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Towards Improved Recognition And Diagnosis of Autism Among Females – A Novel Approach Using Machine Learning

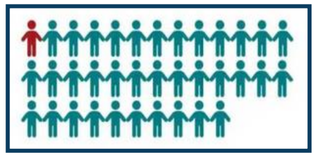
Aanika Tangirala
Lakeside School, Seattle, WA, USA

All images, graphs and data tables are student generated unless otherwise referenced

INTRODUCTION: BACKGROUND

THE BIG PICTURE

Autism Spectrum Disorder (ASD) affects 1 in every 36 children[1]



Autism Parenting Magazine, 2024

Early intervention and **diagnosis** is key for successful outcomes in life[2]

ASD is diagnosed solely on **behavioral observation** – no reliable blood tests or MRIs

For the **27% undiagnosed by age 8,** therapeutic intervention has dissipated

Current diagnostic process is **time consuming, inaccessible, costly,** and **subjective**

It can take up to **13 months** to get a diagnosis

THE HIDDEN ISSUE - GENDER BIAS IN DIAGNOSIS

Females with autism are often **misdiagnosed** or **miss** diagnosis due to biased diagnostic tests[4]

LEADING THEORIES:

- Female Autistic Phenotype exists[5]
- Females tend to camouflage and mask[5]

Delayed diagnoses and support - higher % of **anxiety** and **depression** in teen girls with autism[6]

Difference **CANNOT** only be attributed to something inherent in females that decreases the chances of developing autism.

All figures student-generated except where cited

INTRODUCTION: AUTISM DIAGNOSTIC TOOLS

The **Diagnostic and Statistic Manual of Mental Disorders, Fifth Edition (DSM-5)** provides criteria for diagnosing ASD based on impairments in social and verbal communication and restricted, repetitive patterns of behavior

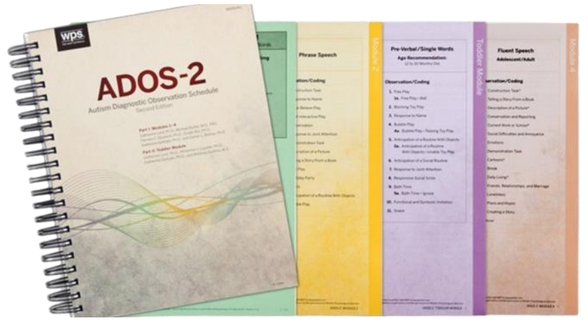
Autism Diagnostic Observation Schedule (ADOS)
Clinical Observation
→ ADOS_COMM: communication ability
ADOS_SOCIAL: social ability
ADOS_STEREO_BEHAV: repetitive behavior

Autism Diagnostic Interview-Revised (ADI-R)
Caregiver Interview
→ ADI_R_SOCIAL: social ability
ADI_R_VERBAL: verbal ability
ADI_R_RRB repetitive & restrictive behavior:

Gold standard for autism diagnosis

Social Communication Questionnaire (SCQ)
Caregiver Survey
→ SCQ_TOTAL: social and communication ability

Social Responsive Scale (SRS)
Caregiver Survey
→ SRS_AWARENESS
SRS_COGNITION
SRS_COMMUNICATION
SRS_MOTIVATION
SRS_MANNERISMS

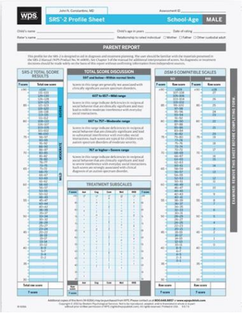


Autism Diagnostic Observation Schedule (ADOS-2) 2nd Edition

Pearson Clinical

Sample SCQ Form

Children's Hospital of Philadelphia Research Institute



Sample SRS-2 Form

Mind Resources

Clinicians use a combination of above to diagnose autism

INTRODUCTION: RESEARCH QUESTION AND GOALS

RESEARCH QUESTION

Which features of existing Autism Spectrum Disorder (ASD) diagnostic tests are most useful for predicting autism in female populations?

GOALS

(1) Establish tangible behavioral difference between females and males with autism.

(2) Identify minimal set of behaviors and features most predictive of autism in females.

(3) Create a more accurate diagnostic predictive machine learning model for females.

METHODS: MACHINE LEARNING PIPELINE DESIGN

DATA SOURCE

- **ABIDE** – the Autism Brain Imaging Data Exchange[7]
- Public online repository of phenotypic autism behavioral data collected over **17** global sites
- Contains **73** features from ADOS, ADI-R, SRS, SCQ
- Dataset size = **1112 individuals; 948 males, 164 females, 539** individuals with autism, **573** without

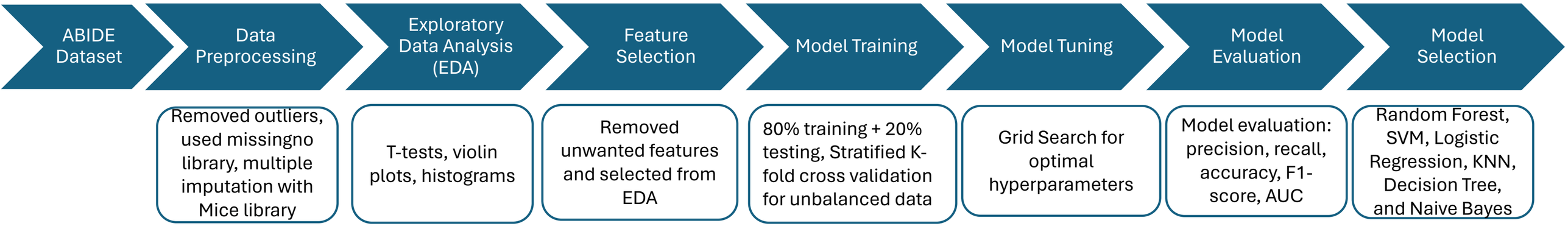
DATA PREPROCESSING

- Removed outliers
- Removed features not related to ADOS, ADI-R, SCQ, SRS tests, from 73 to 23 features
- Used multiple imputation methods for missing data based on correlation heatmap

EXPLORATORY DATA ANALYSIS (EDA)

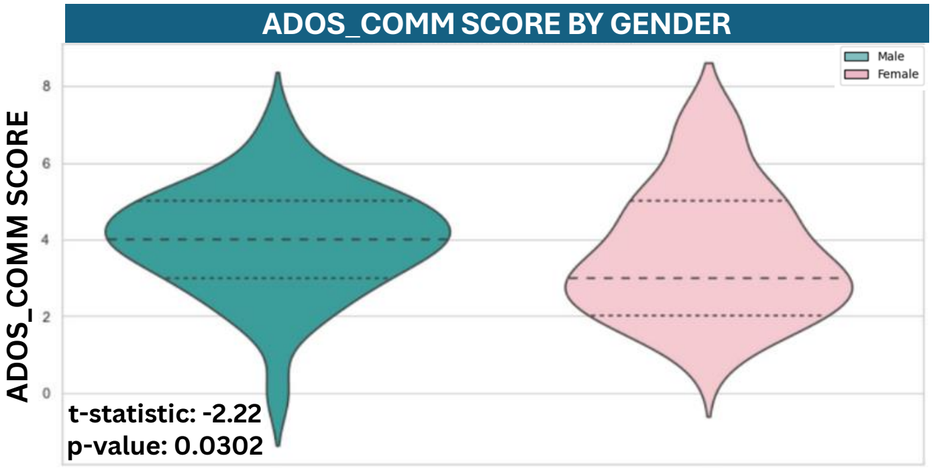
- Descriptive statistics of the features
- Visualized the diagnostic features by gender using histograms and violin plots
- Checked for candidate gender specific features for feature selection and towards Goal 1

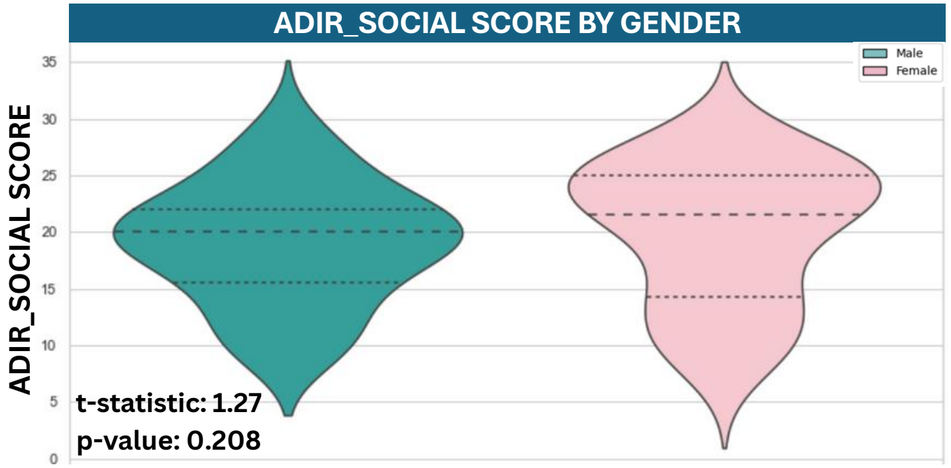
BUILDING MACHINE LEARNING PIPELINE



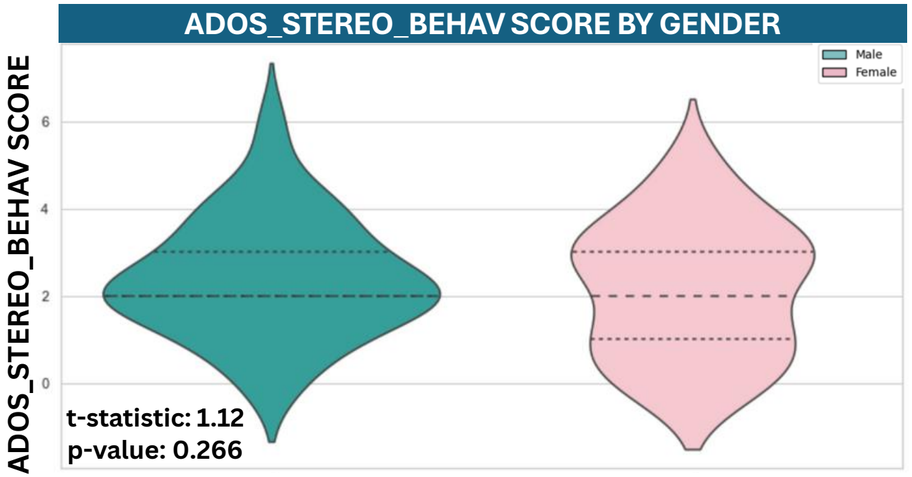
Development Tools and Environment: Python, Pandas, Scikit, seaborn, matplotlib, Jupyter Notebook

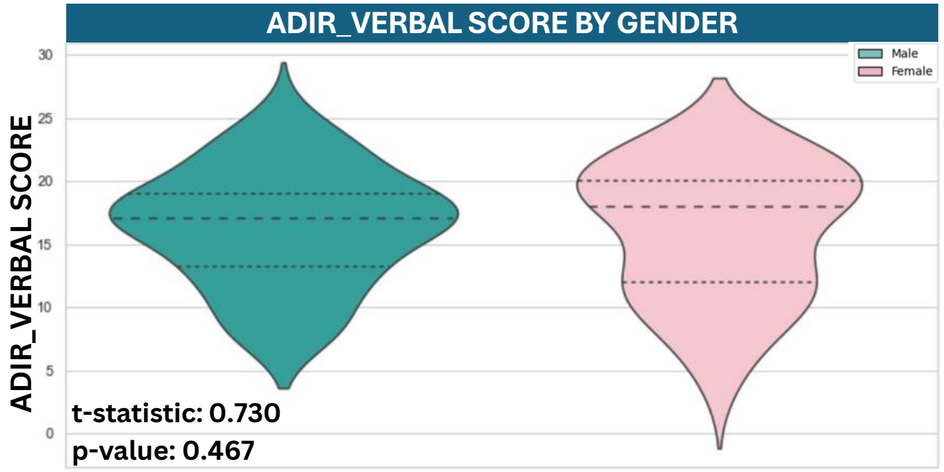
EXPLORATORY DATA ANALYSIS: ESTABLISHING GENDER-BASED DIFFERENCE





- Males have much sharper distributions centered around the means
- Females have bimodal distributions
- Females have higher scores in ADI_R tests
- Statistical difference in ADOS_COMM between males and females

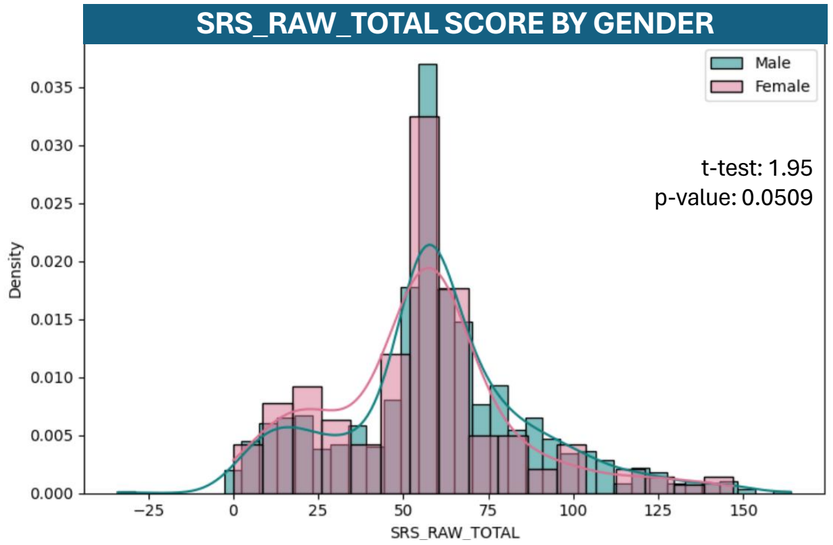




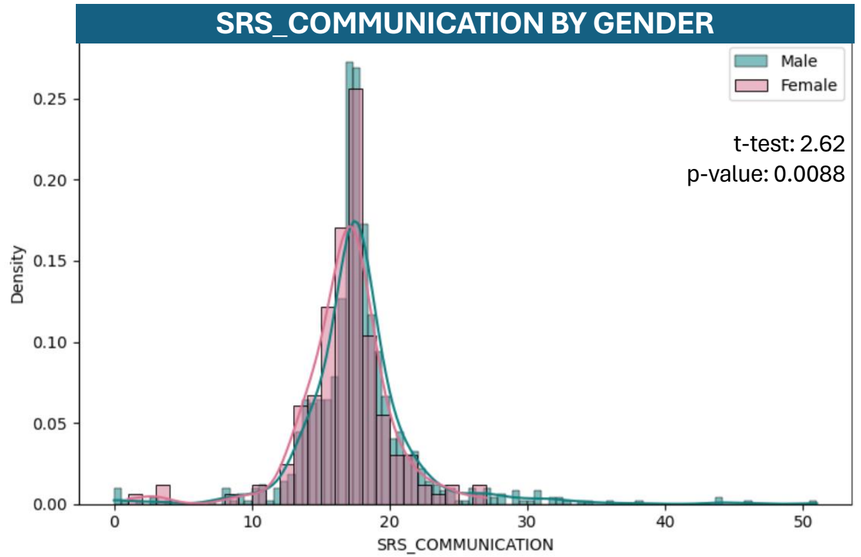
Diagnostic tests capture and classify female autistic behavior differently than males

EXPLORATORY DATA ANALYSIS: FINDING SPECIFIC BEHAVIORS

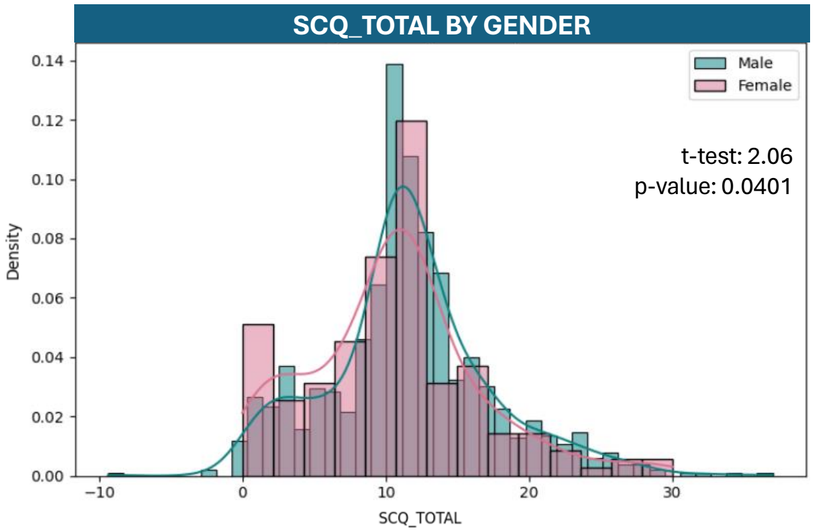
SRS_RAW_TOTAL SCORE BY GENDER



SRS_COMMUNICATION BY GENDER



SCQ_TOTAL BY GENDER



Statistical significance ($p \leq 0.05$) between genders identified in questionnaire-based features – **SRS_RAW_TOTAL, SRS_COMMUNICATION,** and **SCQ_TOTAL**: potential candidates for **feature selection** for female model

RESULTS: PROVING DIAGNOSTIC GENDER BIAS

(1) Built Random Forest classifier on processed ABIDE dataset with all 23 features to predict autism

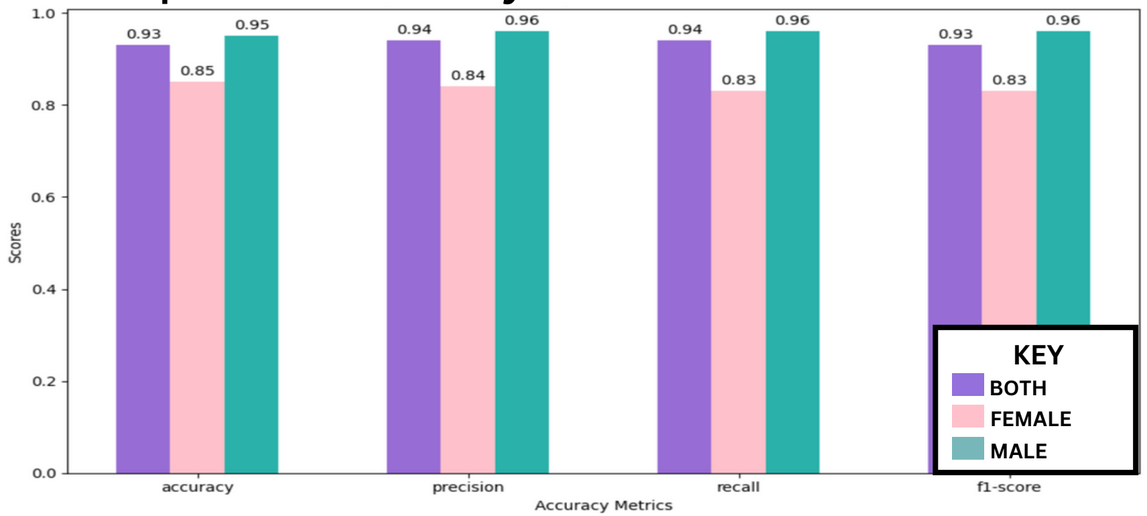
(2) Trained and tested on male and female data combined (Model 1), on female dataset only (Model 2), on male dataset only (Model 3)

(3) Evaluated model accuracy, precision, recall, F1 scores

(4) Checked top 10 most impactful features for each model

(5) Using Top 10 and candidates from EDA, built minimal feature set of **12 features**

Comparison of Accuracy Metrics for All-Feature Models



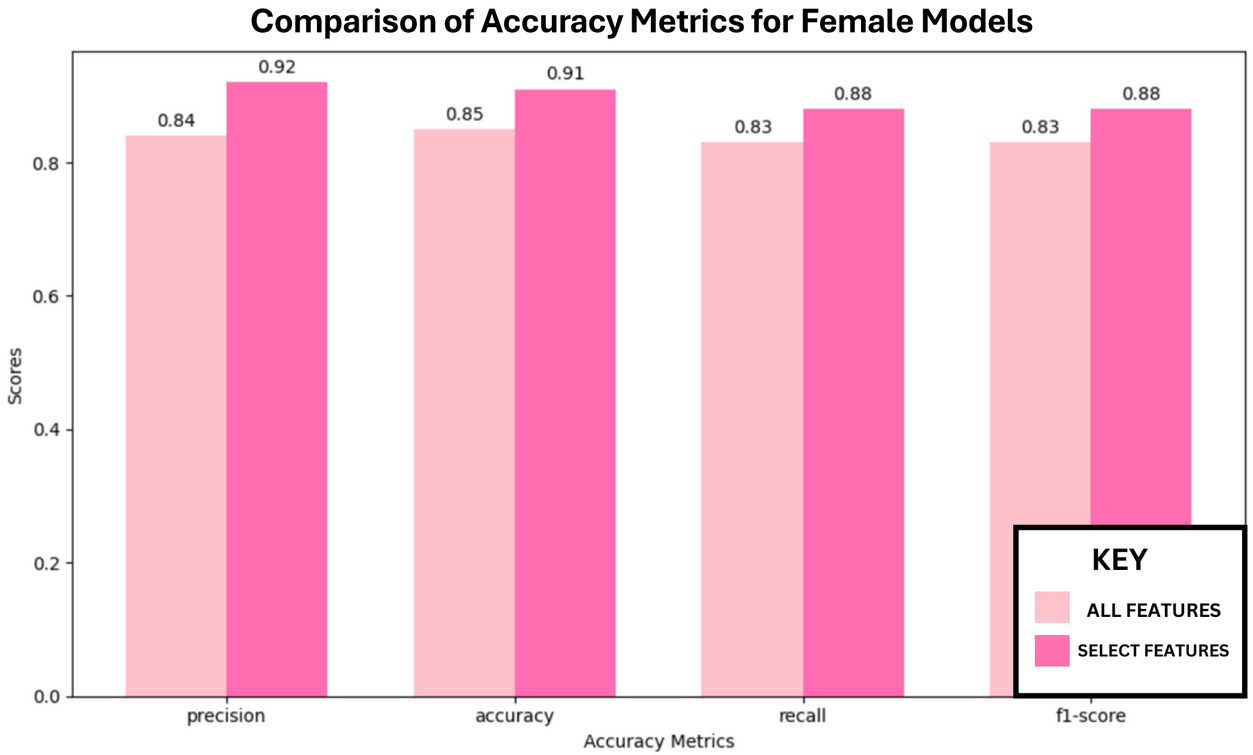
Model	Accuracy	Precision	Recall	F1 score
1:Both	0.93	0.94	0.94	0.93
2: Females	0.85	0.84	0.83	0.83
3: Males	0.95	0.96	0.96	0.96

Female dataset had least accuracy on all-feature model, males have most accuracy; **Validates gender bias of tests**

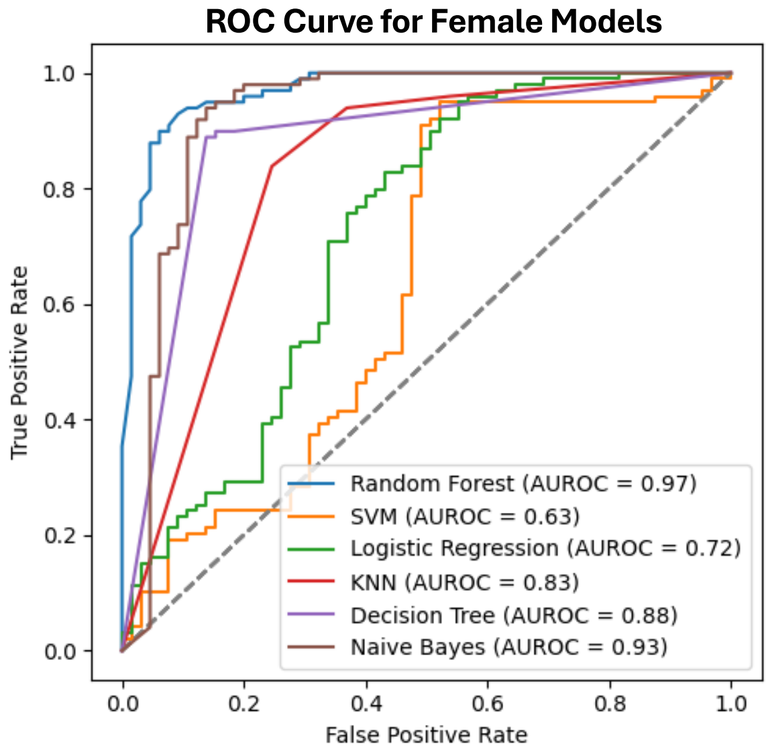
Top 10 features for males + females	Top 10 features for females	Top 10 features for males
AQ_TOTAL	ADI_R_SOCIAL_TOTAL	AQ_TOTAL
ADI_R_VERBAL_TOTAL	ADI_R_VERBAL_TOTAL	ADOS_GOTHAM_SEVERITY
ADOS_SOCIAL	SCQ_TOTAL	ADOS_SOCIAL
ADI_RRB_TOTAL	ADOS_COMM	ADI_RRB_TOTAL
SCQ_TOTAL	SRS_RAW_TOTAL	ADI_R_VERBAL_TOTAL
ADOS_COMM	AQ_TOTAL	ADOS_COMM
ADOS_GOTHAM_SEVERITY	ADOS_SOCIAL	ADOS_TOTAL
ADOS_TOTAL	ADOS_GOTHAM_RRB	SRS_RAW_TOTAL
ADI_R_SOCIAL_TOTAL	ADOS_GOTHAM_SOCAFFECT	SCQ_TOTAL
SRS_RAW_TOTAL	ADOS_GOTHAM_SEVERITY	SRS_COGNITION

- ADOS_TOTAL, ADIR_RRB not impactful for prediction in female dataset but impactful for males
- ADI_R and SCQ features most impactful for female model – **interview** and **questionnaire-based**

RESULTS: BUILDING A FEMALE PREDICTIVE MODEL



Minimal set of 12 features model is more accurate than All-feature model for females



Random Forest is most accurate classifier on Minimal Features Set model

MINIMAL SET OF 12 MOST PREDICTIVE FEATURES FOR FEMALES ESTABLISHED

- SCQ TOTAL
- SRS RAW TOTAL
- SRS AWARENESS
- SRS COMMUNICATION
- ADIR SOCIAL TOTAL
- ADIR VERBAL TOTAL
- ADOS COMM
- AQ TOTAL
- ADOS SOCIAL
- ADOS GOTHAM RRB
- ADOS GOTHAM SOCAFFECT
- ADOS GOTHAM SEVERITY

CONCLUSIONS

- Significant differences in behavior of males and females with autism and performance on social, communication, and repetitive subtests; **Supports Female autistic phenotype hypothesis**
- Gender bias in current diagnostic tests proven, model was more accurate in diagnosing males than females (**95% vs 85%**)
- Random Forest classifier with minimal set of 12 features (from original 23, **48% reduction**) was more accurate in predicting female autism (**91% vs 85%**)
- **Questionnaire** and caregiver **interview-based** tests were better indicators for female autism
- More female data across multiple sites and access to **item-specific scores** would potentially lead to even deeper insights

FUTURE RESEARCH AND APPLICATIONS

Future Research

- Working with Children's National Neurodevelopmental Program (Washington DC)
  - Deeper item level sub-score analysis
- Similar analysis and models for removing bias based on race and socioeconomic factors
- Generative adversarial networks (GANs) to address lack of female data issues
- Combination of behavioral and neuroimaging data to provide more accurate diagnosis

Applications of Research

- **Modify DSM-5 and current diagnostic tests for females** - remove overreliance on ADOS test and repetitive behaviors sub-tests
- Weight **questionnaire** and **interview-based responses** more heavily; use these for early screening
- Develop **digital and mobile health approaches** for faster and expedient screening
- **Raise awareness** for caregivers to identify **female autistic behaviors** to screen for earlier diagnosis

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