Adaptive Smoothing Applied to fMRI Data

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Abstract: One problem of fMRI images is that they include some noise coming from many other sources like the heart beat, breathing and head motion artifacts. All these sources degrade the data and can cause wrong results in the statistical analysis. In order to reduce as much as possible the amount of noise and to improve signal detection, the fMRI data is spatially smoothed prior to the analysis. The most common and standardized method to do this task is by using a Gaussian filter. The principal problem of this method is that some regions may be under-smoothed, while others may be over-smoothed. This is caused by the fact that the extent of smoothing is chosen independently of the data and is assumed to be equal across the image. To avoid these problems, we suggest in our work to use an adaptive Wiener filter which smooths the images adaptively, performing a little smoothing where variance is large and more smoothing where the variance is small. In general, the results that we obtained with the adaptive filter are better than those obtained with the Gaussian kernel. In this paper we compare the effects of the smoothing with a Gaussian kernel and with an adaptive Wiener filter, in order to demonstrate the benefits of the proposed approach.

1 INTRODUCTION

Functional Magnetic Resonance Imaging (fMRI) is a method to map the brain which does not require any invasive analysis. This is a very useful technique to identify brain regions of interest activated by different types of stimulation or activity and also during resting state. The indicator used to identify the local activity is the Blood Oxygenation Level Dependent (BOLD) contrast, which is based on the brain oxygenation of the neuronal processes associated with the experimental tasks. Oxygen and other nutrients is what neurons need to work. Thus, when brain neurons are activated, there is a change in blood flow and oxygenation that causes a change in the Magnetic Resonance (MR) signal received by the receiver coils. A major level of oxygen in blood in a particular area means that there is an increase in neural activity in this zone and a lower level means the opposite (D'Esposito et al., 1999).

To obtain the BOLD contrast, the subject under study lies in the magnet under the influence of a powerful magnetic field and perform a task or is exposed to an external stimulus. At the same time, a large amount of images are acquired using ultra-fast sequences through magnetic resonance. For some of these scans the stimulus is present and for some others the stimulus is absent. The low resolution brain images of the two cases can then be compared in order to see which parts of the brain were activated by the stimulus.

After the experiment has finished, the set of images is pre-processed and analyzed.

One problem of fMRI data is that includes contributions from many other sources including the heart beat, breathing and head motion artifacts, which can cause wrong results (S.A Huettel. et al., 2004). In order to reduce as much as possible the amount of noise and to improve signal detection, the fMRI data is spatially smoothed prior to the analysis.

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The most common and standardized method to do this task is by using a Gaussian kernel. The principal problem of this method is that some regions may be under-smoothed favoring the presence of false positives, while others are over-smoothed causing a loss of information. This problem is due to the fact that the extent of smoothing is chosen independently of the data and is assumed to be equal across the image.

Several studies have proposed approaches which are different from the Gaussian proposal based on the same theoretical principles, the extent of smoothing is choosen independently of the data, fact that can carry on the problems discussed. Some of these methods are the prolate spheroidal wave functions (Lindquist and Wager, 2008), wavelets (Van DeVille, Blu, and Unser, 2006), Gaussians of varying width (Poline and Mazoyer,1994; Worsley et al., 1996) and rotations (Shafie et al.,2003). To solve these problems and limitations, some authors have proposes to use adaptive smoothing methods as the use of the Gaussian Markov random field specifies (Yue et al., 2010) and Propagation-separation procedures (Tabelow et al.,2006).

In this report we present an alternative procedure to denoise the fMRI images that differs from the ones used in the traditional fMRI analysis. This method is based on an adaptive Wiener filter which smooths the images adaptively minimizing the loss of information caused by the over-smoothing and the apparition of the false positives when the images are under-smoothed. In this paper, we compare the effects of the adaptative smoothing based on the Wiener filter and the effects of the non adaptative smoothing of the use of the Gaussian kernel, combinend in both cases with an Independent component analysis.

2 MATERIALS AND METHODS

The study was performed in a 3 T MRI scanner (Magnetom Trio Tim, Siemens Medical Systems, Germany) at the Diagnostic Imaging Centre at Hospital Clínic of Barcelona (CDIC) using the blood-oxygen level-dependent (BOLD) fMRI signal.

Whereas the pre-processing of MR images and the regression model were performed using SPM8 software (SPM8, Wellcome Department of Cognitive Neurology, London), the data analysis was carried out using Group ICA of fMRI Toolbox (Calhoun et al., 2001). Both pre-processing and analysis software were run on a Matlab platform (R2009b version).

2.1 Participants

Forty right-handed healthy undergraduate students [50% women; age range 18–25, mean (±S.D.) 19.6 (±1.7)] were recruited from the University of Barcelona. Subjects with chronic disorders, nervous system disorders or history of mental illness were excluded, as well as regular drinkers and those on medication. All participants were non smokers and low caffeine consumers (< 100mg/day), had intermediate circadian typology and reported an undisturbed sleep period of at least 6 h during the night prior to the fMRI scan sessions.

Caffeine may affect the performance of the task (Serra-Grabulosa et al., 2010a); Adan and Serra-Grabulosa, 2010). For this reason the participants abstained from caffeine intake for a minimum of 12 h and fasted for at least 8 h prior to the first fMRI session.

The study was approved by the ethics committee of Hospital Clínic de Barcelona. Written consent was obtained from all participants, who were financially rewarded for taking part.

2.2 Experimental Design

The functional magnetic resonance imaging was obtained using gradient echo sequence single-shot echo-planar imaging, with the following parameters: TR (repetition time): 2000 ms, TE (echo time): 40 ms, FOV (field of view): 24 x 24 cm, matrix 128 x 128 pixels, flip angle 90, slice thickness: 2 mm, gap between sections: 0.6 mm, 36 axial slices per scan. A total of 243 volumes were purchased, with 46 slices each.

During the acquisition of fMRI, in order to obtain the BOLD contrast, the subjects performed a sustained attention and working memory task (CPT-IP, Continuous Performance Test-Identical Pairs), which is a modification of the Cornblatt task (Cornblatt *et al.,* 1989) and a control task. CPT-IP task was created with the software Presentation (Neurobehavioral System, USA). All stimuli were presented to the subjects through glasses specially designed for use in the scanner.

The CPT-IP task was performed using a block design. It started with a block of 35 seconds of accommodation to the scanner, which had a blank screen that the subject had to stare at. After this first block, 9 blocks of CPT were alternated with 9 blocks of control (Figure 1). Preceding each block, subjects received instructions for what to do in the next block for a duration time of 5 seconds.

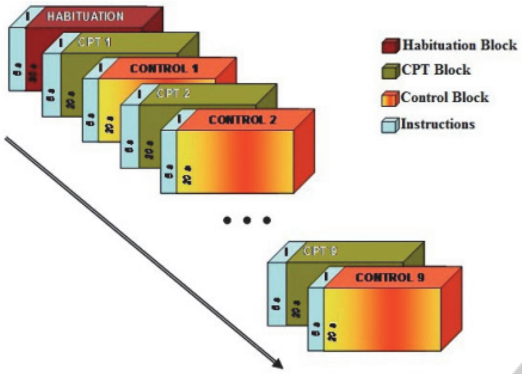

Figure 1: Design of the sustained attention task with alternation between blocks.

Figure 2: The following figure illustrates the design of the task blocks. The top (A) exemplifies the figures presented in the CPT blocks. In this example, you should respond to the stimulus e3. The bottom (B) exemplifies the figures presented in the control blocks.

Each of the CPT blocks had a total of 27 numbers formed by 4 digits (1 to 9, without repeating the same figure), so that 23 of the figures were different and 4 were repeated. The presentation time of each number was 450 ms and the interval between the onsets of each of the 27 consecutive digits was 750 ms. Subjects' task was to detect the repeated figures and respond by pressing a button as quickly as possible (Figure 2A). The position of the repeated figures was randomized over the blocks CPT. Concerning the control block, it always had the same 4 digits (1 2 3 4) and the task of the subjects was only to stare at it throughout the presentation (Figure 2B).

2.3 Data Pre-processing

Image pre-processing was performed with SPM8 (http://www.fil.ion.ucl.ac.uk/spm/software/spm8/) as described in (http://www.fil.ion.ucl.ac.uk/spm/doc/spm8_manual.pdf). The pre-processing steps were (1) realigning and unwarping the images to correct for movement artifacts and related susceptibility artifacts, (2) coregistration of the anatomical to the functional images, (3) segmentation and normalizing of the anatomical image to the standard stereotactic space (Montreal Neurological Institute), (4) application of normalization transformation to the functional images, and (5) smoothing the images with a 8 mm full-width half maximum (FWHM) Gaussian filter and with an adaptive Wiener filter in order to have two groups of the same images with different types of smoothing to compare them later.

2.4 Adaptive Wiener filtering

This filter is a (non-linear) spatial filter which operates on the principle of least squares. Imagine that we have a noisy image ***M'*** of some original image ***M*** and a restored version ***R***. Obviously, what we intend is to have ***R*** as close as possible to the original image ***M***. One way to know if the image ***R*** is close as the image ***M*** is by adding the squares of all differences:

$$\sum(m_{i,j} - r_{i,j})^2 \qquad (1)$$

where the sum is taken over all pixels of ***R*** and ***M*** (which we assume to be of the same size). This sum can be taken as a measure of the closeness of ***R*** to ***M.*** If this value is the minimum the resultant image of the denoising process will be as close as possible to the original image. The noisy image ***M'*** can be written as:

$$M' = M + N \qquad (2)$$

where M is the original correct image and N is the noise which we assume to be zero-mean normally-distributed.

However, the mean may not be zero. Therefore we suppose that the mean is m_f and the variance in the mask is σ^2_f. We suppose also that the variance of the noise over the entire image is known to be σ^2_g. Then the output value can be calculated as:

$$m_f + \frac{\sigma^2_f}{\sigma^2_f + \sigma^2_g}(g - m_f) \qquad (3)$$

where g is the current value of the pixel in the noisy image. See Lim, 1990 for details. In practice, we calculate m_f by simply taking the mean of all grey values under the mask, and σ^2_f by calculating the variance of all grey values under the mask. We may not necessarily know the value σ^2_g. So the Matlab function wiener2 (used to filter the images) which implements Wiener filtering uses a slight variant of the above equation:

$$m_f + \frac{\max\{0, \sigma^2_f - n\}}{\max\{\sigma^2_f, n\}}(g - m_f) \qquad (4)$$

where n is the computed noise variance, and is calculated by taking the mean of all values of σ^2_f over the entire image. This can be very efficiently calculated in Matlab.

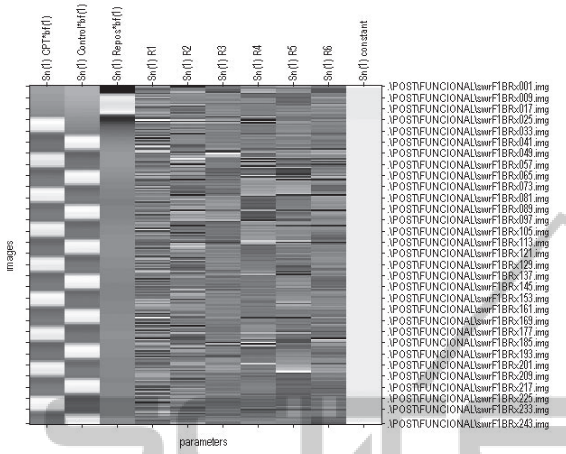

Figure 3: Regression model proposed to explain, for each voxel of the functional MRI images, the variability in the signal along the recorded 243 volumes. Each one of the 10 columns corresponds to one of the input variables in the regression. The first one corresponds to the attention task in which the subject has to respond to repeated stimuli. The second one corresponds to the task of looking at numbers and the third one to the task of initial rest. The next 6 columns are the values applied to correct the head movements in the pre-processing step. The last one represents the error. On the right side of the table the registered volumes are listed from 1 to 243. For each variable, white colour indicates that this helps to explain the variability while black colour indicates the opposite.

2.5 Implementation of the Regression Model

After the pre-processing step, we proceeded to perform the regression model to explain brain activations. To do this, we created a regression line where signal changes observed in each voxel could be explained by changes in the proposed task minimizing the residual error (Figure 3).

2.6 Independent Component Analysis

After pre-processing and regression model creation steps, we applied ICA analysis in both types of the smoothed images. What we intend with this analysis is to check that the components obtained with the Wiener filter have a time course more similar to the task pattern than the time course obtained with the Gaussian kernel (see Figure 4).

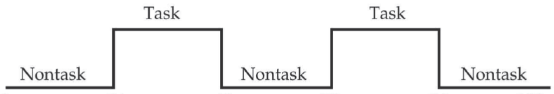

Figure 4: Task pattern followed during the CPT task.

To perform the ICA analysis we used the Group ICA of fMRI Toolbox. This program has the option to make the analysis using different algorithms, as Jade, Erica, Infomax, Simbec, Amuse and others. The chosen algorithm to analyze fMRI data was Infomax because it has been one of the most commonly used algorithms for fMRI data analysis and has proven to be quite reliable (Calhoun et al., 2004).

3 RESULTS

3.1 Selection of the Independent Components

After ICA analysis we selected some of the components in order to evaluate results. For that, we did a multiple regression and a statistic correlation with every paradigm. We excluded the components that had a p-value greater than 0.01, and the ones which were associated to noise. Therefore we selected 3 components for the CPT task coming from every approach.

3.2 Obtention of the Areas of Interest

After the selection of the independent components, we performed a T – test with all the subjects and all the components. We also performed a 'multiple regression' SPM8 analysis to establish the relationship between CPT-IP-related activations.

The fMRI results were interpreted only if they attained both a voxelwise threshold $p<0.05$ (corrected) (cluster extent (k) = 10voxels). The anatomical location of the activated brain areas was determined by the Montreal Neurological Institute (MNI) coordinates. Anatomical labels were given on the basis of anatomical parcellation developed by (Tzourio-Mazoyer et al., 2002).

3.3 Results with the Different Smoothing Methods

In the following images taken from one sample, we can see the results obtained with every smoothing method. The first image (Figure 5) is an example of

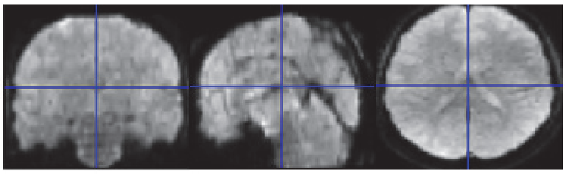

Figure 5: fMRI image without smoothing.

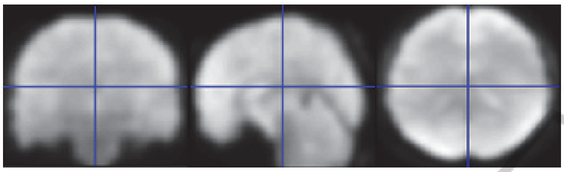

Figure 6: fMRI image smoothed with a Gaussian kernel.

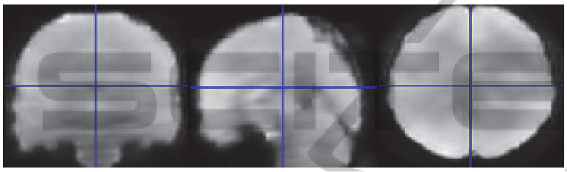

Figure 7: fMRI image smoothed with an adaptive Wiener filter.

a non smoothed image with noise. The next two images (Figures 6 and 7) correspond to the same image smoothed with the two mentioned methods.

As we have mentioned before, we applied an ICA analysis on all the subjects in order to check the components obtained with every method, as is illustrated in the next images.

Activations found in the CPT task with the Wiener filter were located bilaterally in frontal lobe (BAs Left 4, 6, 8, 9, 10, 32, right 45, right 46, 47), parietal (BAs 7, 39, 40), temporal (BAs Left 22, 37) and occipital (BAs Left 17, 18, 19).

Activations found in the CPT task with the Gaussian kernel were located bilaterally in frontal lobe (BAs 4, 6, 8, 9, right 10, right 32, 45, 46, 47), parietal (BAs right 2, Left 5, 7, 31, Left 39, 40, Left 41), temporal (BAs Left 20, 21, 22, Left 37) and occipital (BAs Left 17, 18, 19).

4 DISCUSSION

This paper introduces an approach to smooth fMRI data based on the use of an adaptive Wiener filter. The results from the proposed method were compared with those obtained through the conventionally used Gaussian smoothing.

The principal feature of our approach respect to the classic methods is that it allows varying the extent of smoothing across the brain. This characteristic will help to avoid the problems related with over and under-smoothing that may occur if smoothing is performed using a Gaussian kernel of fixed width. In the following paragraphs we will comment these problems with the achieved results.

If we take a look at the figures (Figures 5, 6 and 7), we can observe that in figure 6 the edges of the images are fuzzy and have less resolution than the images in the figure 7. This fact indicates that the images in the figure 6 are over-smoothed causing probably a loss of information. On the other hand, the images of the figure 7 have more definition and the edges have been preserved after the smoothing process because the adaptive Wiener filter smooths an image adaptively, tailoring itself to the local image variance. Where the variance is large, performs little smoothing. Where the variance is small, performs more smoothing. As a result this filter is more selective than the Gaussian kernel and preserves better the edges and other high-frequency parts of the image.

If we compare the time courses and the activations maps between the components achieved with the Gaussian kernel and the adaptive filter we can see that all of them are very similar except the ones presented in the figures 8 and 9.

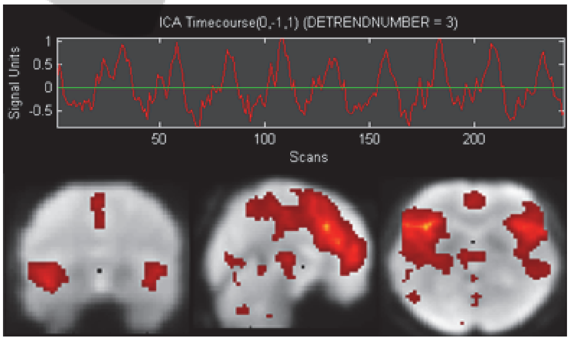

Figure 8: Component from the CPT task obtained with the Gaussian kernel.

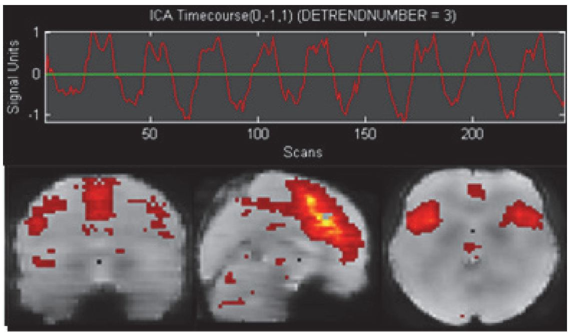

Figure 9: Component from the CPT task obtained with the adaptive Wiener filter.

If we take a look to the activations found, we can see that the adaptive filter found less active regions. These correspond to the zones parietal (BAs 2, 5, 3, 41) and temporal (BAs 20, 21) which are basically present in the figures 8 and 10.

Between all of these areas, the ones which probably could be activated by the task are the BA 5 which is related with the working memory (Yoo et Al., 2004) and BA 20 which is associated with the dual working memory task processing (Yoo et Al., 2004).

However, if we look previous studies (Bartés et al. 2011) which studied the same task using ICA, we can see that the BAs 5 and 20 were not found. By this fact and because the figure 8 has more abrupt changes in the time course than the figure 9 which differs a little bit from the task pattern, we believe that the components of the figures 8 and 10 have some false positives which are removed by the adaptive Wiener filter in the figures 9 and 11.

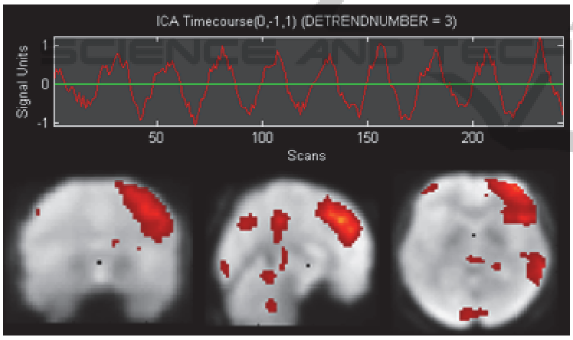

Figure 10: Component from the CPT task obtained with the Gaussian kernel.

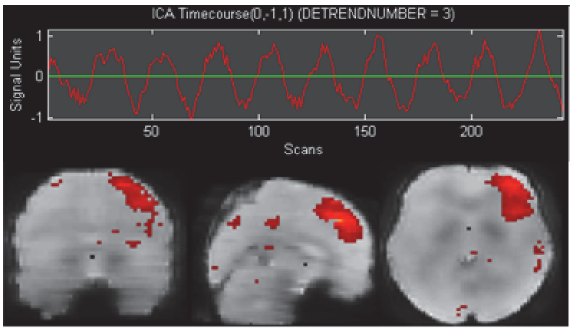

Figure 11: Component from the CPT task obtained with the adaptive Wiener filter.

5 CONCLUSIONS

We have compared the effects of two different denoising approaches: the use of Gaussian kernel and the use of an adaptive Wiener filter. After the analysis, the adaptive Wiener filter demonstrated to be a technique with a great potential. Comparing with the fixed Gaussian approache, is able to remove the noise minimizing the over/under-smoothing. The results provided evidences to state that the Gaussian kernels alter the spatial shape and extent of the activation regions, when applied for denoising fMRI data. Therefore, we believe that the approach proposed in this paper could be a good alternative to the classic smoothing methods.

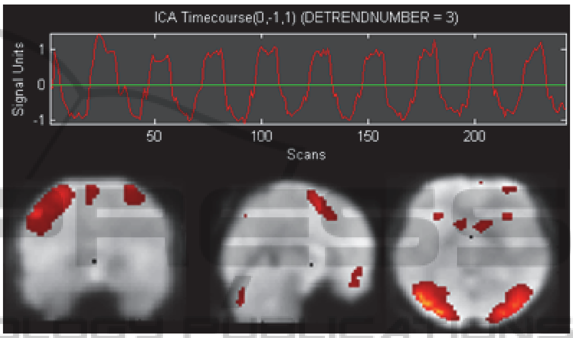

Figure 12: Component from the CPT task obtained with the Gaussian kernel.

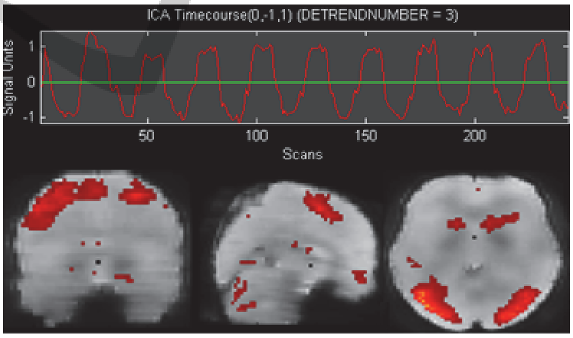

Figure 13: Component from the CPT task obtained with the adaptive Wiener filter.

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