

Multimodal imaging classification of ADHD: brain functional connectivity and cortical thickness

Po-Hsiang Chan¹, Yu-Sheng Tseng¹, Chun-jung Chen¹, Teng-Yi Huang¹, and Tzu-Chao Chuang²

¹Department of Electrical Engineering, National Taiwan University of Science and Technology, Taipei, Taiwan, ²Department of Electrical Engineering, National Sun Yat-Sen University, Kaohsiung, Taiwan, R.O.C, Taipei, Taiwan

Target audience: MR researchers working on classifying groups using resting-state fMRI or cortical thickness

Purpose

This study aims to develop a classification method based on support vector machine (SVM) for attention-deficit/hyperactivity disorder (ADHD) patients. Previous researches identified significant differences in brain functional connectivity¹ (FC) and brain cortical thickness² between normal subjects and ADHD patients. In this study, we proposed to use SVM to classify subject groups based on the brain functional connectivity obtained from resting-state fMRI (rsfMRI) datasets and brain cortical thickness (CT) obtained from 3D T1-weighted MPRAGE datasets. We identified an approach to optimize classification accuracies based on parameter selections. We developed a template-based brain parcellation approach to render the whole analysis fully automatic.

Material and Methods

We used the ADHD database available to download through the ADHD-200 Consortium³. All rsfMRI and 3D T1-MPRAGE scans were performed in New York University Child Study Center. Data of 159 subjects, including 68 diagnosed as ADHD-combined and 91 typically-developing subjects. For each subject, two image sets are available: (1) rsfMRI acquired using BOLD EPI with scan parameters (TR = 2000 ms, TE = 15 ms, slice thickness = 4 mm, 33 slices, FOV=240 × 240 mm², voxel size=3 × 3 × 4 mm³, scan time = 6 min); (2) brain structure images acquired using 3D T1-weighted MPRAGE with scan parameters (TR= 2530 ms, TE=3.25 ms, 128 slices per slab, FOV = 256 mm, voxel size = 1.3×1.0×1.3 mm³). Preprocessing of rsfMRI data, including motion correction, image filtering, and normalization, were performed using SPM8. We then used the automated anatomical labeling template⁴ (AAL) to parcellate the preprocessed dataset into 90 cortical and subcortical ROIs in the cerebrum. The next procedure calculated the average of voxels in each ROI for every dynamic measurements and produced 90 time series. Finally, we generated a 90 × 90 FC matrix by correlating the 90 time series with each other. This procedure generated 4005 features [(90 × 90 – 90)/2 = 4005] for the SVM algorithm. For the T1-MPRAGE data, the voxel-based cortical thickness measurement was employed to generate the cerebral CT maps, followed by the parcellation of 78 cortical regions using AAL template. Note that the CT in each subject were normalized by its maximum, rendering all CT values in the similar range of absolute FC values (0 to 1). We then have 78 CT features for the following SVM analysis. We evaluated the performance of classifications with three combinations of these features (FC: 4005, CT: 78, FC + CT: 4083 features). Figure 1 displays the flow diagram of SVM analysis. First, we used all features for a linear SVM training. The initial SVM generated an “hyperplane” to separate two types of the subjects. A “weight” of each feature was obtained from the hyperplane. We then sorted the features according to their absolute weights and selected an amount of features with larger absolute-weights for a second SVM analysis. Of all the 159 subjects, we randomly selected 100 subjects as training datasets and the remaining 59 subjects as challenge datasets to evaluate the accuracy of SVM-based classifications. The classification accuracy was estimated by the receiver operating characteristic (ROC) analysis. For each selected amount of features, we repeatedly performed random selection procedure for 300 times to obtain an average accuracy for each SVM training scheme.

Results

Figure 2 plots the average classification accuracies against the number of selected features using 3 datasets (FC, CT, FC + CT). Selecting features according to their sorted weights, the maxima of the average accuracies are FC: 99.3 ± 6.4 %, CT: 67.5 ± 6.3 %, FC + CT: 99.3 ± 6.3 %. The numbers of selected features corresponding to the maximum accuracies are FC: 471, CT: 18, FC + CT: 524. Notice that the result is obtained using the all 159 subjects for the feature selection procedure. When we selected the features according to an initial SVM training using the 100 selected images of the training set, the maxima of the average accuracies reduced to FC: 59.1% ± 5.8 %, CT: 57.2% ± 6.3 % and FC + CT: 60.4% ± 5.8 %. Figure 3 displays maps with a color scale representing the selection counts of AAL regions. The maximal accuracies using FC and FC + CT as SVM features are significantly higher (P < 0.01) than obtained using CT as SVM features. The classification accuracies obtained using FC and FC + CT exhibit no significant difference.

Discussion

In this study, we aimed to develop an approach to classify ADHD subject groups according to rsfMRI and structural T1WI. Using the selected features, the maximal accuracies increased to 68 – 99 %. The results supported that the feature selection according to absolute weights of a pre-trained SVM hyperplane is an efficient method to increase the classification accuracies. When we modified the feature-selection procedure close to real world situations (using only the training dataset for the feature selection), the classification accuracies reduced to approximately 60%. Nonetheless, the accuracy was anticipated to be increased as the training dataset grows because the selected features could be linked to ADHD-related network. For example, in Fig.3, we found prominently large selection counts in a structure pairs (indicated by white arrows) in AAL regions (Frontal_Inf_Tri_R and Frontal_Inf_Tri_L). It has been reported that functional abnormality in right inferior frontal cortex may be a specific neurofunctional biomarker of ADHD⁵. A limitation of this study is that only ADHD-combined subjects were included. The remaining two subtypes of ADHD (i.e. hyperactive and inattentive) were not analyzed. Adding subjects diagnosed as the remaining subtypes merits further investigations.

References

- [1] Castellanos FX et al., Biol Psychiatry. 2008 Feb 1;63(3):332-7
- [2] Almeida LG et al, J Psychiatr Res. 2010 Dec;44(16):1214-23
- [3] The ADHD-200 Consortium, Front Syst Neurosci. 2012; 6:62
- [4] Tzourio-Mazoyer N, et al. ,Neuroimage. 2002 Jan;15(1):273-89.
- [5] Rubia K et al. Hum Brain Mapp. 2010 Feb;31(2):287-99

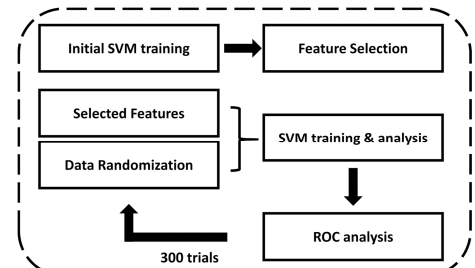


Figure 1 The flow diagram of SVM training and the procedures of feature selection and accuracy evaluation.

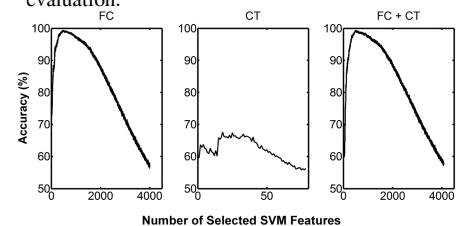


Figure 2 The classification accuracies using FC, CT, and FC + CT feature sets and different number of selected SVM features.

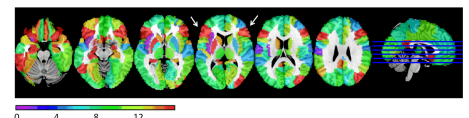


Figure 3 The feature-selection counts of AAL regions obtained using the FC dataset.