Comparing functional connectivity in normal and dyslexic readers with cluster analysis using a continuous phonological task

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Introduction

The purpose of our imaging research in dyslexia is to fully describe the brain reading network and identify the deficiencies in cognitive systems that lead to the learning disability. The Phoneme Mapping task [1] employed here involved a number of cognitive components and neural connections used in linguistic processing. This task was also presented in a continuous activation mode as opposed to the conventional "on-off" block paradigm form and, thus, could not be analyzed by model-driven methods. Here we used a Hierarchical Clustering method combined with Dendrogram Sharpening [2] to examine the patterns of correlations between the signal changes across the entire brain. In the context of the dyslexia studies, we seek to cluster voxels according to their temporal responses of the fMRI BOLD signal. We hypothesize that associated activation has significant spatial and temporal structure that can be grouped into a few types of responses. Subsequently, temporal and spatial characteristics of the obtained clusters can be analyzed with regard to descriptive parameters.

Theory

Dendrogram sharpening [2] is a model free approach that does not require prior assumptions about the number and location of the clusters. The 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.

Methods

Functional MRI was performed using a commercial 1.5T G.E. MRI scanner. Scanning parameters for echo-planar images were: EPIBOLD, TR/TE 2s/40 ms, FA 82deg, FOV 24x24, 64x64 imaging matrix, thick 6mm/1mm, 20 axial slices, BW+/-62.5, 453 volumes. Ten healthy adult male subjects were selected for the study, six dyslexics and four unaffected controls. Each subject underwent a thorough training before the scanning. Our Phoneme Mapping paradigm starts with a 5 minute resting period followed by 6 seconds of aurally and visually presented instructions. During the next 5 minutes a continuous phoneme-matching task is executed as follows. Word-pairs are visually presented every 6 seconds. In each of the words in a pair, certain letters are colored in pink, e.g. TAL**K**, RO**CK**. The subject has to indicate by pressing a button whether these highlighted letters stand for the same phoneme. Each participant was presented with 50 word-pairs

Cluster analysis

Only voxels with cross-correlation coefficient of at least 0.4 were considered. As a consequence, the number of voxels was reduced to about 1000. 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 (2,40) and (10,40), 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* [2]. 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.

Results and Conclusion

Activation maps with slight variability were consistent across all four control subjects. We observed much larger variability in the dyslexics. All of the affected participants showed significant underactivation in IFG, STG, FFG and OTC compared to controls. Five dyslexics showed largely uncorrelated activations in the cerebellum and brain stem. These preliminary qualitative results indicate possible functional differences between the control and dyslexic subjects. The results suggest a failure of the language network, perhaps in the very initial stage. The objective of our future work is to quantify the observed differences using ROI analysis of anatomical brain regions. The proposed method might ultimately result in a powerful diagnostic tool for therapeutic interventions.
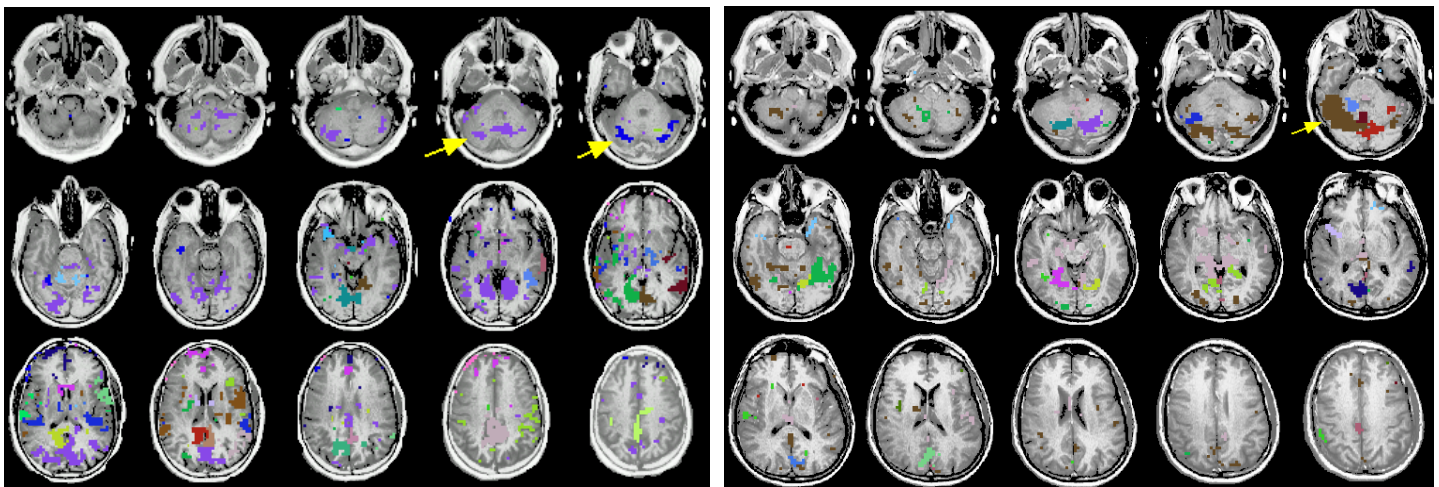
Fig.1 Clustering results for two selected subjects, control *(left)* and dyslexic *(right)*. Clusters were color coded and overlaid on the anatomical images. The control subject shows a symmetrical cluster in the cerebellum that extends to the FFG, lingual gyrus, OTC, and occipital lobe (purple/blue clusters, see arrows on left fig.). The map also indicates different correlated clusters in the cingulate cortex, Insula, IFG, STG and parietal lobe. The dyslexic reader shows much less correlated clusters in IFG, STG or OTC. However, there is an unproportionally large cluster in the right cerebellum (brown cluster, see arrow on right fig.), which does not extent any further.

References

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