

BrainPrint: Computable hypervolume Phenotypes

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Abstract

Machine learning methods applied to neuroimages for disease diagnosis or prevention have been extensively researched in recent years. Among them, many have focused on Alzheimer's Disease, from which we witnessed the vital roles of convolutional neural network in computer assisted intervention for brain disease diagnosis. Also, there are some works on predicting other phenotypes, such as gender, age and Brain Lesion. However, less work has been done on predicting phenotypes that intuitively irrelevant or less relevant to brain volume, such as Autism spectrum disorder(ASD), intelligence quotient (IQ), etc. We proposed a 7 layers Convolutional Neural Network (ChpCNN) architecture and predict ASD on fMRIs, on which we achieved overall 64% and Autism disease group 69% accuracy. Further, by using ensemble method, both the overall accuracy and sensitivity improved ~1%. We compared the performances with that of multiple machine learning methods and VGG16. Also, compared it with various ML methods and LeNet on 2D axial slices. Ensemble ChpCNN outperforms all benchmarks. Finally, we applied 3D wavelet transform and denoise wavelet coefficients to obtain 3D sparse brain expressions, which we named as BrainPrint. Comparable performances were achieved for BrainPrint.

Future, we hope to understand more from the BrainPrint. Our ambition is to pre-train multiple models for various phenotypes so that later researches or different sites based computer intervention diagnosis can use the pre-trained model directly or by transfer learning based on small scale additional data points.

Key word: computable phenotype, convolutional neural network, fMRI, Autism, wavelet

Introduction

A growing number of machine learning studies based on neuroimaging data aim to both help brain fMRI classification, automatic volume segmentation, and understand the mechanics of diseases. Recently, many publications focus on prediction of Alzheimer's Disease[10,9,5,1,3]. To the best of our knowledge, Payan[10] first studied Alzheimer's disease with 3D CNN and compared the performance with that of 2D experiments. Later, Multiclass diagnosis of Alzheimer's Disease was performed on the multi-modal neuroimaging features. 70%-85% accuracy were achieved[9]. Recently, functional MRI Alzheimer's Disease data was fed to CNN, by which more than 95% accuracy was achieved for binary classification. Other phenotypes studies include Automated Pulmonary Nodule Detection[4], Autism spectrum disorder risk for infants[2], brain age[11], etc.

We are inspired by the research of Kang[8], in which wavelet transform involved, work of Korolev[3], in which they proposed a 10 layers' 3D CNN: VoxCNN to predict Alzheimer's Disease, and deep ensemble learning of sparse regression models proposed by Suk[6].

Table 1. Performance of NC group and ASD group(NC|ASD). Trained on 2D 256x256 axial slices.
The trivial(NULL) random accuracy is 0.519|0.481.

SVM	Random Forest	KNN	LeNet
0.546 0.504	0.5553 0.540	0.535 0.479	0.584 0.511

Table 2. Training on 3D 64x64x64 cube.

SVM	RF	KNN	VGG16 ^{[7]*}	ChpCNN	ENS-ChpCNN
0.632 0.545	0.630 0.540	0.549 0.555	0.674 0.561	0.691 0.597	0.704 0.612

* 3D version VGG16. Due to computing issue, it was trained on 32x32x32 cube. It's an unfair to compare it with other 3D cases.

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CNN trainings were applied on TensorFlow and MXNet, with Python2.7 and R3.4.

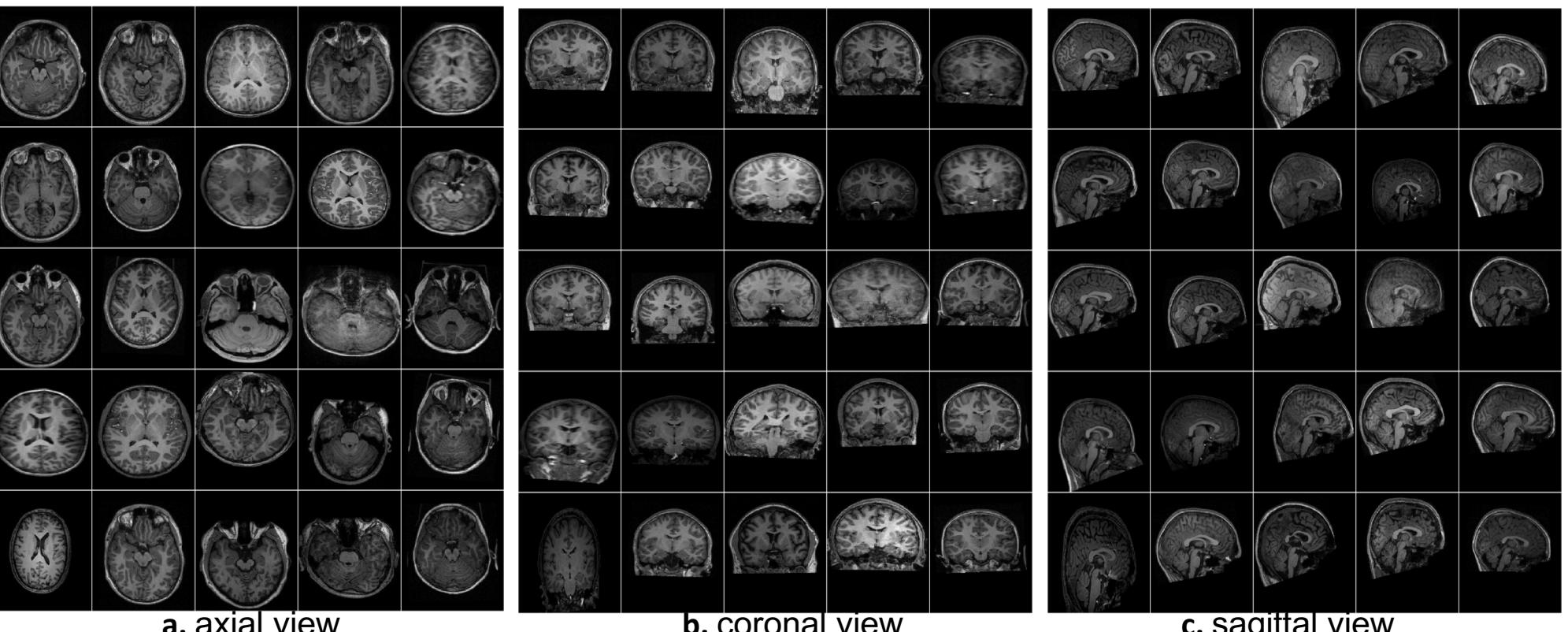


Figure 1. Initial fMRIs

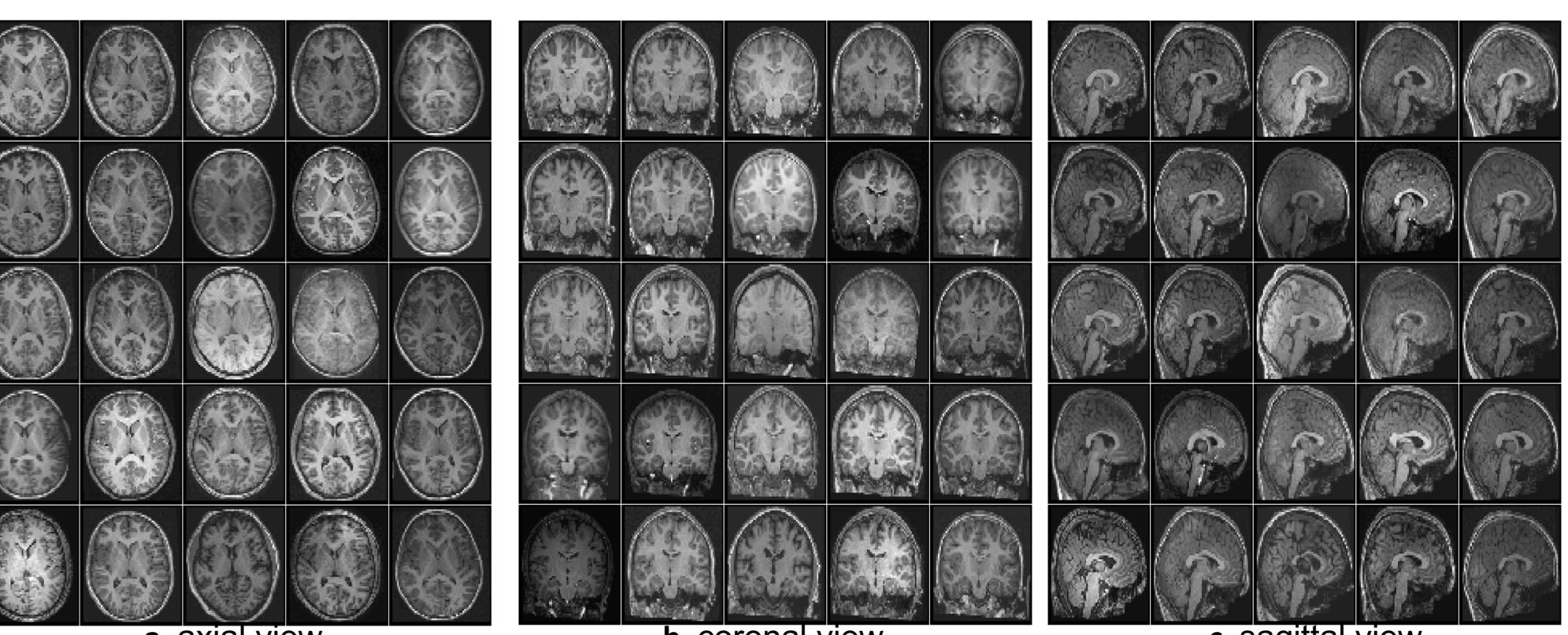


Figure 2. Input data points

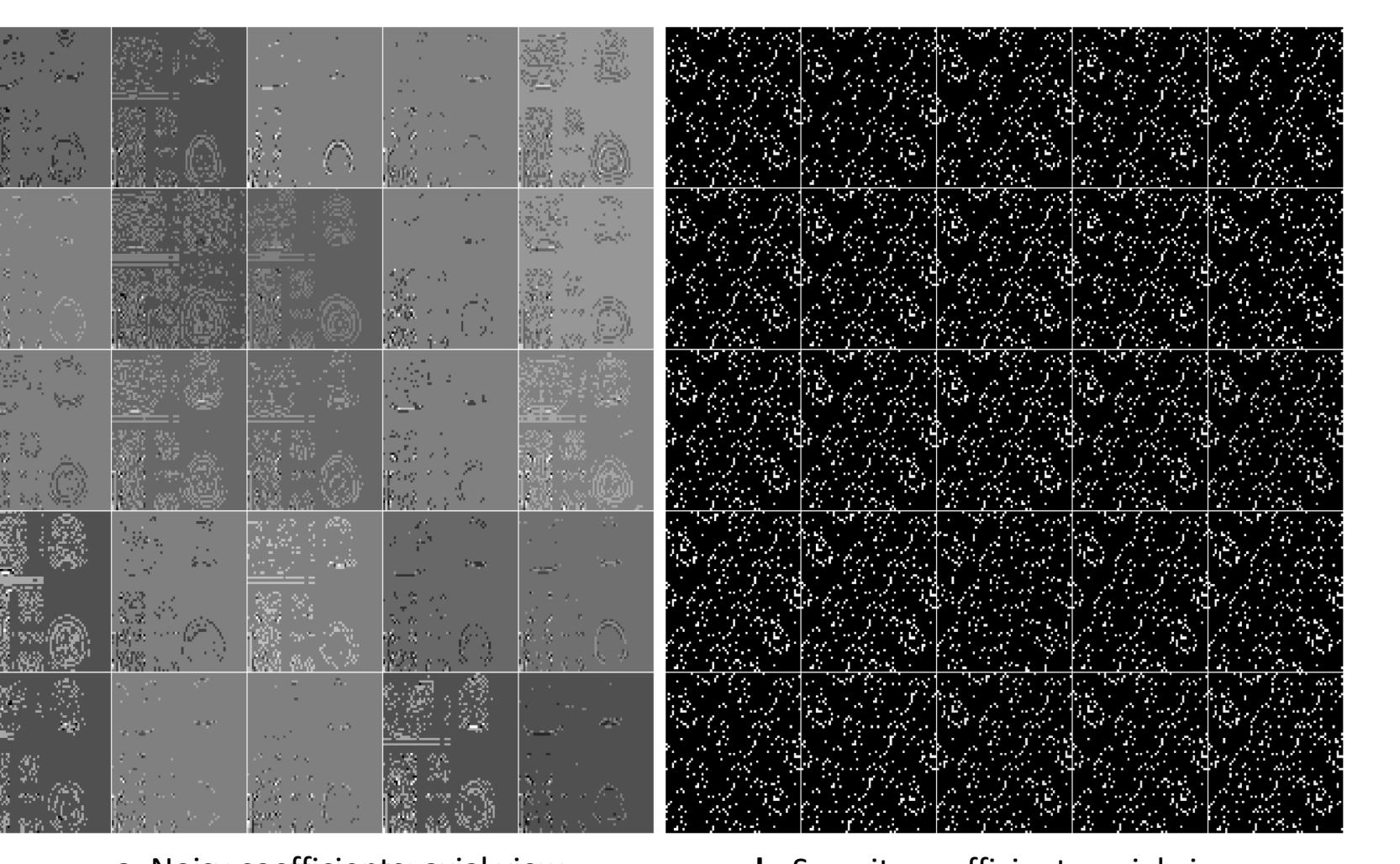


Figure 3. Daubechies Wavelet coefficients

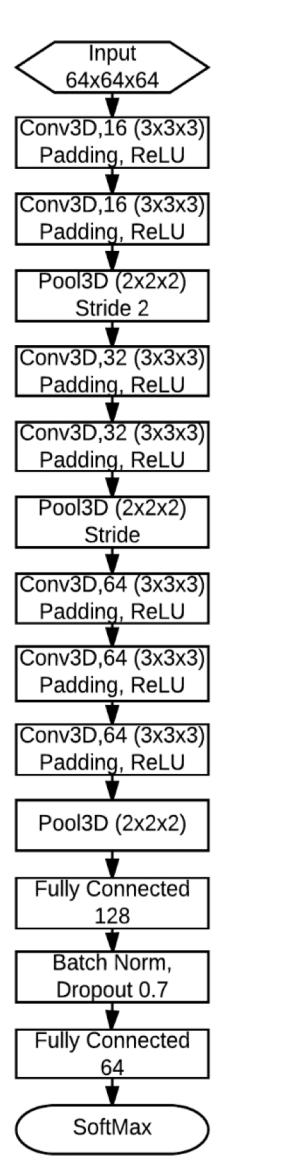


Figure 4.
ChpCNN topology

Methods and Results

Data

The Autism Brain Imaging Data Exchange(ABIDE) includes > 1,000 3D functional magnetic resonance imaging (fMRI) anatomical and phenotypic datasets. This total number of samples we used is 1098, including 528 from individuals with Autism spectrum disorder(ASD) and 570 from Normal Controls(NC). The percent of ASD is 48.1%. The age distributes from 7 to 64 years, where the median is 14.7 across all examples. As ABIDE collected from 17 international sites, the dimensions of fMRIs vary among samples. Some typical patterns include (256,256,124), (128,256,256), (160,240,256), (256,256,160), etc.

Images processing

Processings include registration, normalization, cutting margin/padding and down sample interpolation. The 25 examples of initial datasets are shown in **Figure 1**. Three sub figures display views form 3 orthogonal directions. Preprocessing is required because of various size, unaligned, computing issue, etc. Specifically, we need the aligned and equal length features(pixels) as input. **Figure 1.a** for example, those horizontal slices were drawn from middle layer. Unfortunately, they are not the same layer in human beings' brain, which will invalid some machine learning methods such as SVM, Random Forest as they require aligned features. First, affine 3D global registrations were performed to align fMRIs so that they all had the same dimensions of 256x256x160. Then manually cut background margin or added padding to registration images to improve computing efficiency, while preserve marginal information, after intensity normalization. Finally, perform down sample the images to 64x64x64 cubes by Nearest Neighbors interpolation. **Figure 2.** displays the same 25 examples after processing procedures.

Machine learning Autism diagnosis

The sensitivity and specificity of ChpCNN and ensemble methods are in **Table 2**. Topology of ChpCNN is shown in **Figure 4**. It consists of 7 convolutional layers, followed by 2 fully connected layers. Ensemble ChpCNN(Ens-Chp) combines 5 independent optimized ChpCNN models, trained for arbitrary fixed 800 examples initial with various hyper parameters. We applied SVM, Random Forest, KNN and LeNet, a prevalence two layers CNN architecture, to axial slices(examples in **Figure 2.a**) as benchmarks. **Table 1** shows the performances. 5 folds cross validation was performed. For 3D case, we used simple machine learning algorithms and 3D version VGG16 as comparison.

BrainPrint

Finally, we extracted sparse expression of images by 3D Daubechies wavelet transform. The axial layer noisy coefficients are shown in **Figure 3.a**, exactly corresponding to that in **Figure 1.a** and **Figure 2.a**. Then by setting thresholds to filter out noisy coefficients, we obtained 3D sparse expression, which we called **BrainPrint**. The sparsity of BrainPrint is ~91%. We achieved comparable performances on 3D BrainPrints to that of processed data(examples in **Figure 2**) using machine learning methods and ChpCNN.

Other Prediction

We also tried to predict IQ, Age. However, no acceptable results are obtained. The standard error is 6.6 and 13.7 for age and IQ, while the standard deviation is 8.2 and 14.0, respectively.

Discussion

3D outperformed their 2D counterparts in fundamental improvement, though the lengths shrink from 256 to 64. Both simple CNN architecture and deep learning topology outperforms SVM, RF and KNN, as benchmarks. Using Ensemble methods, we usual get 0.5% to 1% improvement of accuracy and sensitivity. Similar performances are achieved for BrainPrints. It might not be proper to predict IQ and age for unhealthy sample. Also, brain age prediction may be more difficult to teenagers than to elders.

For future work, first, we plan to highly compress BrainPrint to generate highly sparse wavelet coefficients and hope to obtain more fancy BrainPrint. In that way, it's not necessary to down sample the image to size of 64x64x64. We can use more informative cubes such as 128x128x128. Further, Hyper volume(4D) neuroimaging is attractive to be studied. Finally, we will focus on construction of pre-trained models for various phenotypes, such as diagnosis, age, IQ, etc.

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