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Resting state fMRI and connectivity analysis classified autism and control with high accuracy

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Introduction

➢ Autism spectrum disorder (ASD) is characterized by impaired development of social interaction and communication skills and a restricted repertoire of activities and interests. Although the neural and genetic underpinnings of ASD have been extensively investigated, the etiology of the disorder has remained elusive, and clinical diagnosis continues to rely on symptom-based criteria. Functional magnetic resonance imaging (fMRI) of the brain is a powerful tool for exploring biomarkers of psychiatric and developmental disorders. In the present study, resting state (rs-) fMRI and a neural network algorithm were used to classify a large sample of patients with ASD and control subjects

Materials

➢ Rs-fMRI data from subjects with ASD and typical development (CTL) was downloaded from the multi-center research project database in U.S. (Autism Brain Image Data Exchange, ABIDE, http:// fcon_1000. projects.nitrc.org/indi/abide/index.html, Table 1)

➢ ABIDE provides rs-fMRI datasets of ASD and typical controls for the purpose of data sharing in the scientific community. In accordance with guidelines and protocols, all datasets are anonymous, with no protected health information included.

➢ The data used in the present study were obtained from 12 institutes (see Notes).

➢ The diagnosis of ASD was made by using ADI-R and ADOS in all institutes except one.

➢ In the present study, only subjects under 20 years of age were used as participants. (6-19 years old)

Methods

➢ The subject's brain activity was measured during resting condition by using 3 Tesla MRI scanner for approximately six minutes. (Fig. 1)

➢ Correlation matrices of 90 distinct regions computed from rs-fMRI time-series data were entered into a probabilistic neural network (PNN) for classification. (Fig. 2)

➢ A leave-one-out cross-validation procedure was used to compute the sensitivity, specificity, and accuracy.

➢ The effects of several confounding factors on accuracy data were investigated.

➢ Finally, the participants with ASD who were classified as CTL were

Table 1: Demographic data of the subjects

	ASD	CTL	p-value
Number of subjects	312	328	N.A.
Mean age	13.2 (3.1)	12.9 (3.0)	0.32
Male (%)	87.5	81.4	0.03
Rt handedness (%)	84.3	91.8	0.003
Mean full scale IQ	103 (17)	110 (13)	0.001

Table 2: Prediction accuracy

Sensitivity	91.9%
Specificity	86.9%
Accuracy	89.4%
PPV	86.9%
NPV	91.9%

Fig. 1: Workflow of resting state fMRI data analysis

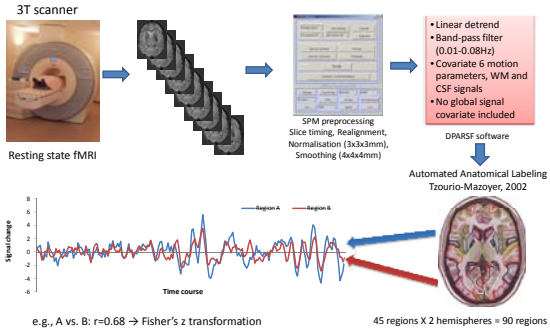


Fig. 2: 90 × 90 correlation matrices

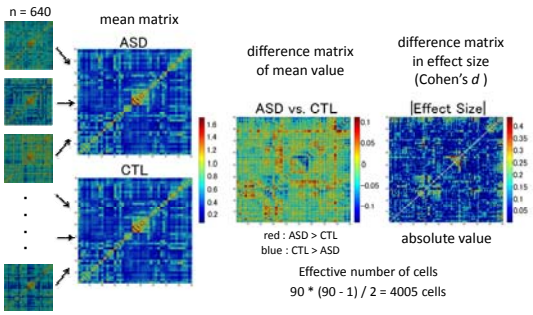


Fig. 3: Best prediction matrix |ES| > 0.16

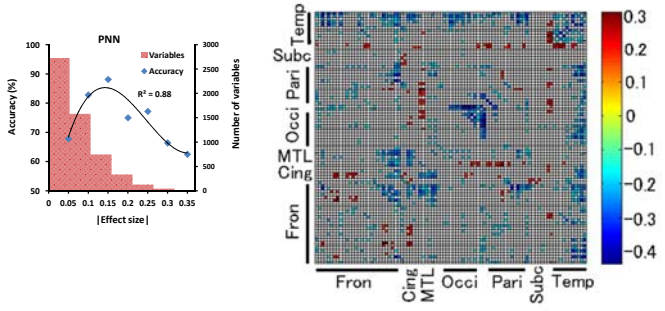


Fig. 4: Effects of confounding factors on accuracy

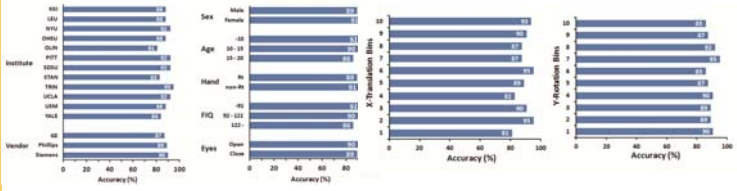
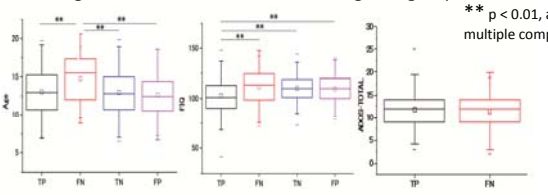


Fig. 5: Characteristics of the false-negative group



Results

➢ PNN algorithm classified a large sample of rs-fMRI data into ASD and CTL with 90% accuracy. (Table 2)

➢ Both increased and decreased connectivities between the regions contributed to high classification accuracy. (Fig. 3)

➢ Several confounding factors (e.g., site, sex, age, IQ, and medication) did not significantly affect the results. (Fig. 4)

➢ False negative (FN) group was characterized by higher IQ and equal level of autistic symptoms as compared with true positive (TP) group. (Fig. 5)

Limitations

➢ Detailed characteristics of the subjects were not available in the database.

➢ The same brain template was used to normalize the image for every subject, despite the wide range of subjects' ages.

➢ Confounding factors such as motion artifacts, the differences in imaging and experimental protocols could not be controlled in the analysis.

➢ The classification results might be attributable to differences in subjects' head motion, attention, anxiety, thought content, or other physiological factors during scanning.

Conclusions

➢ The present study suggests that an intrinsic connectivity matrix computed from rs-fMRI data may yield a possible biomarker of ASD.

➢ These results also support the view that altered network connectivity within the brain contributes to the neurobiological underpinnings of this disorder.

➢ However, further investigation to remove several confounding factors is needed.

References and Notes

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2) Nielsen, Front Hum Neurosci, 7, 599, 2013
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The study was approved by the ethics committee of Nagoya University School of Medicine.

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