Group fMRI Connectivity Maps Showing Abnormal Connections to the Cerebellum in Dyslexic Readers

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Introduction

The purpose of this abstract is to construct the group connectivity maps of brain regions functionally connected with the cerebellum for dyslexic and control subjects using a continuous phoneme mapping paradigm. The task employed here [1] involves a number of cognitive components used in linguistic processing. Data analysis was performed using a Hierarchical Clustering method combined with Dendrogram Sharpening [2] to examine the patterns of correlations in clusters functionally connected with the cerebellum. Our previous results from analyzing individual connectivity patterns in clusters involving cerebellum indicate that the affected population, as compared to the control group, has significantly less voxels involved in the phoneme matching process in certain brain regions, e.g. precentral, frontal and angular gyri, insula, amygdala and occipital cortex. We hypothesize that these disassociations in the BOLD-signal fluctuations could potentially be associated with functional deficiency and, perhaps, could be explained by the impairment of the white matter pathways [3] that slow down or disrupt neuronal transmission from the cerebellum to selected (not all) language centers involved in reading.

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. 25 healthy adult male subjects were selected for the study, 13 dyslexics and 12 unaffected controls. Each subject underwent a thorough training before the scanning. The Phoneme Mapping paradigm consists of a continuous 5-minute stimulation period (*without any interleaving rest periods*) during which the word-pairs are visually presented every 6 seconds. In each of the words in a pair, certain letters are colored in pink, e.g. DOAK, SOTE. 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 from 15,000 to 2,000. 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* [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

For each subject we considered only clusters showing activation in the cerebellum. Upon selecting clusters of interest for each of the participants, the spatial location of the clusters was co-registered and transformed to the standard brain coordinate system (Talairach space). Each data set was segmented into 116 different regions using the anatomical segmentation tools developed by MRIcro (Chris Rorden, University of Nottingham). Number of pixels from the clusters of interest was counted in each anatomical region. A *t*-test showed that the number of voxels correlated with the cerebellum was significantly larger for the control readers in various brain regions including amygdala, superior, middle and inferior frontal gyri, occipital lobule, insula, precentral and angular gyri. Further, for each group of subjects group connectivity maps were calculated by averaging the individual cluster maps (voxel by voxel) which were first transformed to Talairach space.

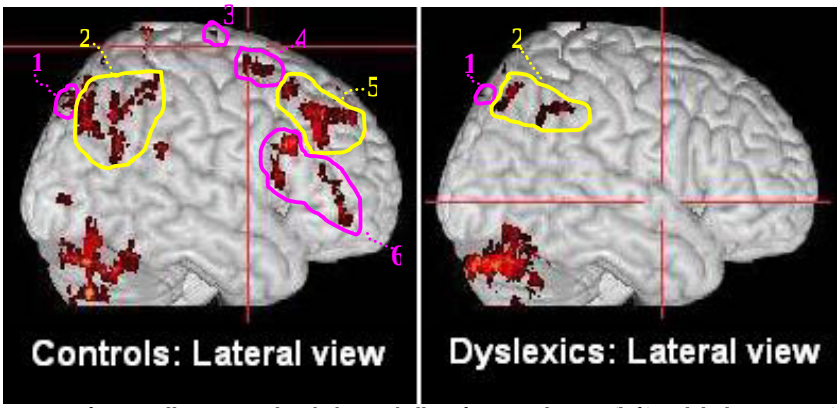

Fig.1 Group connectivity map of the regions functionally connected with the cerebellum for control group (left) and dyslexic group (right). Lateral view of the 3-d standard brain surface was chosen so that differences between dyslexics and controls could be easily observed. Illustrated maps were thresholded with the relatively large minimum cluster size set to 200 voxels. Areas of interest circled on the map include occipital cortex (1), parietal lobe (including the angular gyrus) (2), precentral gyrus (3) and superior(4), middle (5) and inferior(6) frontal gyri. There is an obvious underactivation in occipital cortex and parietal lobe in the dyslexic subjects. Controls have strong activation in precentral gyrus and superior, middle and inferior frontal gyri, whereas dyslexics have no voxels passing the threshold at all in these regions. In the deeper brain structures, i.e. insula and amygdala (not shown on the 3-d surface map), the observations were similar with dyslexics having lesser voxels than controls.

References

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