fMRI Data Analysis Techniques and the Self-Organizing Maps Approach

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Functional Magnetic Resonance Imaging (fMRI) is a widely used technique to know more about how the brain function supports mental activities. Although fMRI is a powerful tool to detect functional activation within the brain, the obtained data from fMRI experiments cannot be easily directed analyzed because of a number of factors: weakness of the signal, abundant noise in the data and the difficulty of separating activations of interest from other types. To overcome some of these difficulties powerful analysis techniques are used to interpret the fMRI data.

In this paper, besides describing some of the most regular approaches, we will provide a more detailed analysis of one technique in particular: the self organizing maps (SOM). To conclude about the performance of this approach we developed a data mining tool implementing the SOM algorithm and tested it with real fMRI data. A presentation and a discussion of these results will be provided.

Keywords: **Neuroimaging, fMRI, data analysis techniques, self-organizing maps.**

Functional magnetic resonance imaging (fMRI) is one of the most successful tools in the investigation of cognitive function, enabling brain imaging with a high spatial resolution in a non-invasive way. The acquisition of data is commonly achieved with techniques that measure the blood oxygen level-dependent (BOLD) signal changes.

The development of the BOLD contrast fMRI technique represents a considerable advancement in the area of cognitive neuroscience, but is far from giving precise responses about the mechanisms involved in the functionality of the brain. Nevertheless, a large number of experiments and studies, based on this technique, have been one of the main sources of knowledge about brain function we have today and considered an important means of knowing even more.

The analysis of fMRI data has the objective to extract functional correlates from the obtained data sets [1] and identify brain regions involved in functions of interest. One of the main difficulties, when analyzing the fMRI data, is to separate the noise from the signals of interest. Other problem is the interpretation of the relation of these signals with some experimental behavior. In order to conduct the analysis of fMRI data, assumptions about the brain function must be made and sophisticated analysis techniques must be employed.

Inferential methods like statistical parametric mapping (SPM), clustering techniques and transformation based methods, like ICA (independent component analysis) and PCA (principal component analysis) are among the most applied approaches today in fMRI analysis.

Statistical parametric mapping (SPM) [2] is based on the general linear model (GLM) and is one of the most commonly used approaches for fMRI data analysis. SPM includes methods like ANOVA, correlation coefficients and t-tests.

The fundamental principle of SPM is that a signal depending simultaneously on various variables can be decomposed in terms of the variables contributions. This is only valid if sufficient sampling of the signals is obtained with different contributions of the independent variables.

The center of the GLM is a simple equation that relates observations to expectations by expressing the observed response Y as a linear combination of expected components (or explanatory variables) X and an associated residual error ε:

$$Y = X\beta + \varepsilon \quad (1)$$

In terms of an fMRI experiment, Y represent the time-course (TC) of the voxel we want to analyze. The matrix X is called design matrix and contains the explanatory variables that represent the experimental conditions under which the observations were made. Each row of the design matrix represents a different scan and each column some effect of the experience or an effect that may confound the results. The explanatoy variables or predictors are obtained by using a box-car function with a standard time-course of the hemodynamic response. A simple condition box-car of the time-course could be defined with values of 1 when an experimental condition is verified (on) and values of 0 in other cases (off). β is the set of coefficients to be determined, relating the voxel TC values to the experimental independent variables. In other words β characterizes preference profiles of the voxel for the experimental conditions modeled in the design matrix. Finally ε is a set of random error terms conforming to a Gaussian or normal distribution.

The estimation of β and its variance can be used in a vast range of statistical analyses. Despite this possibility the main focus here should be a good formulation of the design matrix X in order to model with a good precision the experimental design and obtain the best results from the inferences made. If the design matrix does not contain all relevant predictors, changes in the signal of the voxels will be accounted for errors instead of the model. Inferences about the contributions of the predictors to the observed signal are made using F or T statistics.

Methods based on the general linear model, like SPM, are currently one of the most used analysis strategies. One of the reasons is that the method offers an intuitive approach to the analysis of fMRI. On the other side these approaches are based on a set of tenuous assumptions. The first is that the observations

have a known distribution (e.g. Gaussian). Second SPM assumes that the time-course of different sources can be reliably estimated in advance. This involves fitting the acquired data into a canonical hemodynamic response function, making an assumption about the temporal evolution of the fMRI data. The third assumption is that the variances and convariances of the BOLD signal between repeated measurements are equal. The last assumption is that the signals at different voxels are considered independent. All these assumptions can lead to invalid or inefficient statistical tests. Finally, one other thing to take into account when using SPM is that it relies on smoothing of the data, which may degrade the inherently good spatial resolution offered by fMRI.

Tranformation based methods transform original data into a high-dimensional vector space in order to separate different functional responses and types of noise from each other. The new vector space will be composed of several components, each one representing typical spatial or temporal responses of functional activity and various noise sources. There are two transformation-based methods applied to fMRI: principal component analysis (PCA) and independent component analysis (ICA). Both methods use a transformation matrix to remove diffuse and complex patterns of correlation between the element vectors of the original data.

PCA uses only second-order statistics and decorrelates the outputs using an orthogonal matrix. Let X be the fMRI data matrix $M \times N$, with zero empirical mean (the empirical mean of the distribution has been subtracted from the data set), where N is the number of column vectors in the data set and M is the number of elements in each column vector (dimension). The PCA method is used to generate a new feature space Y using the following equation:

$$Y^T = X^T W \tag{2}$$

where W is the $M \times P$ matrix of basic column vectors composed by a set of P eigenvectors from the $M \times M$ covariance matrix C of the data.

One of the main problems when using PCA for fMRI analysis is the difficulty to capture small changes in signal variance related to some task related experiences. This happens because the principal components are projected onto orthogonal eigenvectors that express only the greatest variance in the data. The orthogonality between the principal components is also the cause of other limitation. If the signals of interest and the signals from other artifacts, such scanner or physiological noise, are non-orthogonal, this will result in loss of important signal. Finally this approach based on voxel-pair covariance will certainly miss some overall patterns of association (e.g. some voxels becoming simultaneously activated during an experiment).

ICA attempts to make the outputs as statistically independent as possible while placing no constraints on the transformation matrix:

$$C = WX \tag{3}$$

Here X is the matrix t (time-points) $\times$ n (voxels) of observed data, W is the unmixing matrix derived from ICA and C is the c (components) $\times$ n component matrix (Fig. 2). We can only observe the variables in X and must estimate W and C using X.

The analysis of fMRI data with the ICA approach has some pros and cons. The spatial division of the data into non-overlapping and specific sets provides a very nice method to identify spatial nodes that are independent and sparse. The correlation between time-courses of different components removes the constraint that artifacts non-related to the experiment have to be orthogonal to those derived from the experiment (in fMRI analyses any confounding between signals of interest and artifacts means loss of signal) [3]. One weakness of this approach is that the attempt to find maps that are maximally independent tends to fragment some broad areas of activation into multiple maps with all having strong correlated TCs. The ICA approach difficults the identification of non-linear activation relationships between active areas, which is an important issue regarding the theory of functional integration of the brain.

Clustering algorithms attempt to classify the time-course (TC) signals of the voxels into several patterns according to the similarity among them. This information is organized in clusters and is independent of their spatial neighborhood. These clusters can be described by an average TC or a cluster center obtained by averaging all the TCs of the cluster in question. The resultant output maps can be calculated by labeling the pixels of the same cluster (membership map) or by plotting the distance of the TCs to a given cluster center (distance map).

All the clustering algorithms share the same principle, the minimization of an objective function. We will describe de K-means clustering (KMC) variant. Let the set $\{x_j\}$ be composed of N vectors from $\Re^i$ where each vector corresponds to a voxel time-course (TC) and i is the number of images taken by the MRI scanner. Next we consider K clusters, and their respective center $c_k \in \Re^i$ and $1 \leq k \leq K$. The data is partitioned by clusters such each x_j (voxel's TC) is assigned to exactly one cluster C_k. The clustering algorithm objective is this assignment while minimizing an objective function to give the low-dimensional approximation to the data. So we have the K-means objective function:

$$I_w = \frac{1}{N} \sum_{k=1}^{K} \sum_{x_j \in C_k} d^2(x_j, c_k), K \leq N \tag{4}$$

where d^2 is the squared distance of two vectors and C_k represents the number of elements in the respective cluster. The distance d is typically the Euclidean but other types are also used.

The results of clustering approaches, like KMC, depend largely on a number of factors. The number of clusters must be specified before the algorithm and a choice that does not reflect the data structure will result in weak or meaningless results. Regardless the ex-

istence or not of structure the algorithm will perform data partitioning. This makes the validation of the results necessary. The choice of the distance d metric will also have a deep influence on the results. The use of the distance function also demands pre-processing of the data [4]. As it is the partitioning is based on the average of the TC signals. Normally this is not the objective since what is wanted is to gather in one cluster TCs with similar waveforms (temporal profiles). The use of raw inputs based on the distance metric will merely segment the brain [5]. The final factor to consider is that the K-means algorithm is non-deterministic and the results are dependent of the cluster initialization.

Self-Organizing Maps

The self-organizing maps (SOM) algorithm introduced by Kohonen [6] is an analog, in this case ironically, to the human brain way of organizing information in a logical manner. It is theorized that cognitive cells in the human brain, like the ones in the visual cortex, are trained in a supervised manner, while others function in a self-organized unsupervised manner. These cells are organized topologically in a way such adjacent areas perform related cognitive functions. The SOM method emulates this unsupervised learning. In terms of the algorithm it tries to reveal structure to the data by bringing together characteristics of two other algorithms. Kohonen's maps do not partition the data into independent subsets but model its interrelation, like cluster algorithms, while performing in it a lower-dimensional projection like topological preserving mapping algorithms. The SOM approach differs from cluster approaches in the way that accounts for the neighborhood of cluster centers. One interesting thing in its use is that addresses some difficulties of the conventional clustering:

- The choice of the number of expected clusters.
- The clusters validity.
- The detection of small and large clusters within the same data set.

Kohonen's maps consist of one layer of neurons (neuron map), usually a two-dimensional grid, and each neuron has a feature array. In the case of fMRI analysis this array represents the voxel's time-course (TC). Each neuron in the map is a cluster center and has as many input connections as the data-samples that will be used in the map training. The training procedure is performed in several steps and has the objective of organize the voxel's TC such that similar ones are close to each other.

The first steps consist in fixing the SOM and training parameters dimension. Each node of the map is initialized with random noise. The training of the map is then made iteratively by selecting a random TC from the measured data from the entire imaged volume or from a region of interest. All the selected voxel's TC used as input for the training will also be normalized. For each iteration the algorithm looks for the neuron that is more similar to the input and declares it the winner. The determination of the degree of similarity Can be done using metrics like the Euclidean distance or the scalar product of the input with the tested neuron for example.

The winner cluster center will be moved towards the selected input as all the centers of the neighbor neurons by an amount inversely to the distance to the winner neuron using

$$n_k(t+1) = n_k(t) + h_{ck}(t) * (x_i(t) - n_k(t)) \quad (5)$$

where t is the current iteration value, h_{ck} is a neighborhood function that controls how much the winner and his neighbors are updated and to what degree, and x_i is the selected TC. As the algorithm goes on, the centers of the winning cluster and the considered current neighbors will change less, as a means of achieving the map convergence and preserving the quantization of the data. As the iterations progresses, the neighborhood function shrinks the neighborhood and at the end only individual nodes are updated. This function could be defined in numerous ways, being a shrinking Gaussian neighborhood function one of the most used [7]:

$$h_{ck} = \alpha(t) * exp(-\frac{\|r_k - r_c\|^2}{2\sigma^2(t)}) \quad (6)$$

where $0 < \alpha(t) < 1$ is the learning rate, that decreases over time, controling how faster the neurons learn, and $r_k \in \Re^2$ and $r_c \in \Re^2$ are neuron coordinates from the winner and updated neuron respectively. Finally $\sigma(t)$ corresponds to the width of the neighborhood function, which also decreases with time. The ending of the training processes could be based in a chosen number of iterations or on an evaluation of the quality of the obtained map.

With map training we obtained a set of small clusters as large as the map's size. The clusters can then be combined to form larger super clusters. This can be done in a different number of ways. One approach would be to add small clusters interactively to the super clusters with the support of some visualization technique [8]. Other ways include automatic calculation of the super clusters by means of constraint (need-driven) clustering using metrics like least-mutual distance [9] or least-squares distance [10], or can also be done using data-driven clustering like fuzzy c-means clustering [11].

Implementation

Our analysis of the performance of the SOM algorithm will be based in two experiments, one based in the stimulation of the auditory cortex and other in the stimulation of the visual cortex.

The first data set obtained from the first experience comprises whole brain EPI-BOLD images acquired on a 2T Siemens MAGNETOM Vision system. 96 acquisitions were made with TR = 7s and each acquisition consisted of 64 contiguous slices (64x64x64 3mm x 3mm x 3mm voxels). This was a block design experiment where auditory stimulation was alternated with

rest periods. The blocks of auditory stimulation consisted on bi-syllabic words presented to subject at a rate of 60 per minute. The experiment was conducted by Geraint Rees under the direction of Karl Friston and the FIL methods group. This experiment has not been formally written up and is freely available for education and evaluation purposes. The data set and a more detailed description can be found at `http://www.fil.ion.ucl.ac.uk/spm/data/auditory/`. The chapter 28 of the SPM5 manual (`http://www.fil.ion.ucl.ac.uk/spm/doc/spm5_manual.pdf`) illustrates a step by step analysis of this data set, using the SPM5 package, presenting the respective final results. We will compare these results to those obtained by our SOM approach using the same data set.

The second data set is composed of whole brain EPI-BOLD images acquired on a 3T Philips MRI system. 108 acquisitions were made with TR = 3s and each acquisition consisted of 40 contiguous slices (80x80x40 $\sim$ 2.875 x 2.875 mm x 3 mm voxels). This experiment used a rapid event-related paradigm design where various pairs of faces were presented in one of 6 possible orientations: 0, 60, 120, 180, 240 or 300. The above experiment was previously analyzed using hypothesis driven analysis by other investigation team [12] using FSL (fMRI software library - `www.fmrib.ox.ac.uk/fsl`) for the preprocessing and application of the GLM. In this particular experiment the investigation team tried to find not only activation in the visual cortex (Figure 4C) but also more specialized zones (Figure 5 C) within this cortex related to the face inversion effect (FIE). Using the SOM approach we explored the data in order to find first one zone correspondent to the visual cortex activation and similar to the one found with the GLM approach. Later we also tried to find within this same zone smaller specialized zones of activation.

In both analysis using the model driven approach, it was performed a single subject analysis in the first case and a multi-subject in the second case. We will compare our results with the results of these experiments, but using single subject analysis in both cases. In the second experiment we opted to choose a subject randomly instead of using the data from all of them.

To test the interest and validity of the SOM algorithm in fMRI analysis of the above described data sets and in general, we developed a software package using Matlab and the programming language C. For the two experiments the raw data was preprocessed using the SPM5 package. In both cases the steps were the same:

1. Spatial preprocessing with realignment of the fMRI images.

2. Coregistration between structural and functional data.

3. Normalization of the data onto a standard anatomical template.

4. Smoothing of the data using a Gaussian smoothing kernel of 8.

In both cases each time course was subtracted by its mean. In the fMRI images the signal correspondent to the BOLD response is very low compared to the structural signal. This step of subtracting the mean to the time-courses was done automatically by our application and has the objective of normalize the data to account only for its variance, and to avoid convergence of the SOM algorithm based on the mean values of the time courses. Other step taken before running the algorithm was the application of a threshold to both data sets, as a means of excluding from the analysis voxels outside of the brain structure.

After the steps taken above we applied our algorithm. The metric used to the determination of the degree of similarity between the time courses was the Euclidean distance. The chosen neighborhood function was a Gaussian neighborhood function as it was defined in Equation 6. A quadratic grid of 10 x 10 was used throughout both experiments giving a total of 100 nodes per map, each node representing a mean of about 40-50 TCs. The choice of 100 exemplar time courses represented by each node, in general, seems an ample enough size to classify 5 to 6 possible fMRI cluster types (activation, head motion, functional connectivity, and noise, among other possibilities). The SOM map was initialized with random noise. At each iteration of the algorithm all time courses of interest were presented to the map. The training of the neuron map was made in a two stage process. In the first stage the number of iterations was set to 10, which represents that the whole data was processed 10 times by the algorithm. The initial Gaussian smooth kernel was set to 6 and the initial learning rate to 0.05. In the second phase, called calibration, the total number of iterations was set to 100, the initial Gaussian smooth kernel to 3 and the initial learning rate to 0.001. For the updating of the training parameters (Gaussian smooth kernel and learning rate) was used a power series function.

In the case of the first experiment the results werent total satisfactory, and so a second analysis was made. In this second approach we selected a smaller ROI to be analyzed by the algorithm. Only voxels from the slices that were known to contain the known activation area (auditory cortex) were presented to the SOM, rather than the whole brain. As we will see the definition of a smaller ROI will represent much more conclusive results.

The largest data set analyzed was composed by 108 frames and a ROI of 52779 voxels. In this case it took about 7 minutes to train the map on a virtual machine with an equivalent processor of 2.2 GHz and 1024 MB of RAM.

The final results were analyzed with the support of a homemade visual tool. By trial and error we tried to merge the map nodes into superclusters until we obtained areas of activation similar to those that were expected from the experiments. Nodes that represented scattered voxels in brain were considered some kind of noise and were discarded as a contribution to an activation of interest. Besides trying to identify previously known regions of activation, found in the hypothesis

driven experiences, we also tried to explore the capabilities of the SOM in finding other zones of activation related to the experiment. Although we dont have the expertise or the knowledge to interpret these results, this action has the objective to empathize the SOM capability in discovering non-expected behaviors from the brain that maybe would be worth exploring.

Results

For each experiment a self organizing map of 10 x 10 with 100 nodes was obtained. Like we already mentioned, this map was explored using a visualization tool with the objective of finding zones of activation similar to those found by hypothesis driven analysis. In this subsection we will show our results and well make the respective comparison between the SOM approach and the other inferential data analysis paradigms results.

Experiment 1: auditory fMRI data First we present the results achieved with SPM by applying a t-contrast, with a $p = 0.05$. Using an adequate design matrix the results obtained are shown in Figure 1C and 2C. Analysis of the data was also made using our SOM algorithm. First we trained the map using the time courses from all brain and found similar areas of activation in the auditory cortex (Figure 1B) by defining a supercluster composed by 4 nodes (Figure 1A). Although auditory cortex regions were found by our algorithm, we can see that other areas outside this cortex are also activated. It is possible that this other regions can have a relation to the experiment and the auditory stimulus, since they are strongly correlated. Nevertheless one of our objectives was to demonstrate that our algorithm could deliver similar results to the hypothesis driven ones. To see if we could obtain better results, more like the ones delivered from SPM, we trained another map. This time we only used a data set composed from the slices of the brain we knew that contained the wanted areas of activation, the slices where the auditory cortex is located. Defining a supercluster of 2 nodes (Figure 2A) we achieved more satisfactory results as we can see in Figure 2A and by comparing with Figure 2B.

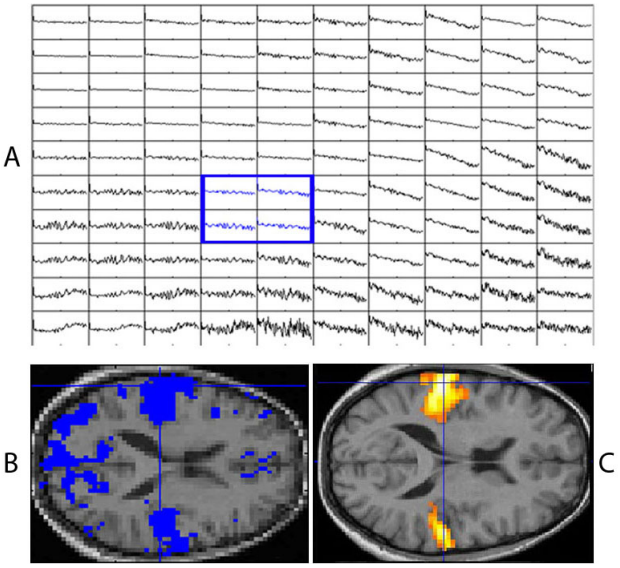

Fig. 1. **(A)** Supercluster formed by merging four nodes of a SOM obtained with whole brain data training (auditory experiment). The supercluster was formed interactivily by trying to find activation zones similar to the ones found with the GLM approach in Figure 1C. **(B)** Zones of activation (SOM approach) of the auditory experiment represented by the nodes of the supercluster in Figure 1A. **(C)** Zones of activation obtained from auditory experiment with GLM approach.

In a second phase of analysis of the trained map we tried to find other unknown homogenous zones of activation as a means of exploring unknown brain behavior. This is a great example of how the SOM can be used we analyzing brain function. We found one other interesting zone (Figure 3B) represented by 5 nodes of the map (Figure 3A). Although we do not have sufficient knowledge to interpret this result, we know for a fact that the found homogeneous area represents a certain behavior of the brain during the experiment. The data driven approaches represent methods that find structure in the data, but they do not give us a meaning to the divisions made. As we will discuss later, the SOM is a good way to explore the function of the brain when information of the experiment is not available or when we have complex experiments difficult to model. Because of this the SOM, like other data driven approaches must be most of the times complemented with model driven methods and the expertise of the researchers, so that can be given meaning to the division of the data.

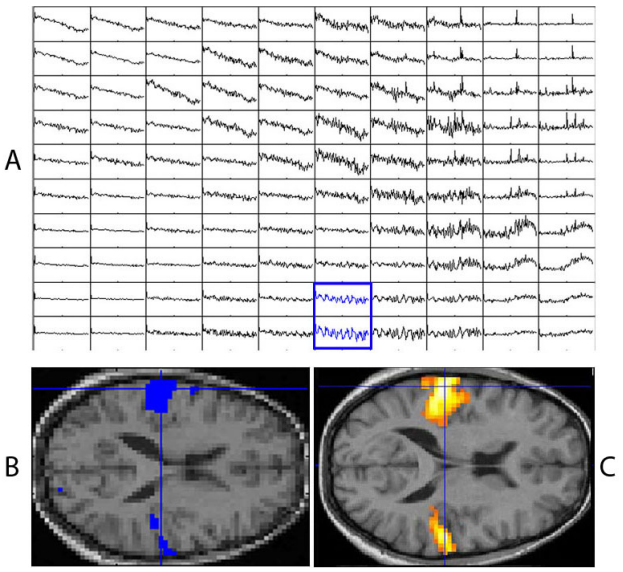

Fig. 2. **(A)** Supercluster formed by merging two nodes of a SOM obtained by training data from slices known to contain activations of interest (auditory experiment). The supercluster was formed interactivily by trying to find activation zones similar to the ones found with the GLM approach in Figure 2C. **(B)** Zones of activation (SOM approach) of the auditory experiment represented by the nodes of the supercluster in Figure 2A. **(C)** Zones of activation obtained from auditory experiment with GLM approach.

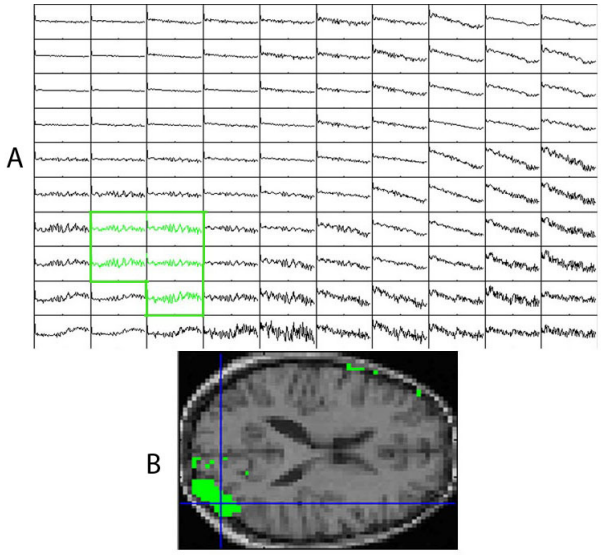

Fig. 3. **(A)** Supercluster formed by merging five nodes of a SOM obtained with whole brain data training (auditory experiment). The nodes were merged interactivily by searching for unexpected homogeneous zones of activation. **(B)** Zones of activation (SOM approach) of the auditory experiment represented by the nodes of the supercluster in Figure 3A.

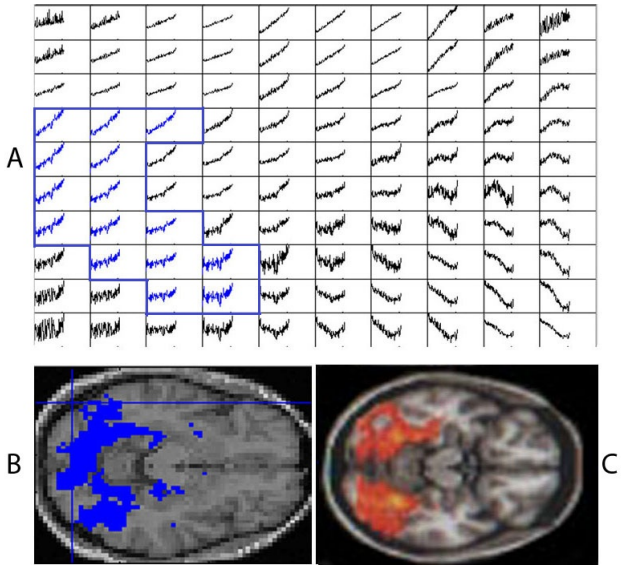

Fig. 4. **(A)** Supercluster formed by merging fifteen nodes of a SOM obtained with whole brain data training (visual experiment). The supercluster was formed interactivily by trying to find activation zones similar to the ones found with the GLM approach in Figure 4C. **(B)** Zones of activation (SOM approach) of the visual experiment represented by the nodes of the supercluster in Figure 4A. **(C)** Zones of activation obtained from visual experiment with GLM approach.

Experiment 2: visual fMRI data The results with a GLM approach using FSL are shown in Figure 4C. The areas of activation are a result of a multi-subject analysis and our analysis was done using data from only one subject chosen randomly. Knowing this, it is reasonable to assume that our results can not be a perfect match to those shown before. In Figure 4B we see the areas of activation found using our SOM analysis algorithm. By grouping 15 nodes into a supercluester (Figure 4A) we can see activations, in the zone of the visual cortex, similar to the ones obtained using FSL and multi-subject analysis.

Also with the GLM approach there were in a second phase identified five functional ROI in the subjects (Figure 5B). These areas are identified in the figure by three different color clusters. We tried to explore the capabilities of the SOM in finding similar areas and smaller clusters within the data set. For this, we tried to divide our 15 nodes supercluester in a set of three smaller superclusters (Figure 5A). As we can see in Figure 5B, we found three homogeneous and symmetric areas of activation with this division. Because we do not have the expertise and we are using a model free approach without any information about the experiment, we cannot give a meaningful interpretation to this division. Nevertheless we know that this found ROIs represent different behaviors, and from this we can propose an hypothesis stating that these areas perform different functions within the visual cortex. Also if we compare the three smaller clusters obtained, we can see some similarities to the zones found by the GLM approach in Figure 5B.

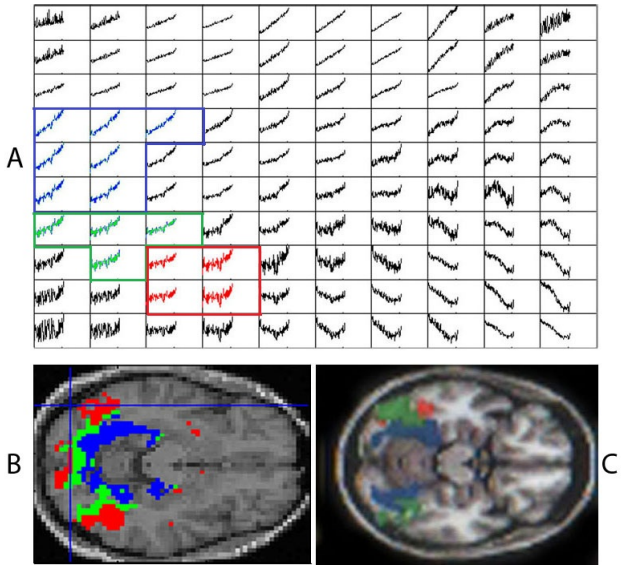

Fig. 5. **(A)** Division of the supercluster in Figure 4A into three smaller superclusters (visual experiment). This division was made interactivily by trying to find zones symetric and similar to the ones found with the GLM approach (Figure 5C). **(B)** Zones of activation (SOM approach) of the visual experiment represented by the nodes of the three superclusters in Figure 5A. **(C)** Three distinct zones of activation obtained from visual experiment with GLM approach.

Discussion

The self organizing map (SOM) approach was applied to two experiments. These experiments were previously analyzed by other investigating teams using

model driven approaches based on the general linear model (GLM). The GLM method requires knowledge about the experiment and involves the construction of a model function that describes the experimental protocol. Our SOM approach did not require any external reference. Model free methods offer a great alternative to fMRI analysis by analyzing the data based on signal alone without user bias. This is a very important characteristic in cases where we have complex experimental protocols or when we are dealing with unknown response functions that hardly can be model correctly by the user (e.g. memory studies). Nevertheless, model free approaches only find structure in the data without giving this structure any meaning. The researchers expertise is needed to interpret the results and these methods may have to be complemented with inferential analysis as a means of associating the partitioning of the data to the experimental protocol. In our analysis we did not have exactly the expertise to interpret the structuring of the data made by the SOM algorithm. In our case, we used the portioning of the data delivered by the SOM and tried to isolate homogeneous zones of activation in the brain that were similar to those found in other approaches and that were located in the known cortexes related to the experiment. The results were within our expectations. With our SOM algorithm we achieved similar results to those found with the model driven methods, finding zones of activation in the brain within the expected cortexes (the auditory in the first experiment and the visual in the second experiment).

More than to find similar zones of activation we also tried to find homogeneous zones not represented in the results delivered by the GLM approach and outside the cortexes supposedly involved in the experiments. We did this regarding the auditory experiment and found a zone of interest outside the auditory cortex that could be somewhat related to the experimental protocol (Figure 3B). Although this is not conclusive, this example has the objective of strengthening the capabilities of the SOM in finding unexpected responses of the brain and its capabilities as a research tool.

The SOM method also offers a good alternative to other data driven approaches. It does not have to deal with the constraints of orthogonality and independency of the data of the PCA and ICA approaches respectively and addresses some of the difficulties of other clustering algorithms as we already mentioned previously. K-Means clustering (KMC) for example would be able to find differently sized and populated clusters. Unfortunately this property cannot be assumed in the case of fMRI analysis, since the clusters in the data are severely blurred and have high mutual proximity. This problem of the KMC is even worst when we normalize the data to make clustering more sensitive to the dynamics of the brain rather than the time-courses mean values. KMC can still do well when separating noise from the signal of interest. However if we set the algorithm to find a small number of clusters it would miss small zones of activation. These zones would simply be grouped into a single larger cluster. KMC by minimizing the sum of squared distances has the tendency to equalize the sizes of identified clusters which difficult the detection of small and larger clusters within the same data set. This can be solved by setting a large number of initial clusters. Although this makes possible to find smaller zones of activation, this zones will be represented by different independent clusters. A way to solve this is to merge these small clusters that are supposed to belong together. In the other hand if we have a larger cluster representative of a larger zone of activation and we want to divide it in smaller specialized zones the solution would be to partition it into smaller clusters. Both options are supported by the SOM approach. This was done in experiment 2 by dividing the larger cluster (Figure 4A) into a set of 3 smaller clusters (Figure 5A). With this operation it was possible to find more specialized zones with different behaviors within the visual cortex. This characteristic of the SOM also deals with the problem of the validity of the portioning of the KMC. By merging nodes interactively it is possible to define which nodes should belong together within the same cluster and which nodes do not contribute to activations of interest.

Regarding the SOM algorithm alone it is visible that the results depend on a number of factors and variables:

- The method of initialization of the map.
- The number of iterations and the size of the map.
- The learning rate and the neighborhood width variables.
- The distance metric.
- Functions that define the updating of the variables and the neighborhood function.
- The method to form superclusters.

All this factors strengthen the idea that running the algorithm with alternative functions and values might be a good idea in order to find the best results. These variables can all be chosen using common sense, by experimenting or with the help of common practice references.

Automatisms can also be used to optimize the algorithm or to reduce user bias. For example a mean squared error (MSQE) [10] between time courses can be calculated at each iteration of the algorithm to access about its convergence. With this mechanism it is possible to stop the algorithm at an iteration where no further appreciable changes in the map occur. The calculation of supercluesters can also be made automatically with the support of methods like contiguity constraint clustering [13] which merges neighboring nodes with least mutual distances. Although the automatic formation of superclusters seems to be a good method to reduce the user bias, we cannot underestimate the power of an interactive method (our approach) based on the researchers expertise and the visual capabilities

offered by the SOMs topographical mapping of high-dimensional data.

The SOM learning rate or neighborhood contraction rate can also be optimized by finding which values attain the lowest total squared error [10] for example. This represents a great alternative when choosing the best values to these variables.

As we also have observed the choosing of smaller ROIs can help to improve the results returned by the SOM, as we eliminate form the training process the contributions of less interesting time courses. Although normally a 10x10 grid of 100 nodes seems to be sufficient to characterize different types of signals, a larger grid can sometimes be a better option to find even smaller and specialized zones of activation.

Extracting extra properties from the maps delivered by the SOM can also help to better characterize the data. Gradient images that calculate the averaged distance between neighborhood nodes and frequency plots that count the number of time-courses for each node can help in defining how many clusters distinct clusters exist in the data. Also calculating the average spatial distance between the nodes in the map could make easier to detect which nodes in the feature space form clusters in the image pane.

Outlook: SOM proved to be a very flexible approach that, as we have discussed, addresses the typical clustering problems while maintaining the advantages of this kind of approach. It also can be use as a method of initialization to other algorithms as the fuzzy C-means clustering. The algorithm topological ordering with the help of visualization techniques proved to be a great means to visualize complex data and to investigate the overall dynamics of an experiment. On the downside the SOM approach is dependent of many factors, like initialization, parameters definition and others. Although this is true, we discussed a number of methods that can be used to introduce more automatisms into the algorithm and reduce the user bias.

We tried to illustrate how SOM can be used to analyze fMRI data, showing some of the results obtained with this approach. We cannot answer with our study the question of statistical significance but we tried to discuss and show why the SOM approach can be interesting in terms of fMRI analysis. With this idea in mind, we hope this paper encourages further research in this matter with the achievement of promising results, bringing us one step closer to understand more clearly how our brain works.

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