Clustering fMRI Time Series in the Wavelet Domain

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Introduction In this paper, we analyze fMRI time series in the wavelet domain using a hierarchical clustering method combined with Dendrogram Sharpening [1]. This clustering method represents a spatial dimensionality reduction technique. Utilizing only the selected part of the wavelet coefficients can be considered as a temporal reduction of the data. When clustering the original (not wavelet-transformed) fMRI data, the functional component corresponding to the paradigm is separated into one independent cluster. However, after wavelet reduction this component is split into two different clusters with nested structure. This result might indicate the ability of the wavelet coefficient to capture differences in the on-sets of the activation.

Theory Dendrogram sharpening is a model-free approach that does not require prior assumptions about the number and location of the clusters. This method removes observations from low-density regions producing a clear representation of the modal peaks. The similarity between two voxels is expressed in terms of the correlation coefficient of the corresponding time courses which is then converted into distance as **d(i,j)=1 - cc(i,j),** where **cc(i,j)** is the correlation coefficient between voxels **i** and **j**. Voxels are grouped into a binary tree using the single linkage method where the distance between two clusters is equal to the minimal distance of all pairs of voxels in two clusters. In order to make the structure of the data more apparent the tree is pruned by discarding all small-sized children-nodes with a large-sized parent node. Clusters in the modified tree are identified using the method of inconsistent edges, where the value of median edge length of the left (right) subtree plus twice the interhindge spread is the proposed threshold, beyond which an edge is considered inconsistent with respect to its left (right) child. Once the cores are identified, voxels discarded during sharpening are assigned to the cluster group, to which they are joined by the link of minimal length.

Clustering in the wavelet domain Wavelet transformation is performed by computing the inner product between a signal of interest, X, and basis functions derived by rescaling and translation from a selected mother wavelet. The vector of the discrete wavelet coefficients, **W**, can be written as $\mathbf{W}=\mathcal{W}X$, where $\mathcal{W}$ is an orthogonal matrix defining the transform. The elements of the vector of the wavelet coefficients are associated with a particular scale and are localized in time. We consider **W** as a projection of the signal vector onto the space defined by the basis function attributed to the selected mother wavelet. Selecting a part of the wavelet coefficient vector could be viewed as a projection of the signal space onto the affine subspace spanned by the selected wavelet basis. This procedure reduces the dimensionality of the data in the temporal domain. The *j*-th level detail reflecting the changes on the 2^{j-1} scale are computed as $D_j=\mathcal{W}_j^T\,\mathcal{W}_j\cdot X$. The lower level details are usually associated with the noise components of the signal. By examining the details of the corresponding transform one can select a scale of interest and utilize the corresponding wavelet coefficients as reduced data to work with.

Methods Scanning was performed on a commercial 1.5T GE MR scanner. The paradigm consisted of five periods of bilateral finger tapping (30sec) interleaved with rest (30sec). The EPI acquisition parameters were: FOV 24 cm x 24 cm, BW +/- 62.5 KHz, TR 2 sec, Flip 82 deg, 20 slices, slice thickness 7mm/gap 2mm, 64x64 resolution. Only voxels with cross-correlation coefficient of at least 0.4 were considered. As a consequence, the number of voxels was reduced from 15,000 to about 1500. Upon the grouping of the remaining voxels into a binary tree, the dendrogram sharpening was performed twice with parameters: *(fluff-value, core-value)* set to (2,20) and (10,20), respectively, where *fluff-value* is the maximum size of a child cluster that is discarded if it has a parent node of a size greater than the *core-value*. Cluster cores were identified using the method of inconsistent edges. The final classification was run on voxels, discarded during sharpening, in order to assign them to the found clusters. We used a continuous Morlet wavelet decomposition to explore the temporal behavior of the obtained clusters. For the clustering in the wavelet domain we used a discrete wavelet transform with Daubechies wavelets of order 8. Wavelet coefficient (Fig.3) of the order 3-6 were selected as the representation of the reduced data based on the multiresolution analysis.

Results Clustering algorithm applied to the original data resulted in clusters clearly associated with motor cortex, SMA, cerebellum and thalamus (Fig1). Wavelet analysis using a continuous Morlet transform indicates that the magnitude of the motor task specific frequency (0.016Hz) varies over time (Fig 2). Aside from this dominating frequency there are noticeable high frequency oscillations especially in the beginning of the paradigm. Multiresilution analysis of the mean time courses (Fig3) shows an interesting difference in the fourth level details for clusters A and C which reflects changes over a 16-second scale. For the voxels in the motor cortex area the detail structure is very similar to the level five. But for the cluster C, the frequency of the oscillations is twice higher and could be explained by the anatomical functions of the thalamus structure, which acts as an internal alarm notifying brain regions about the upcoming event. When a person performs an “on-off “ paradigm he/she anticipates the beginning and the end of each of the 30sec cycle. Every time when the cycle is about to begin or to end, thalamus cells fire an impulse. Because the particular paradigm activates the voxels in the motor area of the brain, the activation in the thalamus appears as a derivative of the time course of activation in the motor cortex.

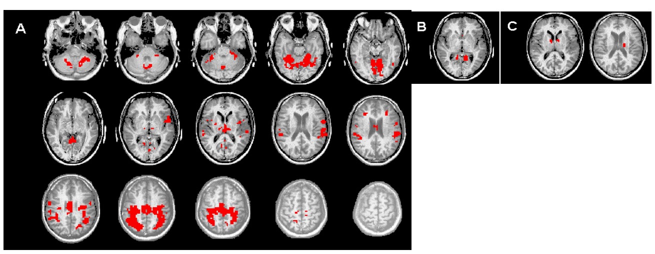

Fig 1 Three clusters resulted from the clustering method. Cluster ***A*** shows strong activation in the primary sensorimotor cortex, SMA and cerebellum. The other two clusters were specific to the retrosplenial area ***B*** and thalamus ***C***. (Only slices containing the active voxels are presented).

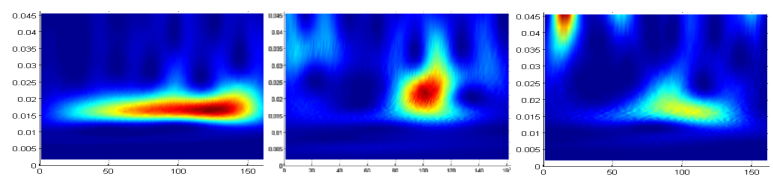

Fig 2 Time-frequency contour plots for the mean time courses of clusters A, B, C, obtained using a continuous wavelet transform with Morlet wavelet. All series have a significant contribution of the different magnitude and duration from the paradigm specific frequency of 0.016Hz, which gradually increases during the first two-thirds of the task time and declines later on. This behavior could, perhaps, be attributed to the habituation or learning effect. Also clusters B and, especially, C exhibit high frequency fluctuations during the first cycle of the task.

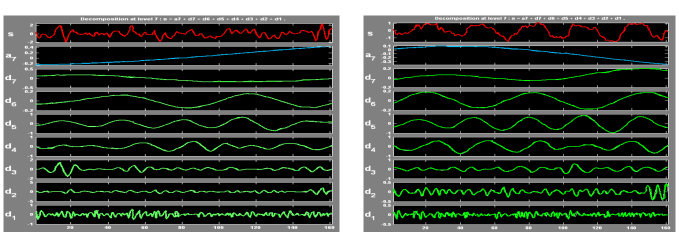

Fig 3 Multiresolution analysis of the mean time courses of the clusters A(*left*) and C(*right*) using DWT with D(8) wavelets. First and second level details could be attributed to the noise presented in the data. Details at the fifth level look almost identical and reflect changes over physical scale of τ_5TR = 16*2=32 secs that is almost exactly a duration of each activation and rest period in the paradigm.

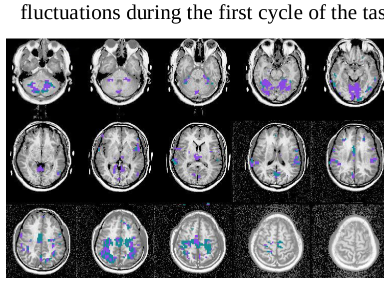

Fig 4 *(Wavelet analysis)* Two clusters (blue and purple) identified in the reduced data set using the identical clustering procedure. Notice that the areas attributed to the motor cortex and SMA are now split in two different clusters. Cluster C (Fig1) does not appear on the activation map.

References

[1] Stanberry et al. Cluster analysis of fMRI data using dendrogram sharpening (2003) Hum Brain Mapp 20(4):201-219

[2] Percival and Walden Wavelet methods for time series analysis (2000) Canbridge University Press