Predicting Autism Behavioral Treatment Response from Baseline Functional MRI

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Rising Stars in Biomedical
Massachusetts Institute of Technology, Cambridge, MA
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Yale University

Autism Spectrum Disorder (ASD) and Treatment

- Neurological developmental disorders characterized by impaired social interactions, difficulties in communication, and repetitive behaviors
  - Prevalence in U.S.: 1 in 68 children
  - Wide range of symptoms and severity
- Promising treatment: Intensive behavioral interventions
  - Our focus: Pivotal Response Therapy
  - Early intervention is important
- However, no “one size fits all” treatment, use trial and error

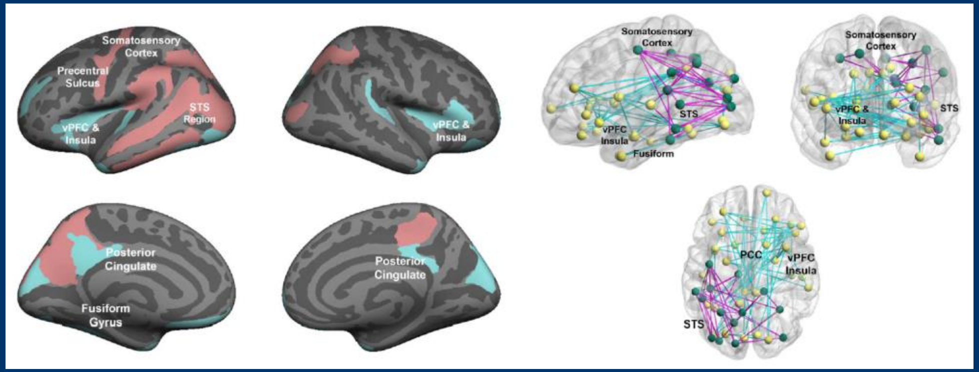
→ Need for *precision medicine*

www.autismspeaks.org

Goal: Predict Autism Treatment Outcome from Baseline fMRI

- Functional magnetic resonance imaging (fMRI) allows noninvasive measurement of brain activity

- fMRI has aided understanding of ASD pathophysiology



Venkataraman et al., TMI 2016

→ We propose first use of fMRI for predicting ASD treatment response

- Data: 19 ASD children underwent 16 weeks Pivotal Response Therapy

Supervised Learning Overview

Inputs X →

Outputs Y →

Learning Algorithm

?

→ Learned Predictive Model

$f : X \rightarrow Y$

Learning Inputs and Outputs

Inputs X:
fMRI
Biomarkers

Outputs Y:
Behavioral
Treatment
Response

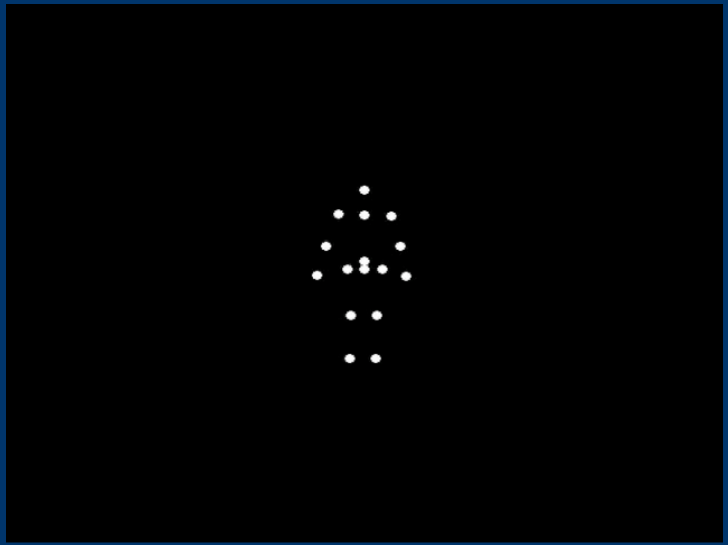
Learning Algorithm

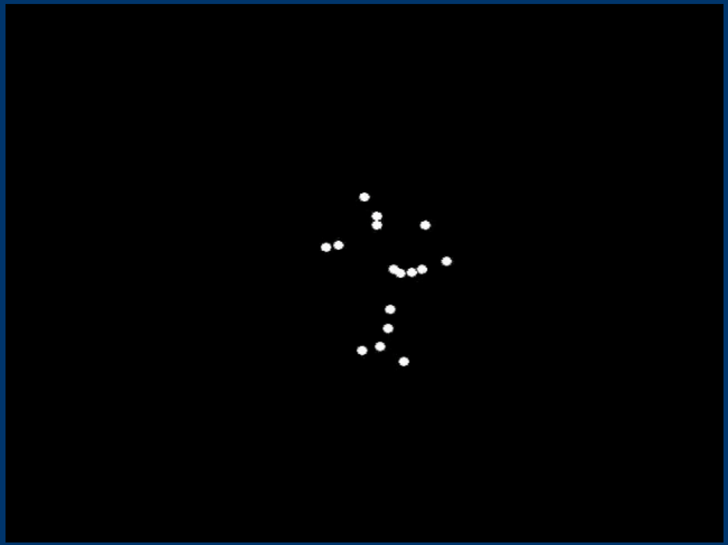
?

Learned
Predictive
Model
$f : X \rightarrow Y$

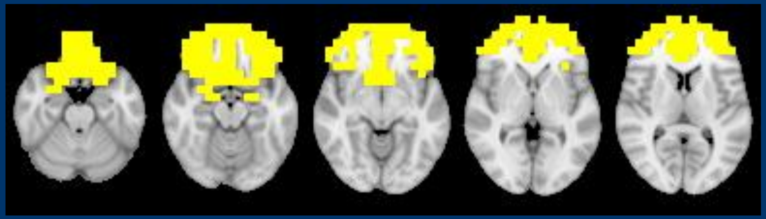
Biopoint fMRI Paradigm

- Biological motion perception task



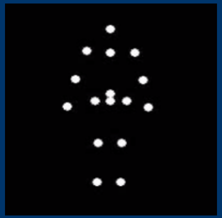


- Focus on social motivation regions:
  Orbitofrontal cortex/ventromedial prefrontal cortex, amygdala, and ventral striatum



Learning Inputs and Outputs

- Inputs: Baseline fMRI-derived biomarkers
  - Acquire fMRI during Biopoint task

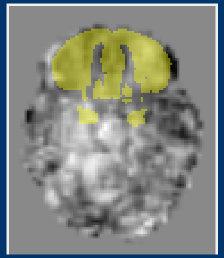
  → Use t-statistics for contrast  >  in social motivation regions

- Outputs: Treatment Outcome
  - Measure Social Responsiveness Scale, Second Edition (SRS) Score pre and post treatment

  → Use normalized change in SRS Score

Learning Pipeline Overview

Inputs *X*:
fMRI
Biomarkers



Outputs *Y*:
Behavioral
Treatment
Response

Learning Algorithm

?

Learned
Predictive
Model
$f : X \rightarrow Y$

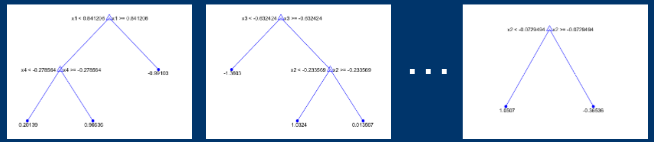
Learning using Standard Random Forests

Inputs *X*:
fMRI
Biomarkers

Outputs *Y*:
Behavioral
Treatment
Response

Learning Algorithm

Random
Forest
Training



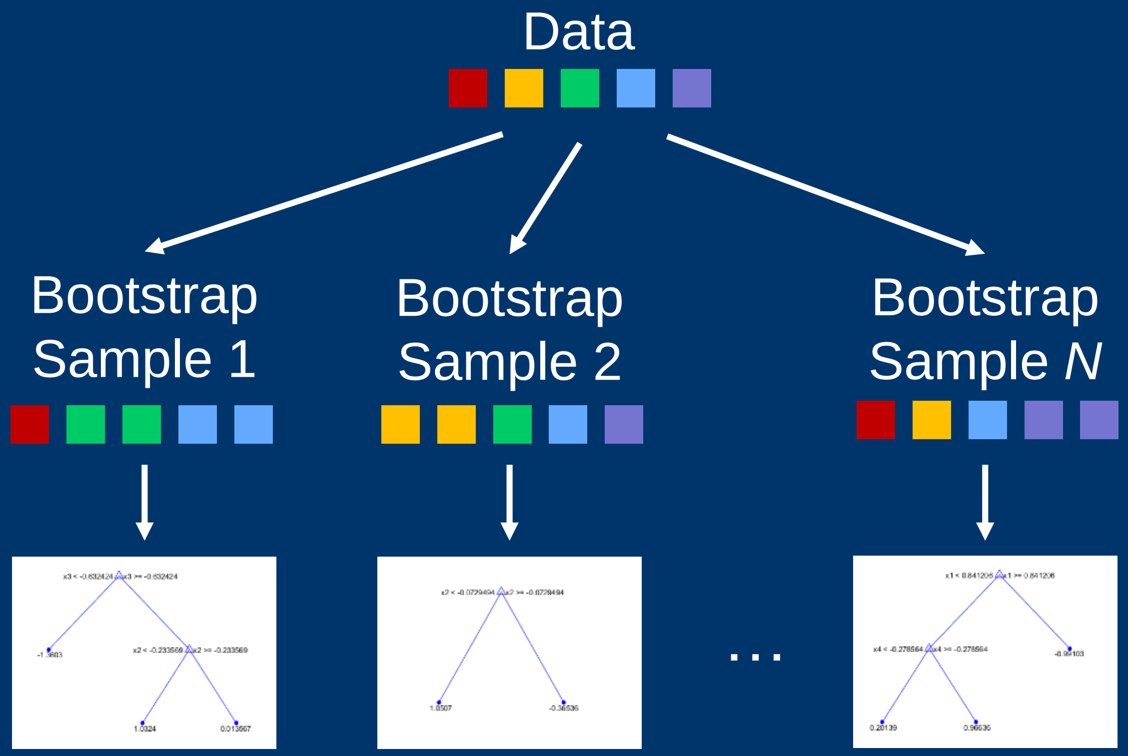
Random Forest

→ *Y*

Learned
Predictive
Model
$f : X \rightarrow Y$

Random Forests for Regression

- Learning method that constructs multiple decision trees with randomness



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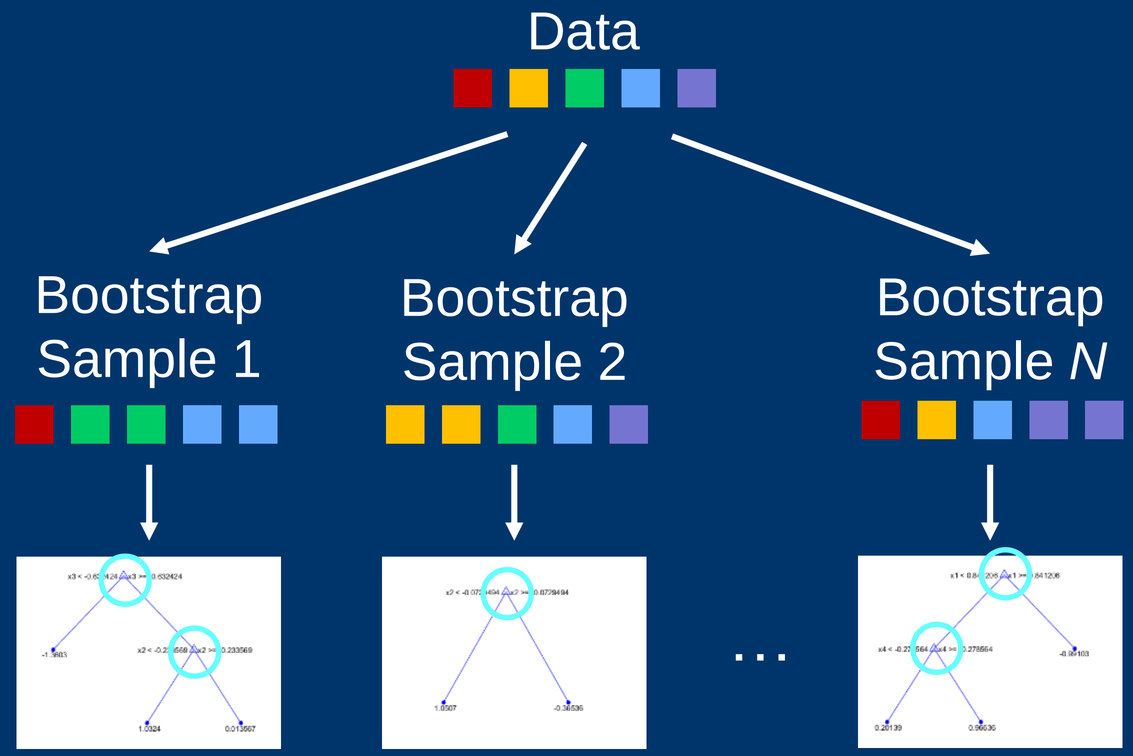
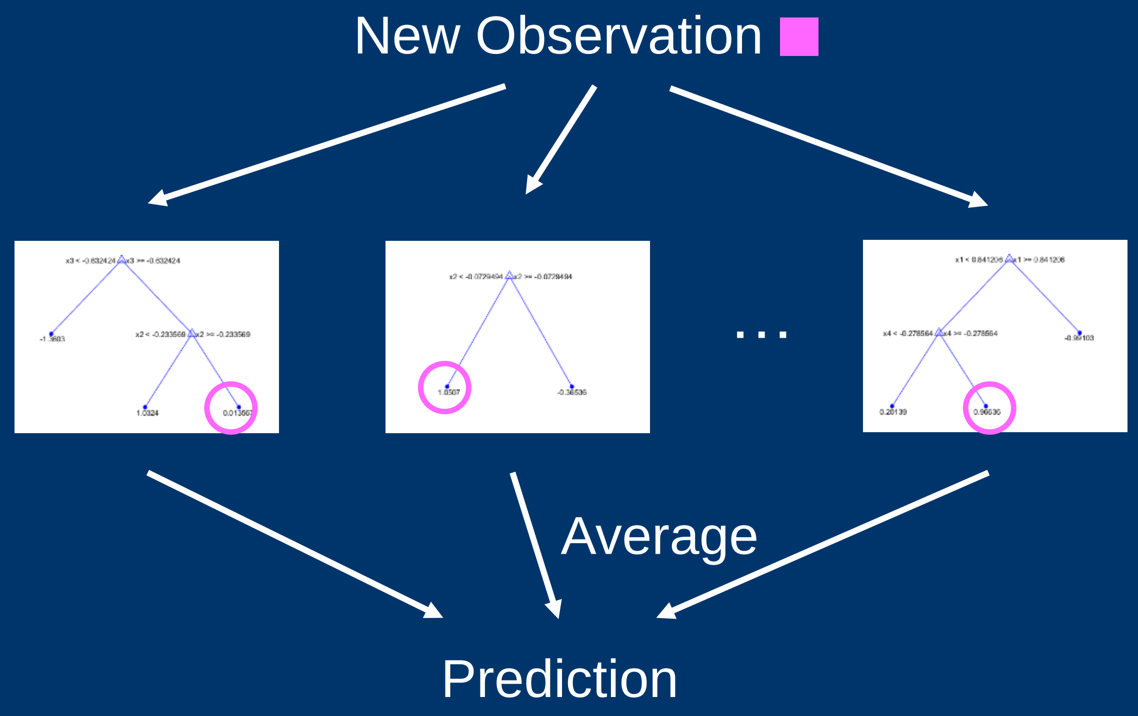


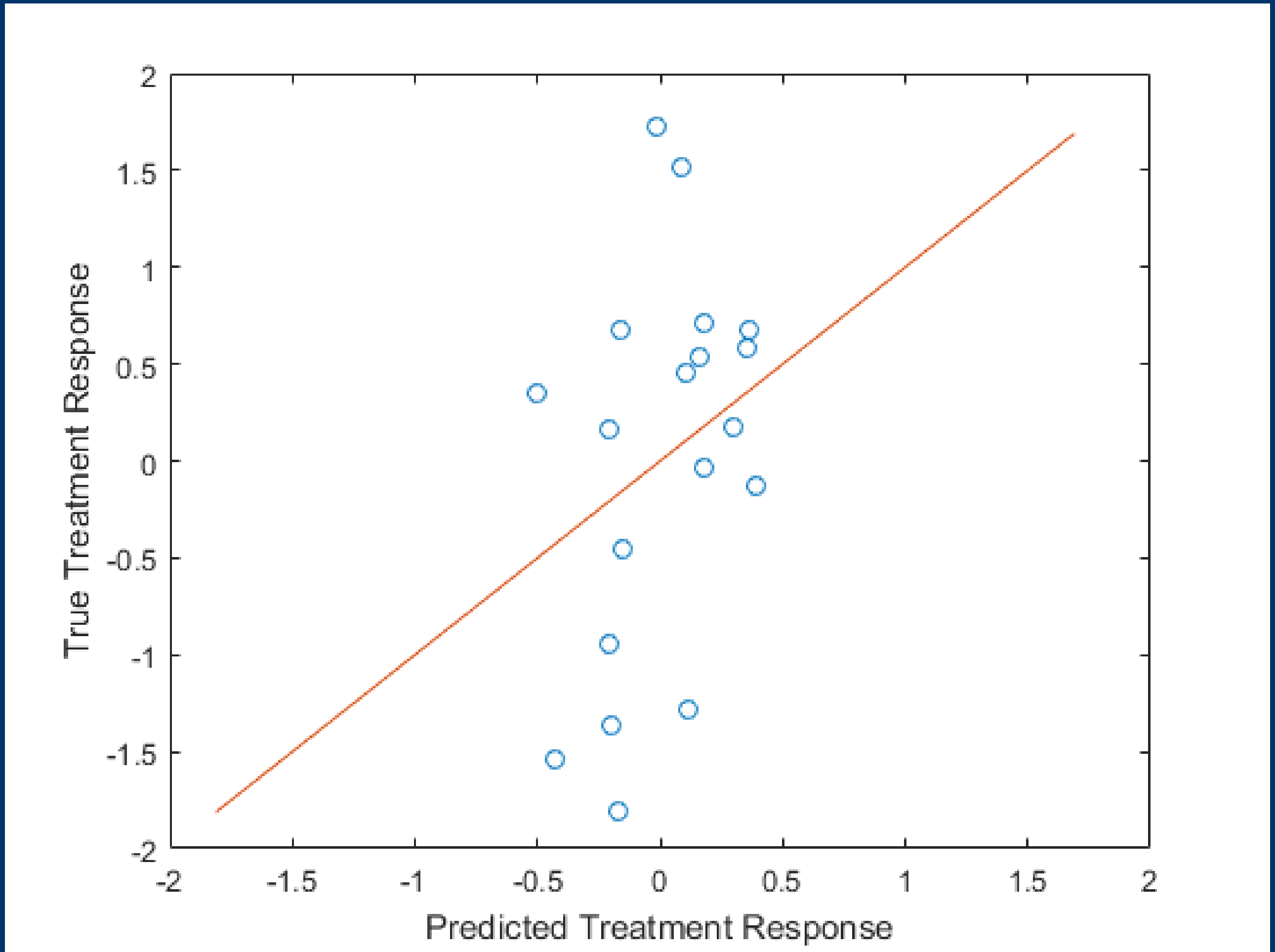
Best split variable chosen from *m* randomly selected inputs

Predictions from Random Forest

- Output average prediction across trees



Random Forests Results in Weak Predictive Power



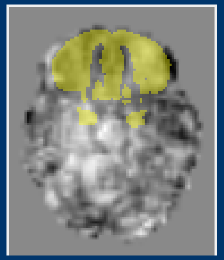
Red line: Perfect prediction

- Leave-one-out cross-validation
- MSE ± SD: 0.82 ± 0.96
- $r = 0.39$, $p = 0.038$

- **Problem**: Too many noisy/irrelevant inputs

Learning using Standard Random Forests

Inputs X:
fMRI
Biomarkers



Outputs Y:
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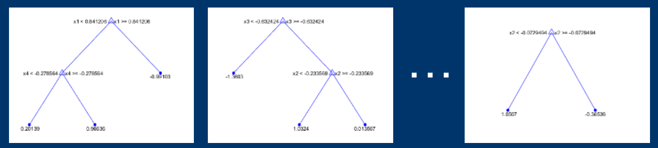

Random Forest

→ Y

Learned
Predictive
Model
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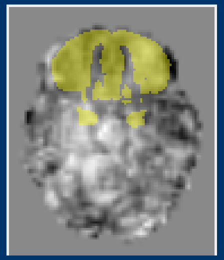
Learning with Variable Selection

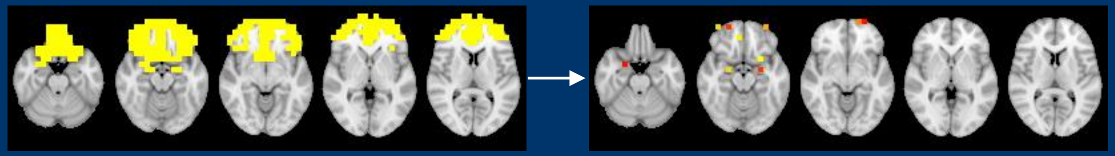
Inputs X:
fMRI
Biomarkers



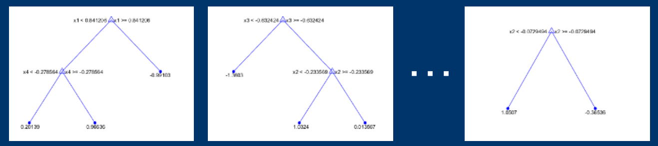
Outputs Y:
Behavioral
Treatment
Response

Learning Algorithm

Variable
Selection



Random
Forest
Training



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Random Forest

→ Y

Learned
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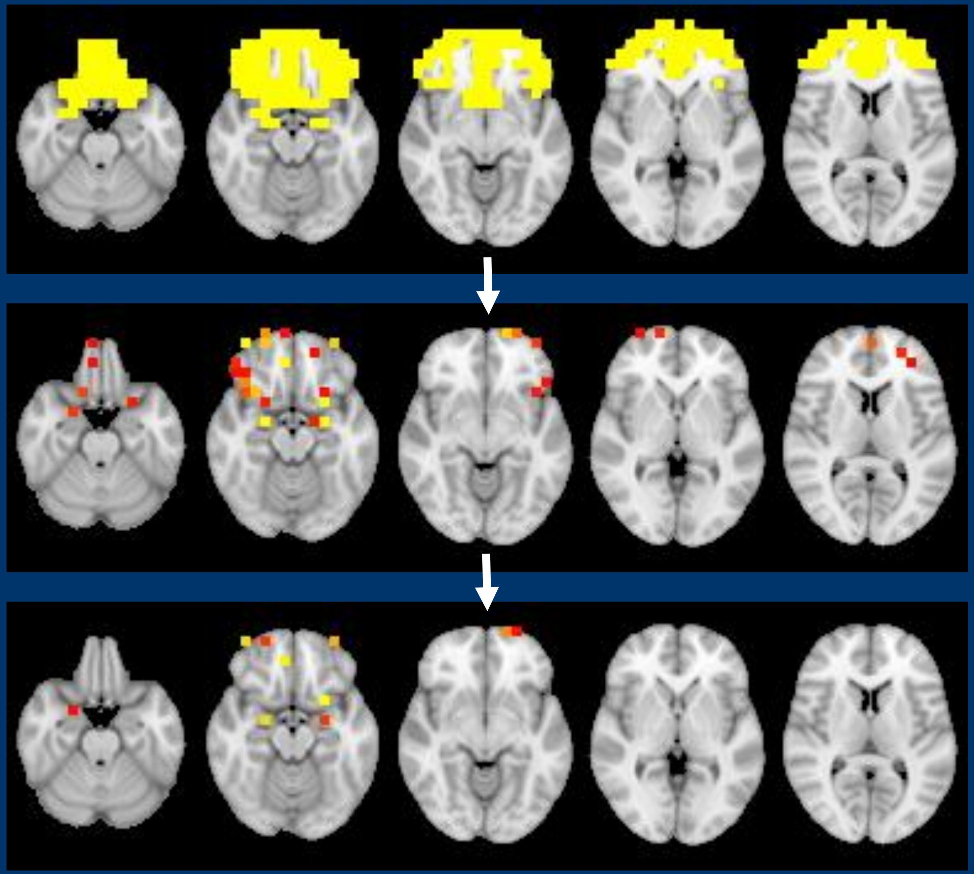
Two-Step Variable Selection Process

Original Inputs: Social motivation regions

1. Variable selection using random forest variable importance

2. Stepwise variable refinement



Red → Yellow: More frequently selected across trials

Learning with Variable Selection

Inputs X:
fMRI
Biomarkers

Outputs Y:
Behavioral
Treatment
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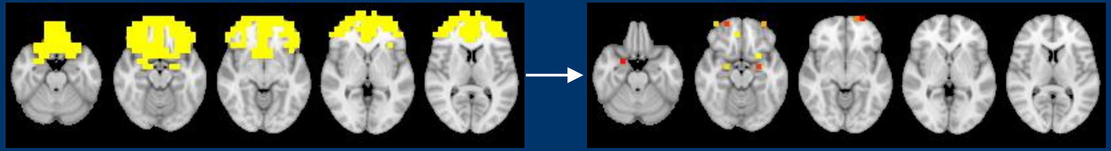
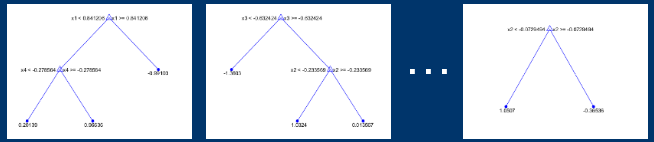
Learning Algorithm

Variable
Selection



Random
Forest
Training



Random Forest

→ Y

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Learning with Variable Selection

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fMRI
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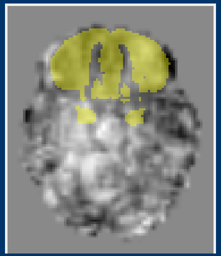

Outputs Y:
Behavioral
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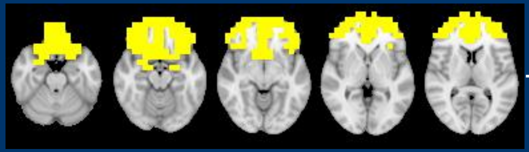
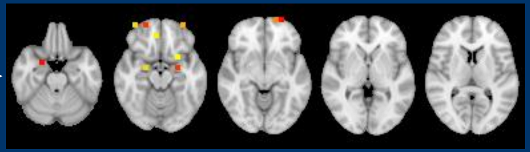
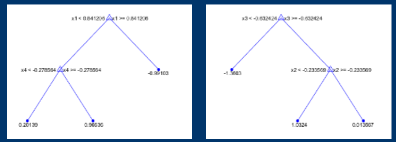
Learning Algorithm

Variable
Selection





"Less-Random"
Forest
Training



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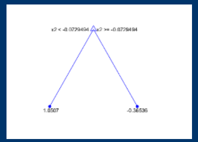


Decision Forest

→ Y

Learned
Predictive
Model
$f : X \rightarrow Y$

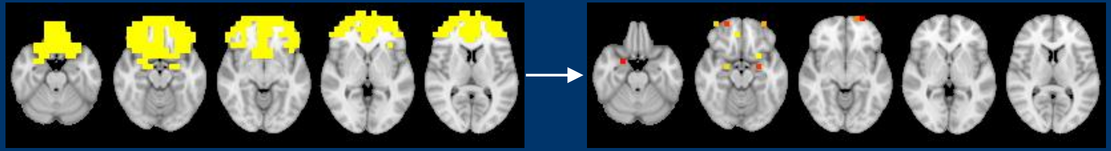
Learning with Bias Correction

Inputs X: fMRI Biomarkers

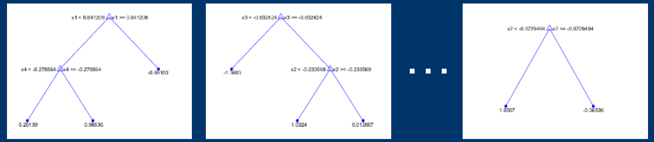
Outputs Y: Behavioral Treatment Response

Learning Algorithm

Variable Selection



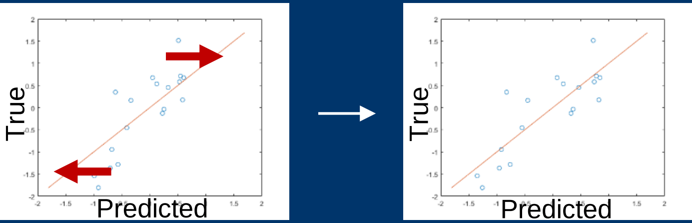
"Less-Random" Forest Training



Decision Forest

→ Y

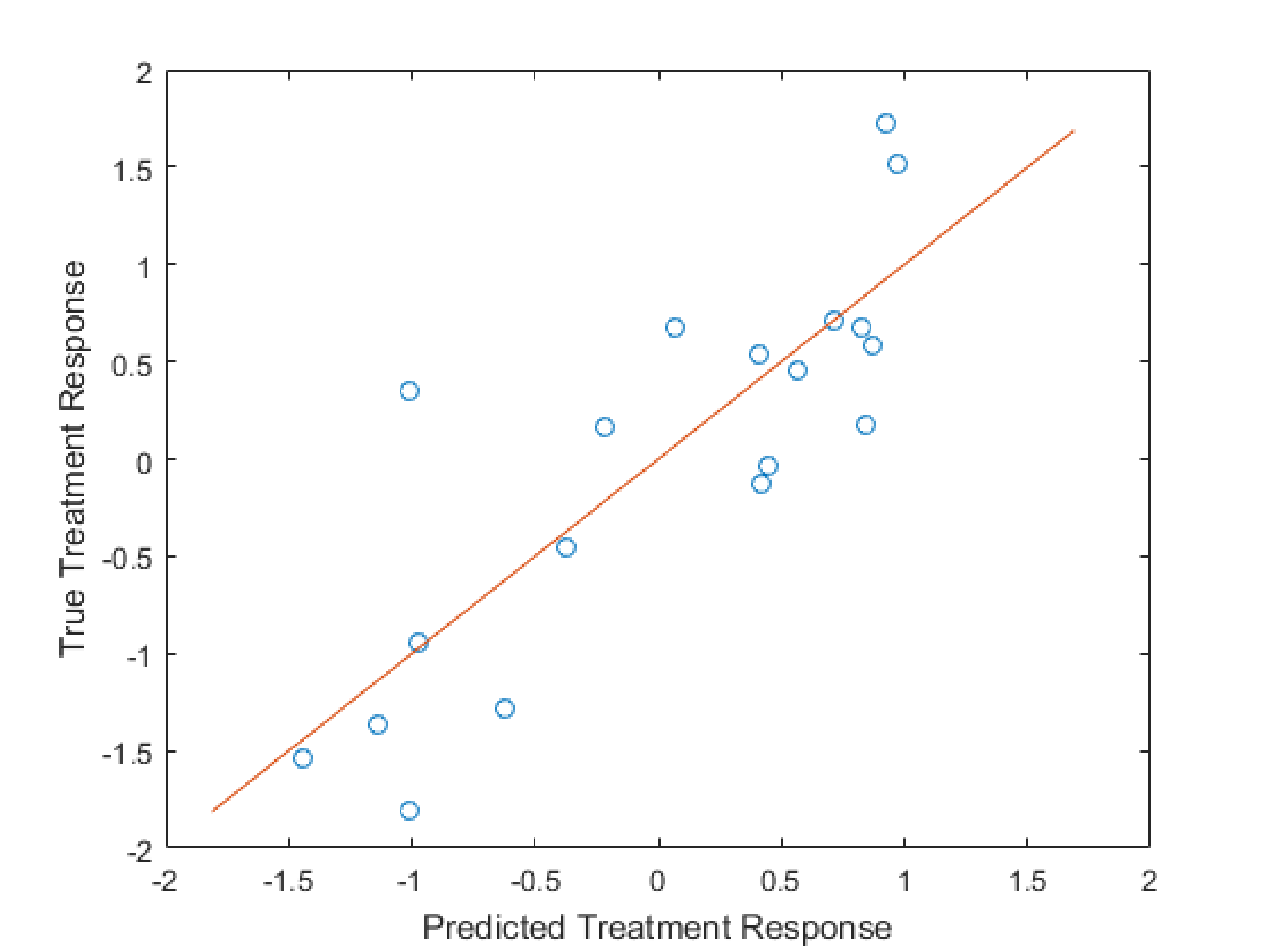
Bias Correction



Learned Predictive Model

$f : X \rightarrow Y$

Proposed Learning Pipeline Significantly Improves Prediction Accuracy



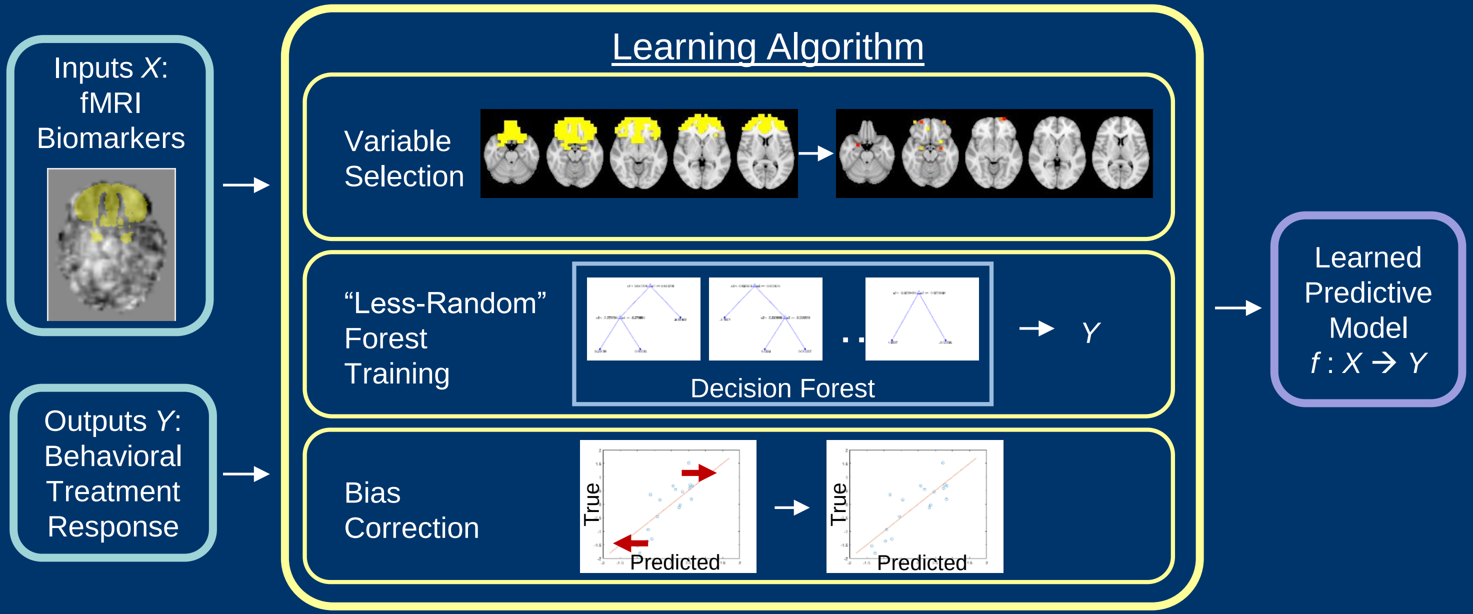
Red line: Perfect prediction

- MSE ± SD: 0.29 ± 0.43
- $r = 0.83$, $p = 0.001$

- Variable selection reduces noisy inputs
- Bias correction improves predictions at the extremes

Conclusions

- Developed learning pipeline to predict response to autism behavior therapy from baseline fMRI
- Move toward personalized treatment



- Future work
  - Other biomarkers for more robust/accurate prediction, e.g., functional connectivity
  - More data, assess generalization

Thank You!

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- Dr. Daniel Yang (fMRI preprocessing)
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