Automatic Diagnosis of Spasmodic Dysphonia with Structural MRI and Machine Learning

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Introduction

Spasmodic dysphonia (SD) is a neurologic disorder of unknown causes and pathophysiology. SD is characterized by involuntary spasms in the laryngeal muscles that are specific to speech production. Highly variable symptomatology and the absence of objective diagnostic criteria make the diagnosis of SD a challenging task, which leads to misdiagnosis and delayed treatment. As neuroimaging studies described SD-specific brain abnormalities contributing to its pathophysiology [1,2], we used a series of machine-learning algorithms to identify automatic objective diagnostic markers of SD based on structural abnormalities.

Methods

Whole-brain T1-weighted MRI images of 52 SD patients (age = 53.9±9.5 years, 33 females) and 52 age/gender-matched healthy controls (age = 52.5±10.0 years, 33 females) were acquired on a 3T scanner. In each subject, FreeSurfer was used to extract cortical thickness (CT) and SPM12 CAT toolbox was used to extract gray matter volume (GMV). The performance of four classifiers was examined: (1) linear discriminant analysis (LDA), (2) linear support vector machines (SVM) with regularization strength C=100, (3) neural network (NN) with one hidden layer of 12 neurons, logistic activation, and Adam optimizer, and (4) an ensemble of convolution neural networks (CNNs).

For LDA, SVM and NN feature selection, we performed a separate meta-analysis (GingerALE [8]) of previous imaging studies that applied voxel-based morphometry and CT analyses in SD patients and healthy controls [2-7]. Meta-analysis found six clusters at the voxel-wise significance level of p=0.001 and minimum cluster volume of 200 mm^3. Using these clusters as a mask, the average CT and GMV measures were extracted, resulting in a total of 12 structural features per subject. The performance of LDA, SVM and NN was computed using a 13-fold cross-validation.

For CNN, the whole-brain GMV and CT images were subsampled by a factor of 2 and split into training (78 subjects) and test (26 subjects) sets. Data were augmented by extracting volumetric patches of 25x25x25 from each image. We trained two CNNs (Figure 1) with Keras, one with CT images and one with GMV images. The outputs of the two CNNs were then averaged across patches associated to the same subject and across CNNs to obtain the ensemble prediction.

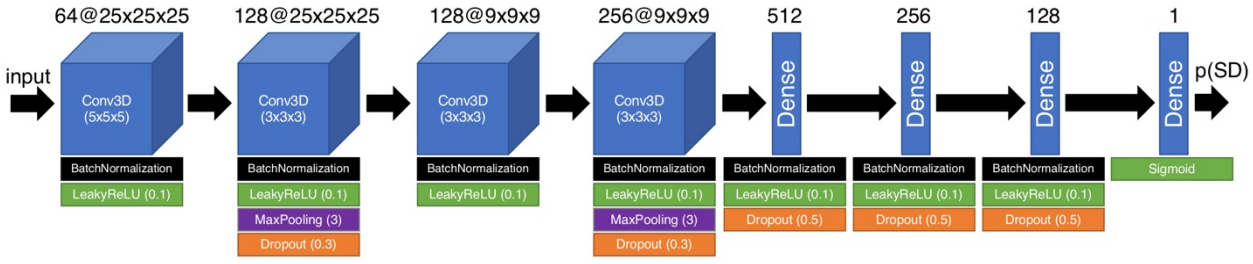

Figure 1. Architecture of the CNN.

Results

Meta-analysis of VBM and CT literature in SD patients vs. healthy controls found significant structural abnormalities mainly present in the left hemisphere, including inferior frontal gyrus (#2), putamen (#3), insular cortex (#4), and inferior temporal gyrus (#5) (Figure 2). The clusters in the premotor cortex (#1 and #6) were found bilaterally in both hemispheres.
Based on these data, the combination of CT and GMV features resulted in average cross-validation AUC of 72.6% for LDA, 70.2% for SVM, 66.4% for NN, and 53.3% for CNN.

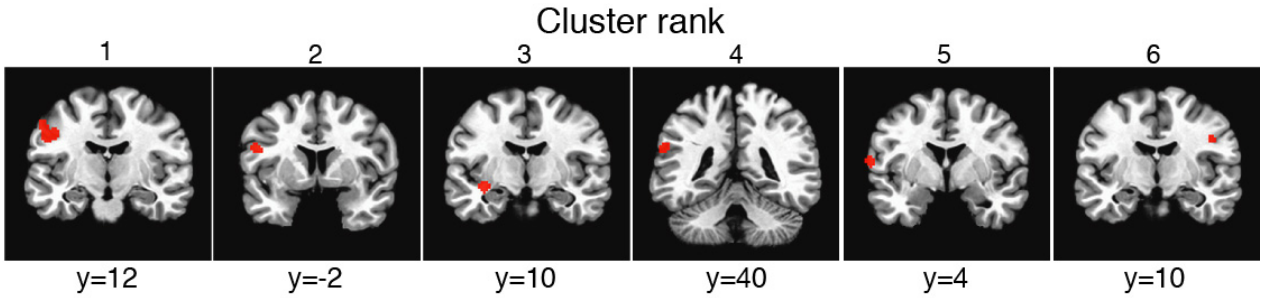

Figure 2. Coronal slices in standard Talairach-Tournoux space with clusters of significant abnormalities between SD patients and healthy controls identified by meta-analysis.

Conclusions

Best-performing machine-learning classifiers based on disorder-specific brain abnormalities correctly diagnosed SD in approximately two out of three patients, showing their translational potential compared to clinical evaluation of dystonic symptoms [9]. LDA outperformed other algorithms and showed superior performance to that previously reported with resting-state fMRI [1]. This suggests that a combination of supervised feature selection and LDA is a promising avenue for the development of objective diagnostic tools for SD. CNN suffered from underfitting due to the small dataset. Overall, structural brain abnormalities identified in SD could be used as imaging markers to build objective diagnostic tools. Future work should be focused on integrating features extracted from other imaging modalities (e.g., fMRI) in the classification pipeline.

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