Classification of schizophrenia and normal controls using 3D convolutional neural network and outcome visualization

Kanghan Oh, *et al*. (2019).
Schizophrenia research, 212, p186-195.

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Introduction

Schizophrenia

Symptoms:

Delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior, negative symptoms

Diagnosis:

Presence of each one of symptoms for a significant portion of time during a 1-month period

Treatment:

Antipsychotic medication and psychotherapy

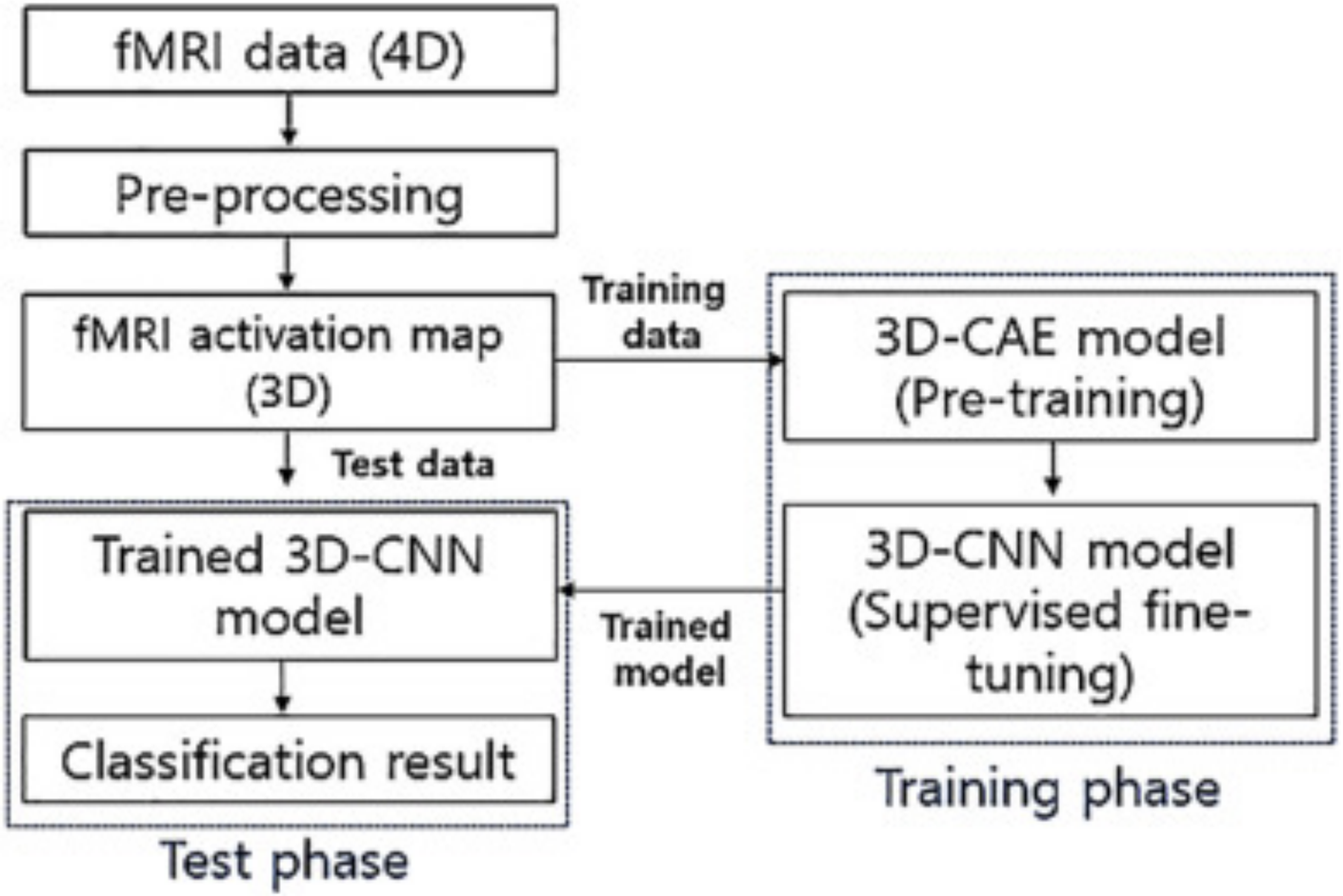
Primary aim

1. Investigating whether self-proposed model proposed higher accuracy compared to SVM

2. Using visualization to make model explainable

Methods

Overview


fMRI data (4D)
Pre-processing
fMRI activation map (3D)
Training data
3D-CAE model (Pre-training)
Test data
3D-CNN model (Supervised fine-tuning)
Trained 3D-CNN model
Trained model
Classification result
Training phase
Test phase

Participants

Patient group:

Number = 103

Age = 18~59

DSM-IV-TR criteria for schizophrenia spectrum disorders checked

Healthy control group:

Number = 41

Age- and sex-matched to the patient group

Participants

Variable	Schizophrenia spectrum disorder (*N* = 103)	Normal control (*N* = 41)	P
Age (years)	32.46 ± 9.21	33.98 ± 8.53	0.470
Education (years)	13.59 ± 2.76	16.22 ± 2.57	0.727
Sex (male/female)	57/46	24/17	0.727
Age of onset (years)	27.20 ± 9.00	–	–
Duration of illness (months)	56.28 ± 50.96	–	–
PANSS-total	49.93 ± 18.98	–	–
PANSS-positive	13.09 ± 6.70	–	–
PANSS-negative	12.09 ± 5.48	–	–
PANSS-general	24.76 ± 9.10	–	–

Values are presented as mean ± standard deviation or number.

PANSS, Positive and Negative Syndrome Scale.

Image acquisition

fMRI data:

Scanner: 3T Siemens Verio scanner with 45mT/m gradients and a 12-channel standard quadrature head coil

Images: Axial 1.0-mm-thick T1-weighted images

Parameters:

TR=1.9s, TE=2.5ms,

field of view=240mm, acquisition matrix=256x246,

Flip angle=9degree

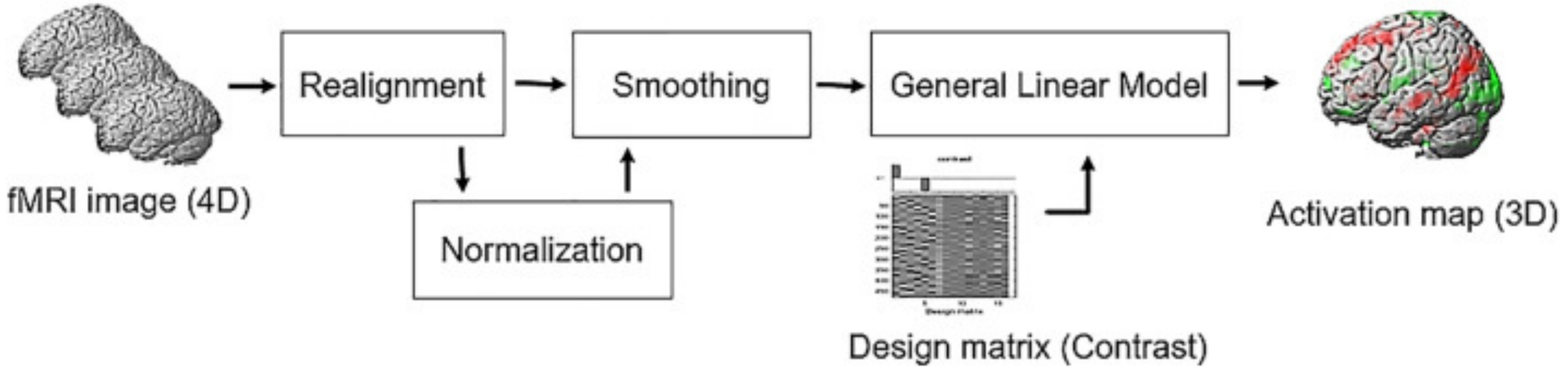
Preprocessing

Software: SPM8

1. T1-weighted images were normalized to the standard T1 template

2. Normalized images were smoothed with an 8-mm full-width-at-half maximum Gaussian filter

3. 3D activation map was constructed based on the contrast images with General Linear Model(GLM)



Input data for DL and SMV model

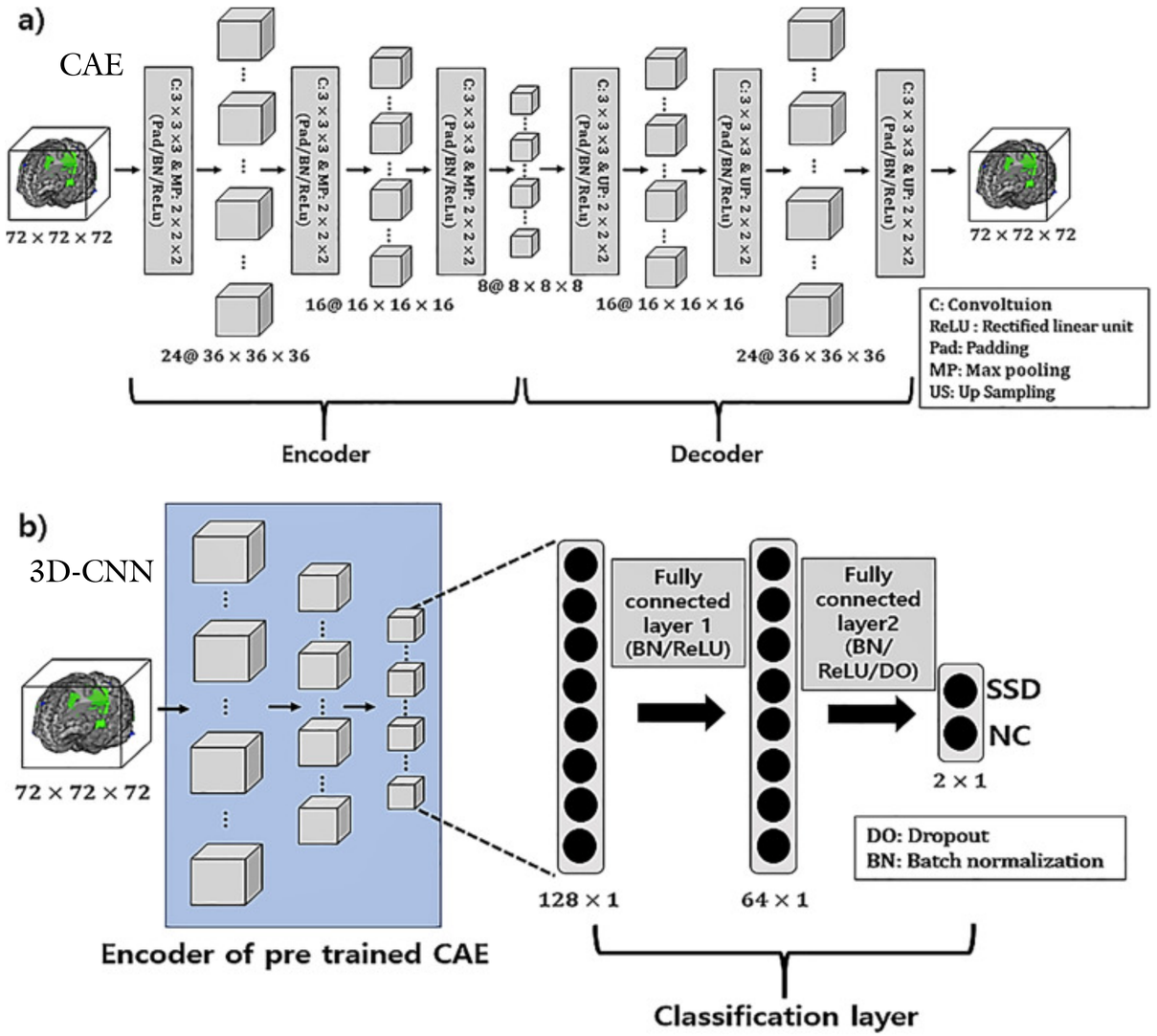
For the SVM applications, we conducted experiments in three ways:

a) directly fed the whole-brain betas to SVM without any preprocessing;

b) used 40 features extracted by applying principal component analysis (PCA) to the whole-brain voxels;

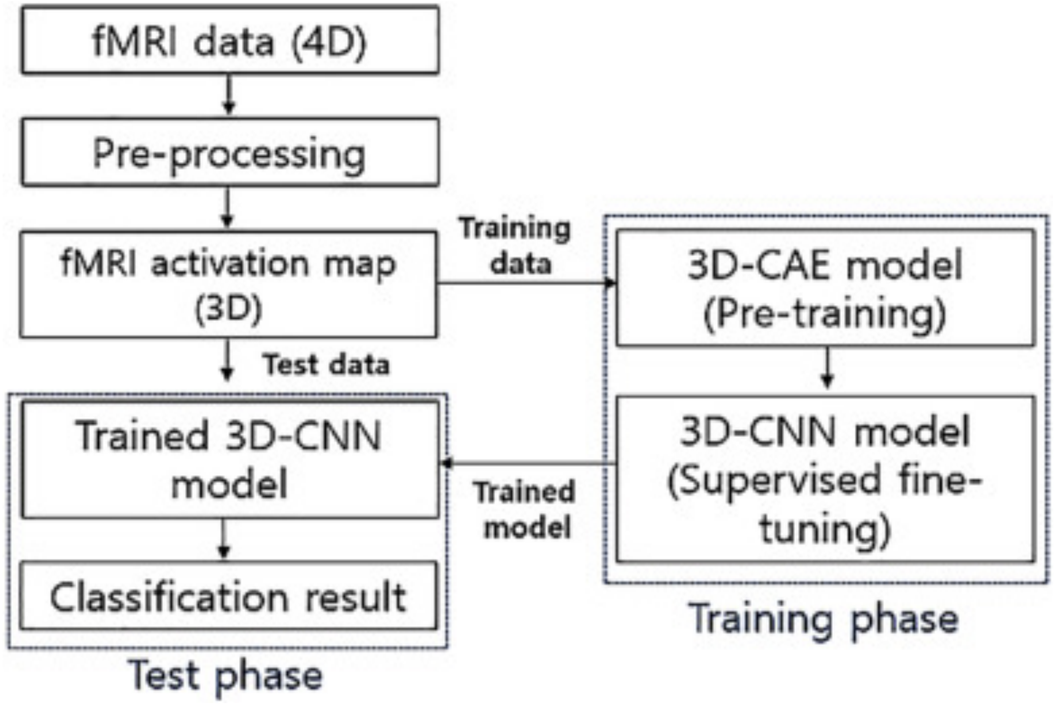
c) used the β-values of five AAL regions chosen based on the significant differences of contrast between patients and controls (uncorrected $p < 0.01$, cluster size >50)

DL model selection



This model was selected by comparing classification performances of 3D-CAE based CNN with or without regularization techniques to those of 3D CNN with or without regularization techniques.

Evaluation



Pretraining 3D-CAE: 62 patients

Evaluation: 41 patients + 41 controls

10-fold cross-validation was performed.

Validation process was repeated 100 times independently. (3D-CNN)

Bayesian optimization with 500 iterations on kernel size and box constraint was applied. (SVM)

ROC curves were plotted to compare.

Visualization

1. Visualizing the feature maps in each layer of the learned neural network

2. Visualizing for explanation on why the neural network reached the decisions—class saliency visualization (CSV) method

CSV method:

class saliency map $M_{i,j,k} = |\omega_{h(i,j,k)}| = |\frac{\partial f_c}{\partial I_{i,j,k}}|$

Results

Model selection

Number of epochs	Accuracy	Sensitivity	Specificity	PPV	NPV
100	82.99%	86.21%	78.87%	80.65%	85.61%
500	83.51%	86.83%	80.41%	80.54%	86.73%
1000	84.43%	88.42%	80.06%	81.14%	88.10%
1500	84.01%	87.59%	80.67%	80.86%	87.45%

CAE, convolutional auto-encoder; NPV, negative predictive values; PPV, positive predictive values.

Number of neurons	FC1: 32 FC2: 16	FC1: 64 FC2: 32	FC1:128 FC2:64	FC1:256 FC2:128
#prams	202 K	390 K	770 K	1542 K
Accuracy	83.80%	83.94%	84.43%	84.17%

FC, fully connected; #prams, number of parameters.

Model selection

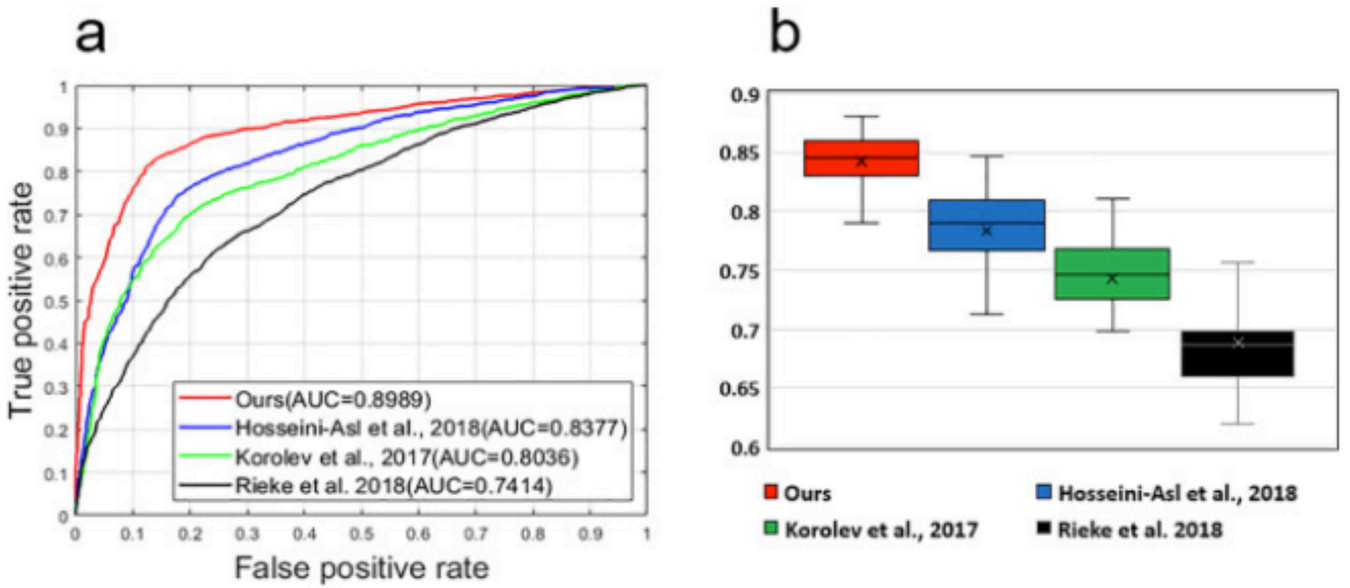
Network model	Accuracy	Sensitivity	Specificity	PPV	NPV
3D-CNN (training from scratch)	60.56%	60.55%	60.57%	60.78%	60.34%
3D-CNN (training from scratch with BN)	68.92%	70.94%	66.98%	67.18%	70.77%
3D-CNN (training from scratch with DO)	66.40%	64.34%	68.44%	66.92%	65.90%
3D-CNN (training from scratch with BN + DO)	67.94%	76.15%	61.28%	61.48%	75.99%
3D-CAE + CNN	76.16%	77.40%	74.92%	75.43%	76.91%
3D-CAE + CNN with BN	81.22%	83.36%	79.17%	79.32%	83.23%
3D-CAE + CNN with DO	78.15%	81.55%	75.00%	75.16%	81.41%
3D-CAE + CNN with BN & DO	84.43%	88.42%	80.06%	81.14%	88.10%

BN, batch normalization; CAE, convolutional auto-encoder; CNN, convolutional neural network; DO, dropout; NPV, negative predictive values; PPV, positive predictive values.

Classification

Network model	Accuracy	Sensitivity	Specificity	PPV	NPV
Korolev et al., 2017	74.85%	77.61%	72.35%	71.79%	78.08%
Rieke et al., 2018	68.30%	71.09%	65.59%	66.06%	70.74%
Hosseini-Asl et al., 2018	78.04%	81.34%	74.92%	75.43%	80.91%
Proposed model	84.43%	88.42%	80.06%	81.14%	88.10%

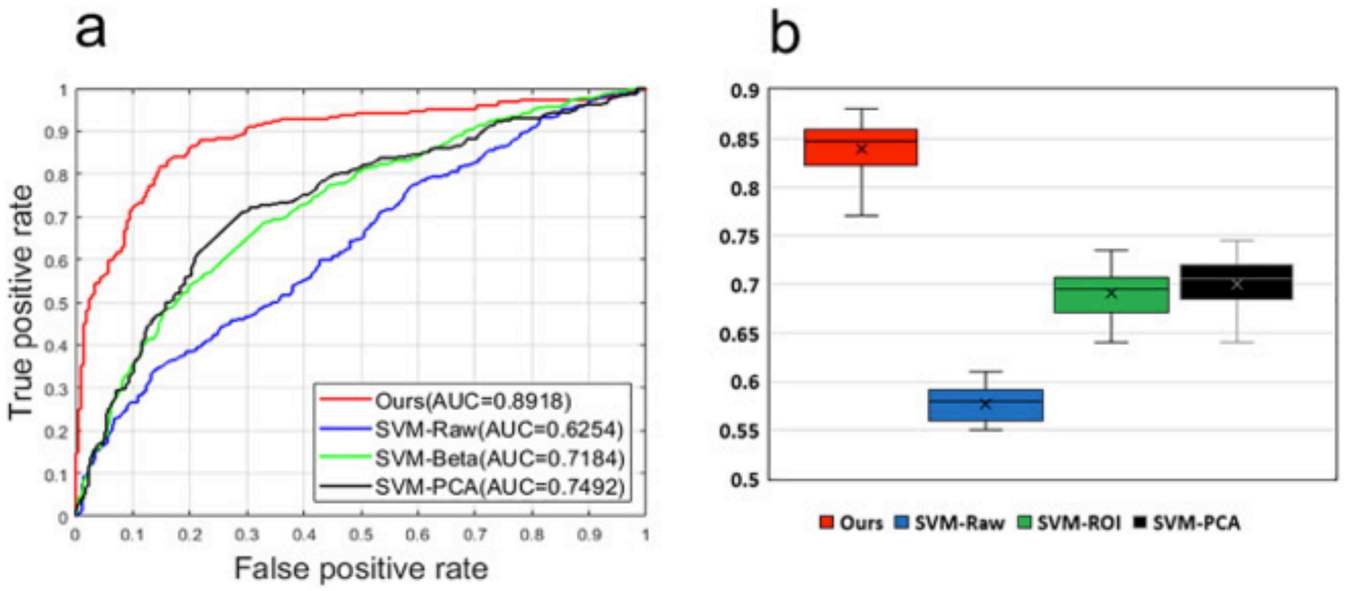
NPV, negative predictive values; PPV, positive predictive values.



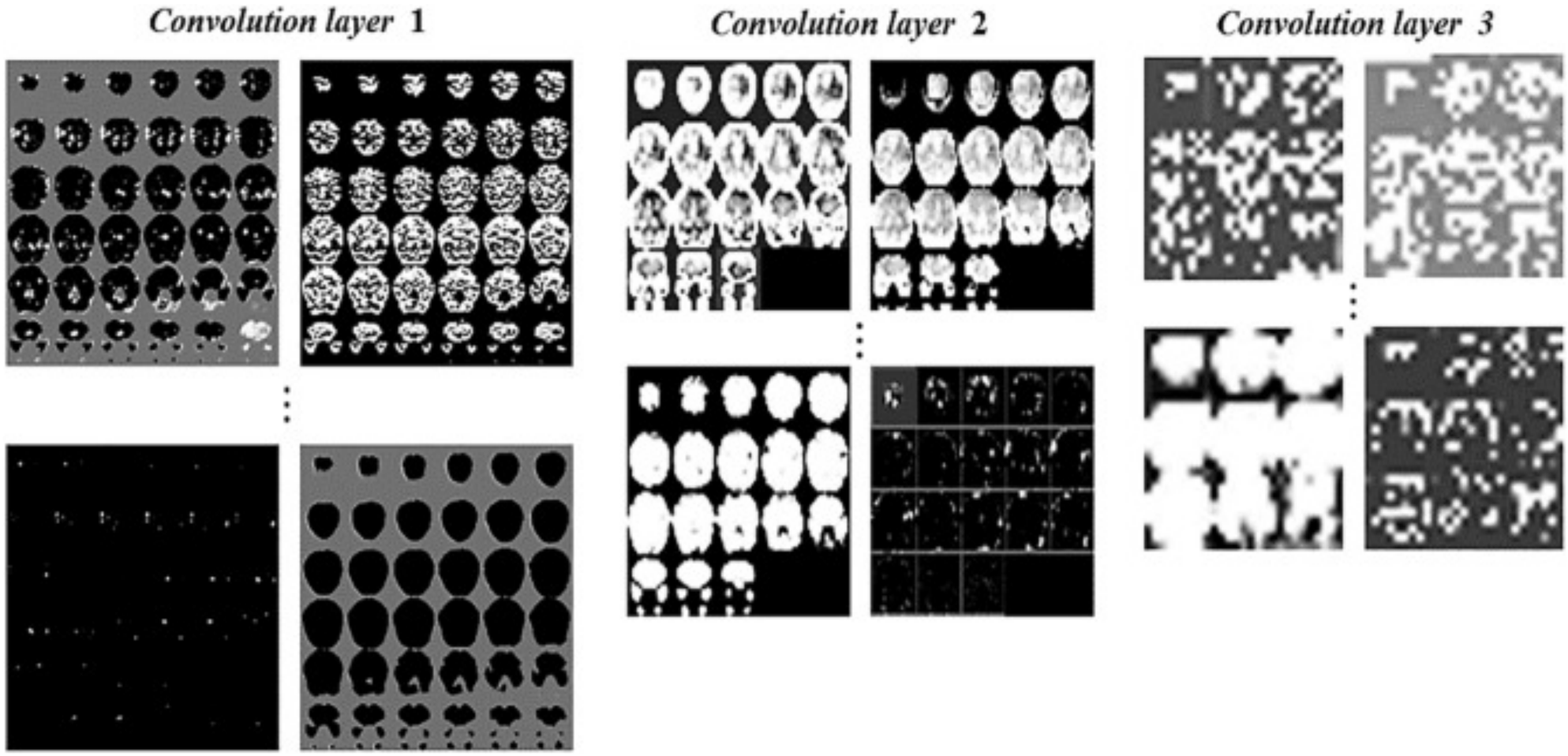
Classification

Network model	Accuracy	Sensitivity	Specificity	PPV	NPV
SVM-raw	57.32%	68.29%	46.34%	56.00%	59.30%
SVM-beta	67.07%	73.17%	60.98%	65.22%	69.44%
SVM-PCA	70.73%	78.05%	63.41%	68.09%	74.28%
Proposed model	84.15%	87.80%	80.49%	81.82%	86.84%

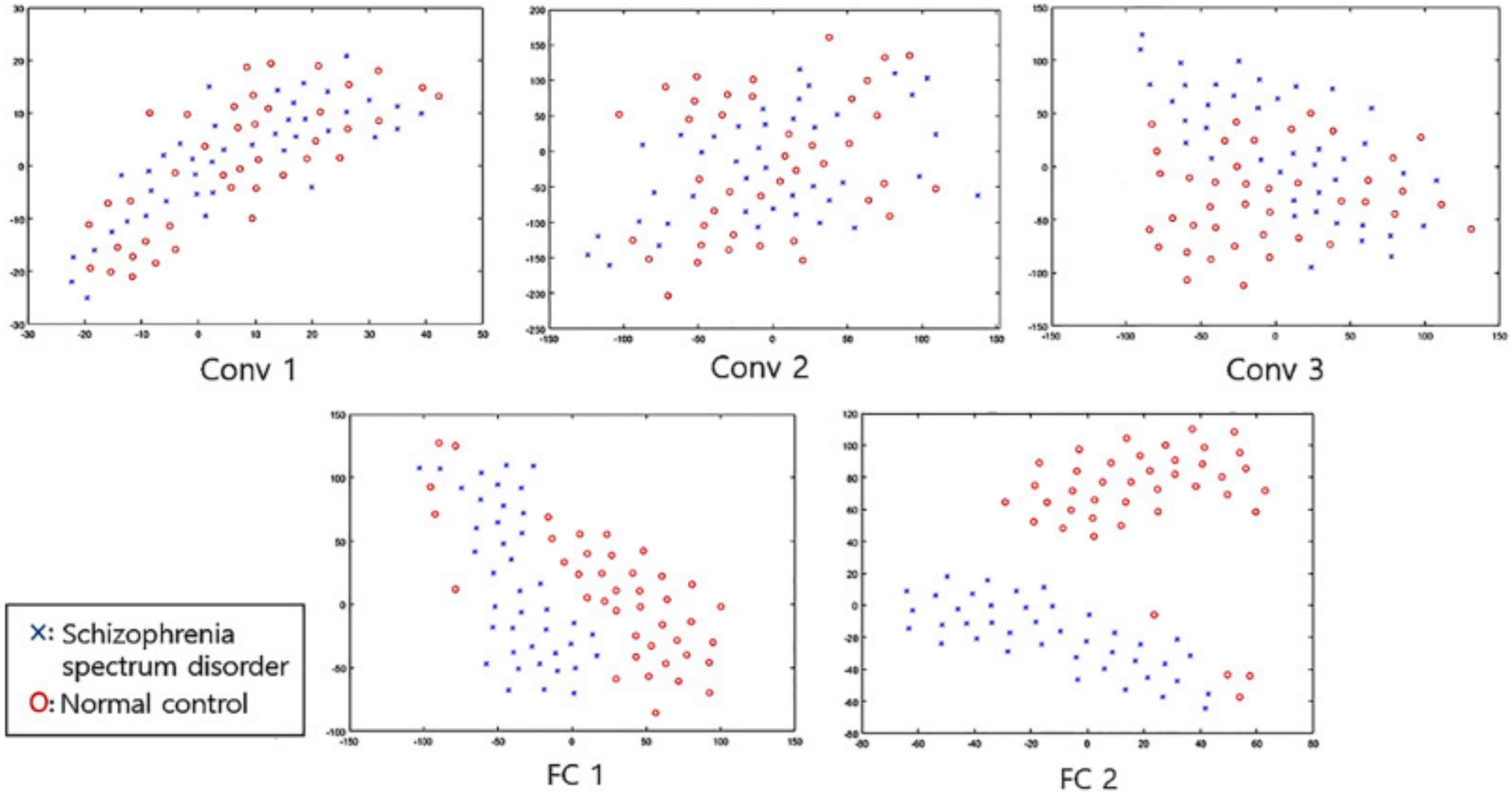
NPV, negative predictive values; PPV, positive predictive values.



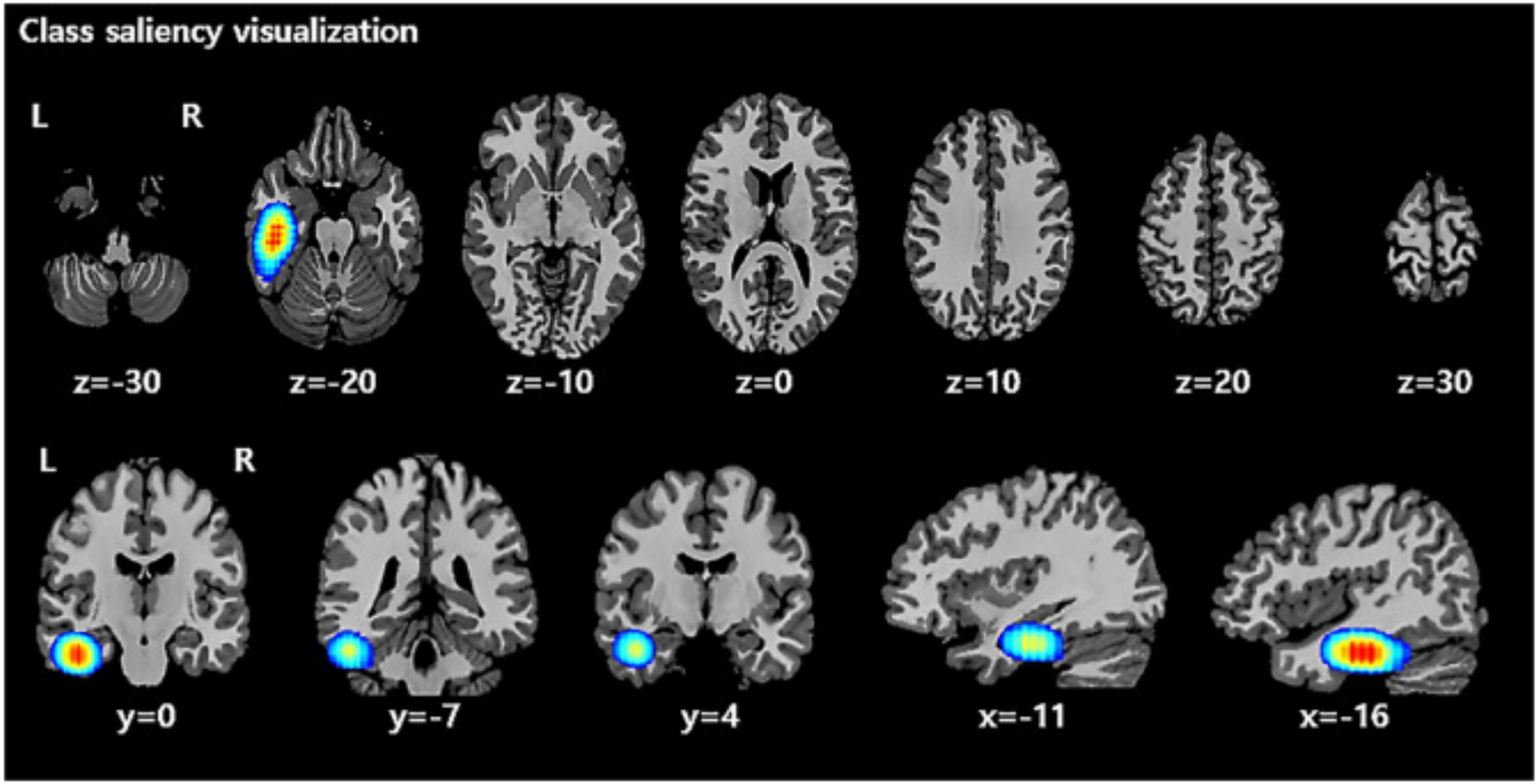
Visualization(feature map)



Visualization(t-SNE)



Visualization(CSV)



Discussion