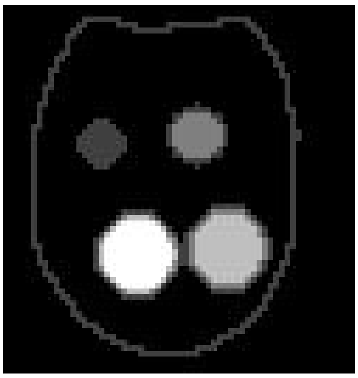

Figure 1. Activation regions (1%, 2%, 3%, 4% activation levels) and phantom contour.

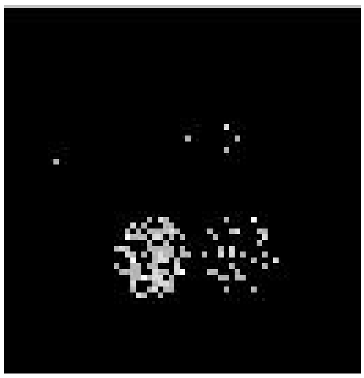

Figure 2. Standard statistical parametric mapping (z-test, $p<0.05$) , 5% noise level.

Figure 3 shows an example of the output of the proposed method in three cases: Daubechies (16 coefficients), Lemarie (16 coefficients) and Gabor. The first two have been selected because they produce reasonably good images and have been mentioned in other references **[5,6]**. Gabor is included because it yields the best results.

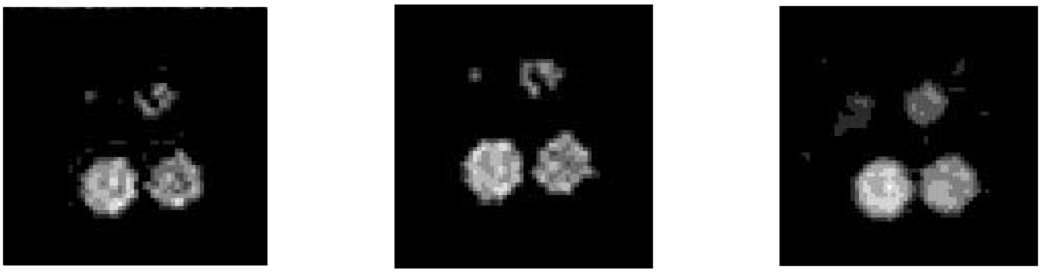

Figure 3. Results of multiscale analysis ($p<0.05$, 5% noise level, Scale=2). From left to right, Daubechies (16 coef.), Lemarie (16 coef.) and Gabor.

Table1 compares the sensitivity and specificity rates of the traditional and multiscale approaches.

Table 1.
Sensitivity and specificity of the analysis (5% noise level, $p<0.05$, Scale=2)

Activity	SPM z-test		Daub. 16 coef.		Lemarie 16 c.		Gabor	
level	Sensitiv.	Specif.	Sensitiv.	Specif.	Sensitiv.	Specif.	Sensitiv.	Specif.
1%	0%	100%	17%	99%	14%	99%	86%	95%
2%	5%	100%	75%	98%	79%	99%	100%	97%

Table 2 and figure 4 compare the results at two different noise levels: 3 and 5 %.

Table 2.
Sensitivity and specificity at different noise levels. The figures are only shown for the region with 1 % activation ($p<0.05$, Scale=2).

Noise	SPM z-test		Daub. 16 coef.		Lemarie 16 c.		Gabor	
Level	Sensitiv.	Specif.	Sensitiv.	Specif.	Sensitiv.	Specif.	Sensitiv.	Specif.
3 %	7%	100%	76%	94%	79%	96%	100%	94%
5 %	0%	100%	17%	99%	14%	99%	86%	95%

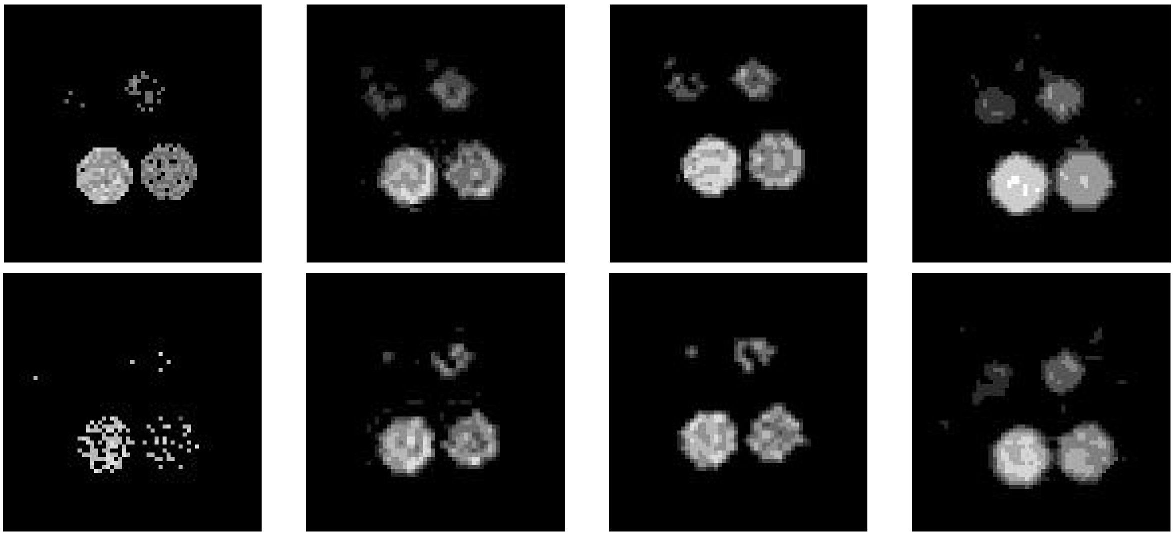

Figure 4. Result images of a phantom with a noise level of 3 % (top row) and 5 % (bottom row). From left to right, SPM, Daubechies (16 coef.), Lemarie (16 coef.) and Gabor ($p<0.05$, Scale=2).

Discussion and Conclusions

With our phantom data, the conventional statistical parametric mapping detected the 4% activation area and only partially the 3% activation area. Multiscale methods clearly improved the sensitivity, being able to locate even the 1% activation area, with different degrees of spatial resolution. The best results were obtained with the multiscale Gabor decomposition, which provided the highest sensitivity/specificity rates, with a good spatial localization and shape determination.

Sensitivity decreases at higher noise levels both with traditional and multiscale methods. However, the advantage of the multiscale approach is more noticeable with low activation levels on noisy images.

The increase in sensitivity obtained is in accordance with some previously reported data **[5, 6].** However, these authors do not provide a quantitative assessment of their results, as they did not had a standard to compare with. Furthermore, they chose 'a priori' a single wavelet family and order, not providing comparative data. Our data show that the Gabor decomposition produces significantly better activation maps than the Daubechies and Lemarie wavelets previously proposed.

It is also interesting to remark that specificity is a very important parameter to take into account, as it is always possible to increase sensitivity at the expenses of an unreasonably low value of specificity. The correct shape of the detected activation areas is also very related to the specificity. This parameter cannot be calculated unless a gold standard is available.

Acknowledgements

The authors would like to thank the collaboration of the Instituto de Optica 'Daza Valdés' (CSIC) and the Signal Theory Group of the University of Vigo, whose implementations of the different wavelet transforms were used in this work.

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