GABA and Socio-Communicative Abilities in High-Functioning Adults with Autism Spectrum Disorder

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INTRODUCTION

“Imitation Game”

Brain

Social Behavior

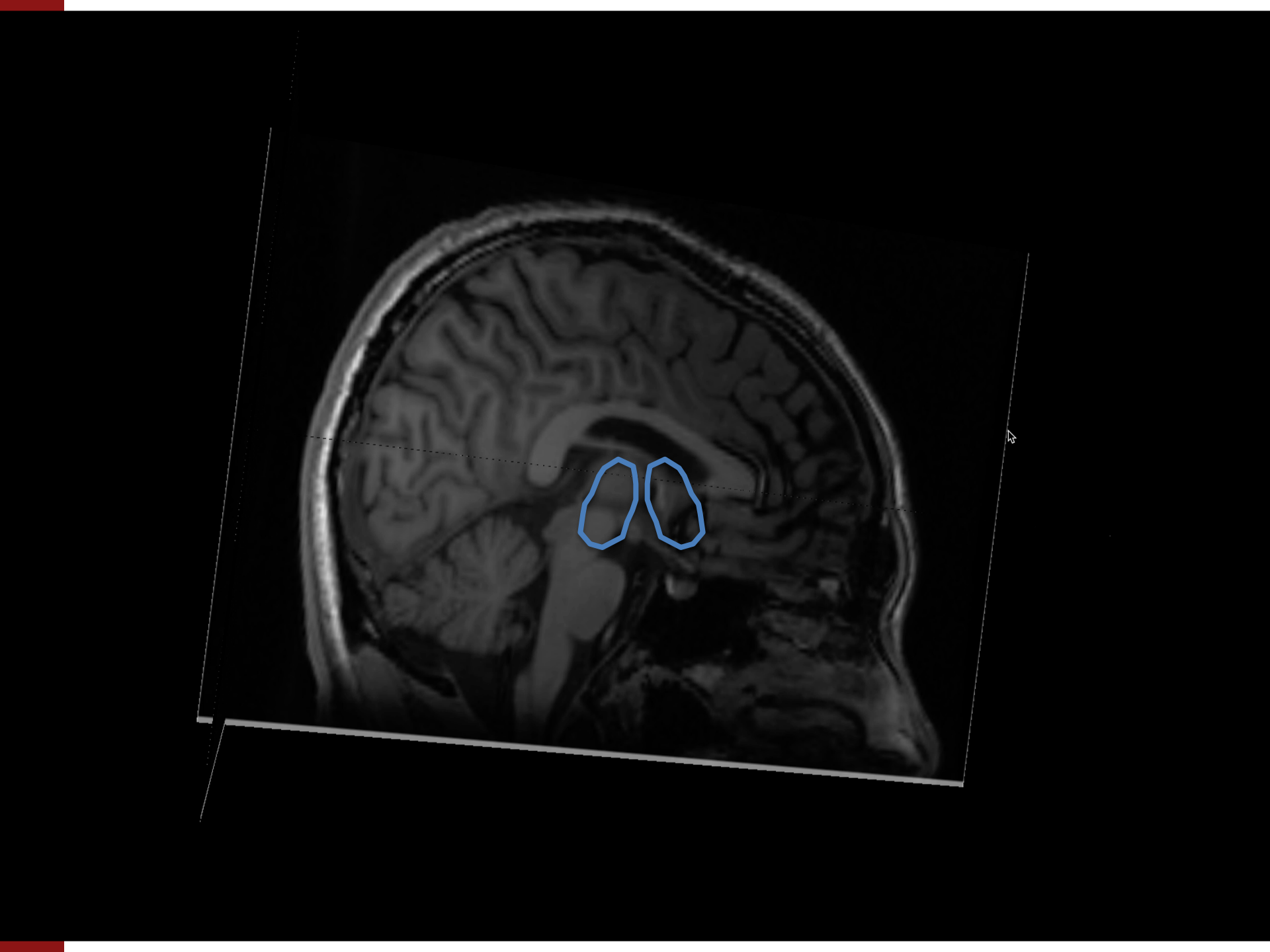
Questions

- What are the **brain regions** responsible for altered **social behavior** in individuals with autism?

- What **causes** these brain regions to function differently in individuals with autism?

- Question: What are the **brain regions** responsible for altered **social behavior** in individuals with autism?

- Hypothesis: The **Thalamocortical Circuits** are responsible for altered social behavior in individuals with autism.



- Question: What **causes** the Thalamocortical Circuits to function differently in individuals with autism?

- Hypothesis: Mechanisms responsible for modulating **excitation / inhibition** balance causes differences in Thalamocortical Circuits in individuals with autism.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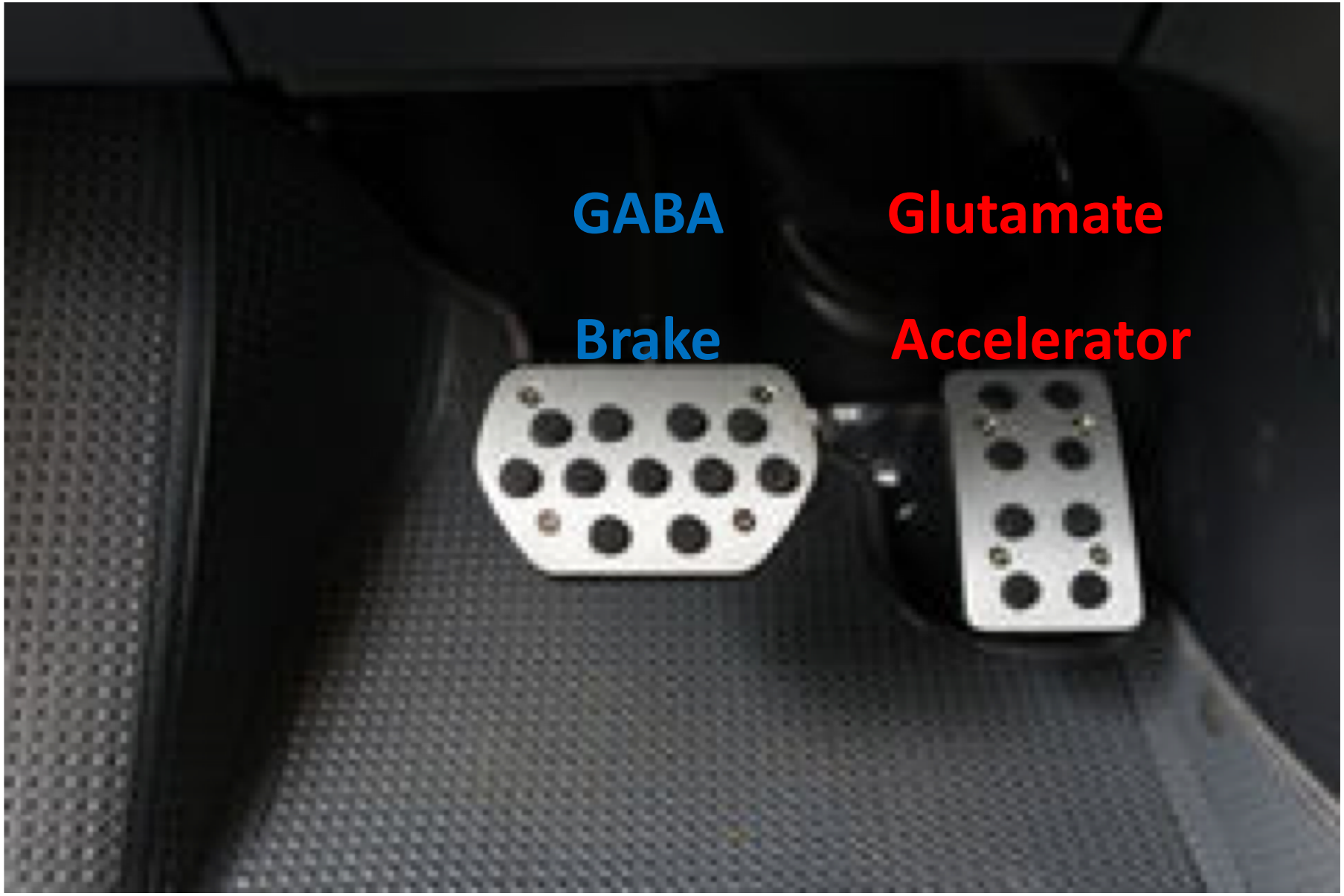
LIGHTYEAR
REAR INSIDE



Inhibition **Excitation**

Aims

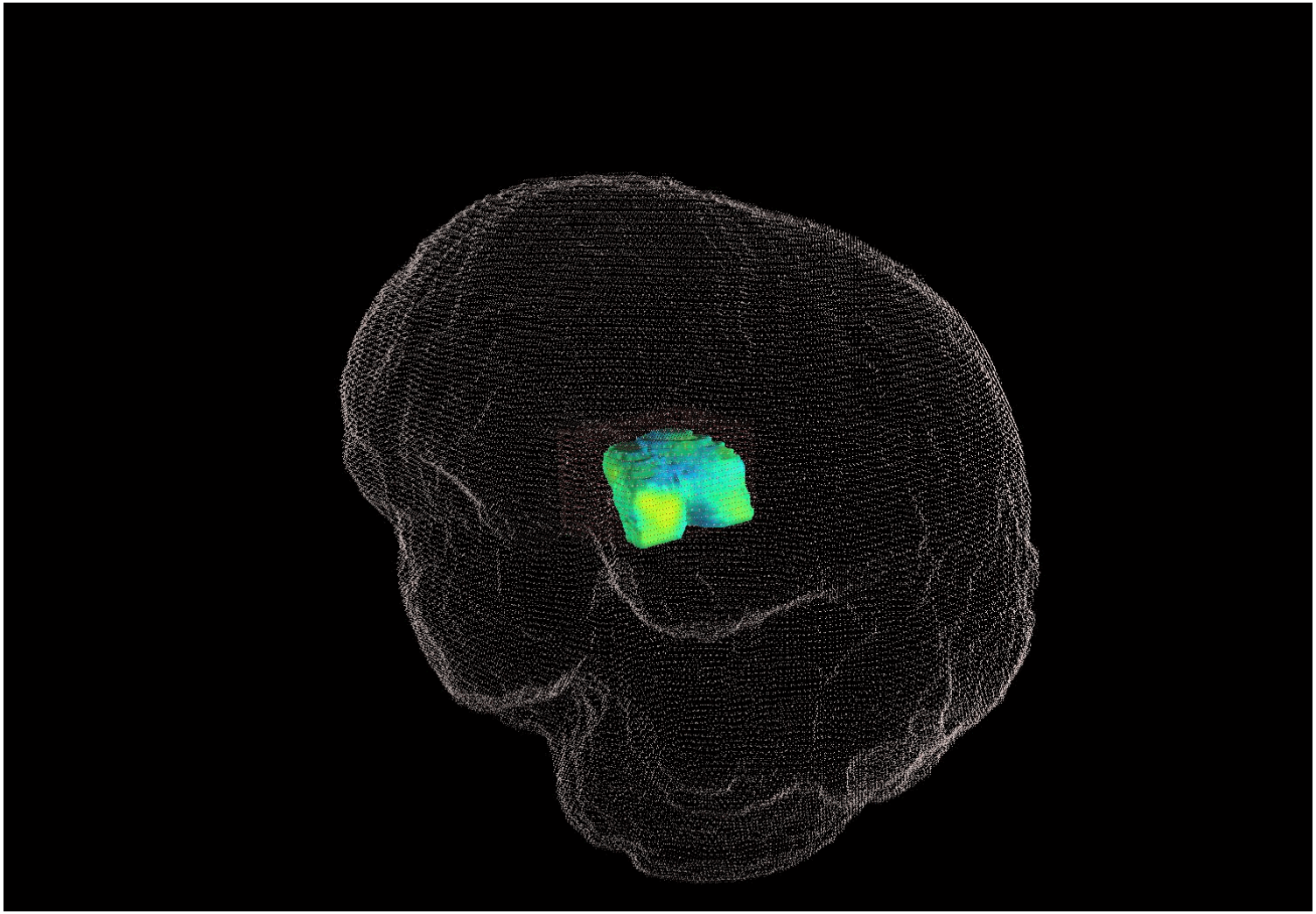
- **Aim 1**: Determine the abnormalities in GABA levels in thalamocortical networks in adults with ASD using proton magnetic resonance spectroscopy (MRS).
- **Aim 2**: Characterize the distribution of $GABA_A$ receptors in adults with ASD using positron emission tomography (PET).
- **Aim 3**: Examine the effects of $GABA_A$ receptor densities and GABA levels in the thalamus and left dorsolateral prefrontal cortex (DLPFC) on socio-communicative abilities.

METHODS

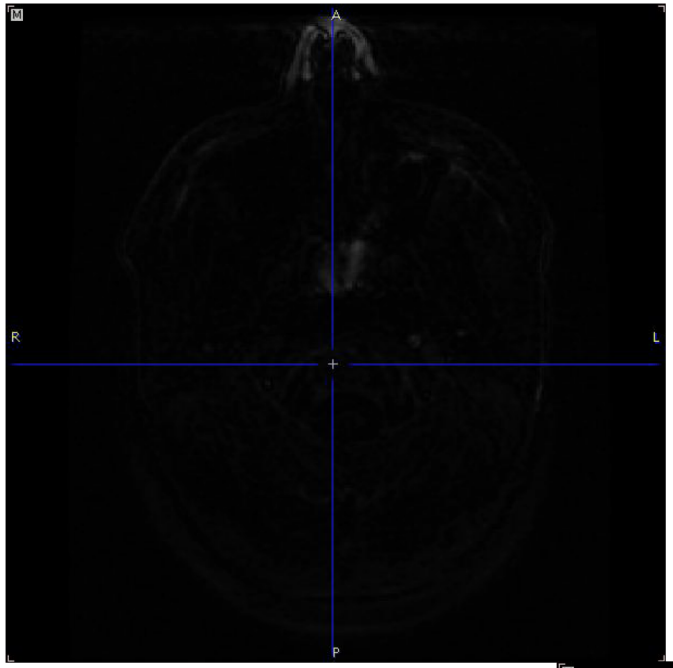
Hybrid PET-MR Scanner (General Electric)

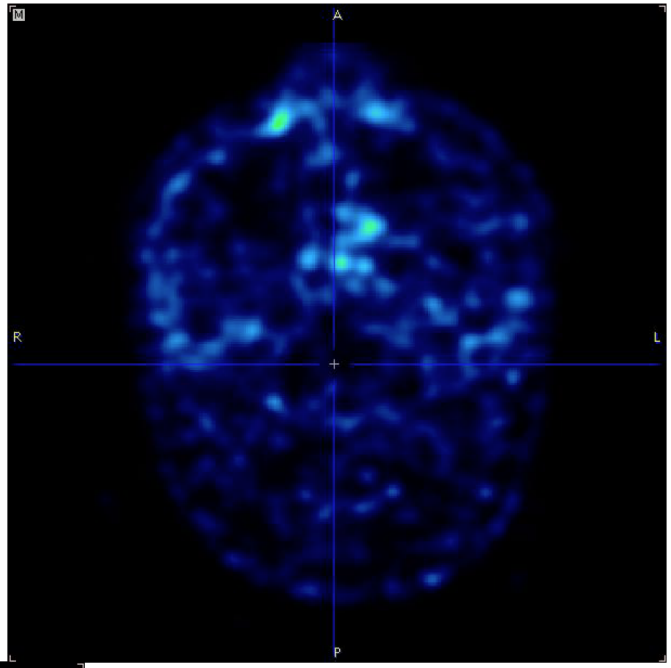
http://www3.gehealthcare.com/en/products/categories/magnetic_resonance_imaging/signa_pet-mr

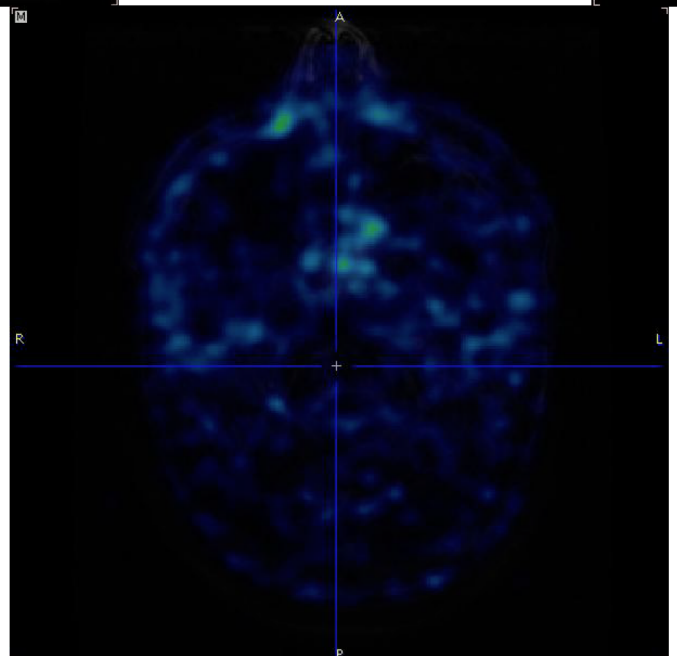
MRS voxel in Thalami



Simultaneous PET/MR Acquisition







Neuropsychological Assessments

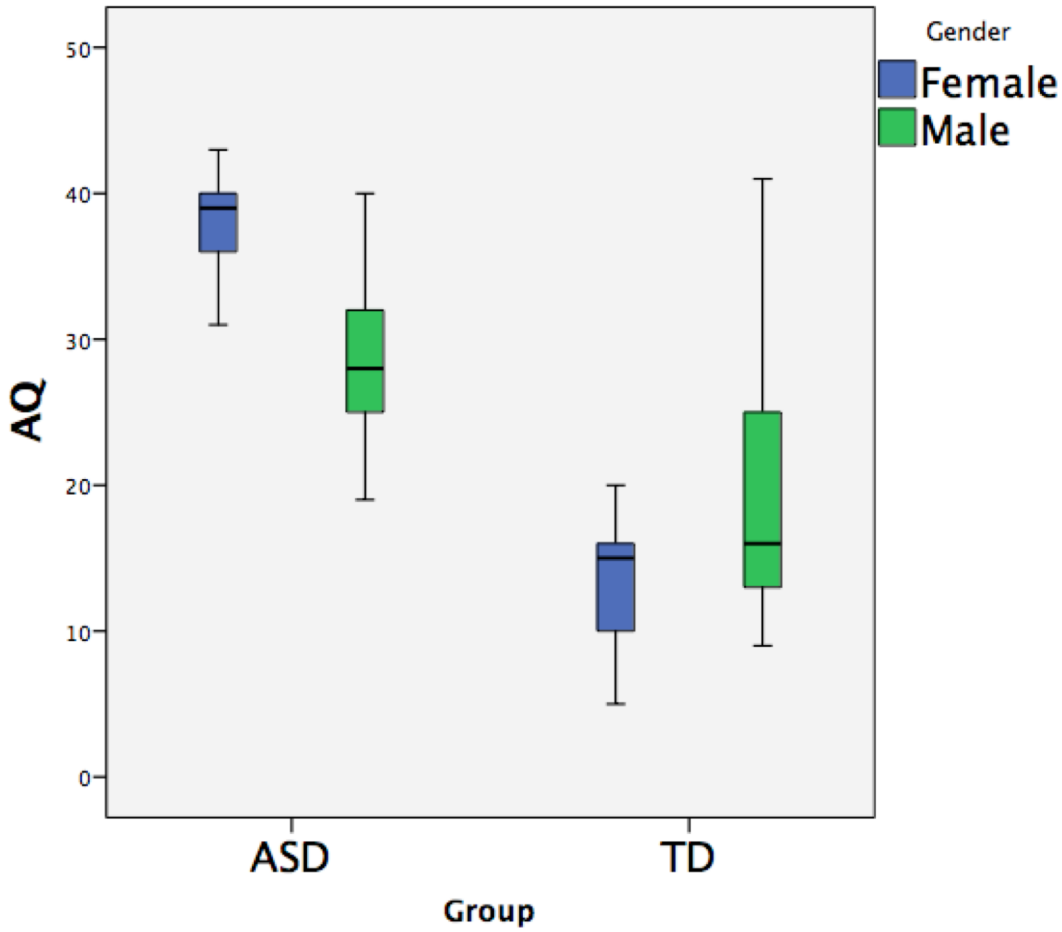
- IQ:
  - Stanford Binet Version 5 (SB5)
- Autism Spectrum Disorder Diagnosis
  - Autism Diagnostic Observational Schedule (ADOS)
  - Autism Diagnostic Inventory – Revised (ADI-R)
- Social interaction abilities:
  - **Ritvo Autism Asperger's Diagnostic Scale (RAADS)**
  - **Autism Quotient (AQ)**
  - Social Responsiveness Scale (SRS-2)
- Emotion regulation:
  - Berkeley Expressivity Questionnaire (BEQ), Aberrant Behavioral Checklist – Irritability (ABC-I)
- Sensory aberrations:
  - Sensory Profile Questionnaire (SPQ)
- Repetitive behaviors:
  - Repetitive Behavior Scale (RBS-R)

RESULTS

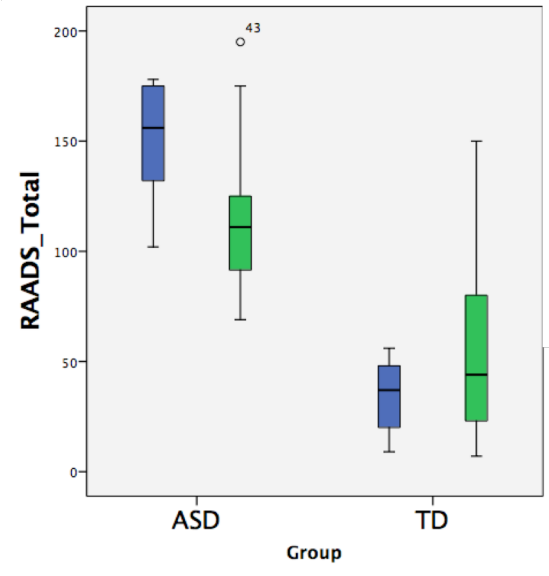
Participant Demographics and Partial Neuropsychological Testing Results

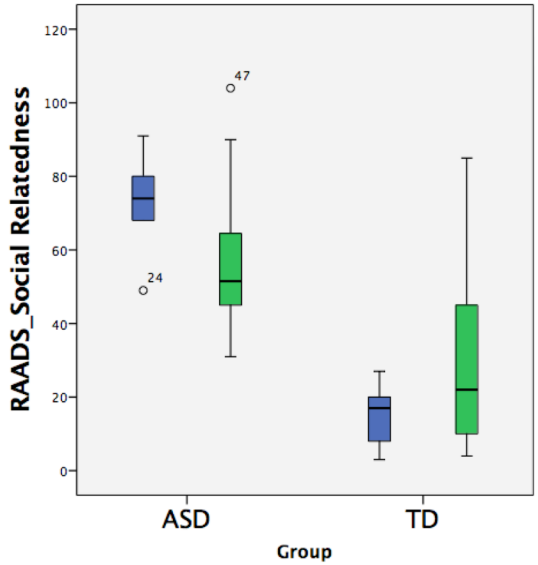
	ASD	TD	p
Age (years)	27.0 ± 8.7	27.4 ± 7.5	.675
Gender	16 M / 9 F	17 M / 9 F	--
FSIQ	102.9 ± 17.6	113.0 ± 12.3	.035
AQ	32.0 ± 6.7	17.9 ± 8.6	<.0001
RAADS total	128 ± 35.1	50.3 ± 41.6	<.0001
SRS total	68.1 ± 9.8	51.0 ± 9.8	<.0001
BEQ – Negative Emotionality	22.1 ± 8.9	21.2 ± 6.0	.656
BEQ – Positive Emotionality	18.9 ± 5.7	21.2 ± 5.2	.142
BEQ – Impulse Strength	29.8 ± 9.3	26.0 ± 8.1	.132
BEQ – Emotional Expressivity	70.8 ± 20.0	68.4 ± 16.1	.638

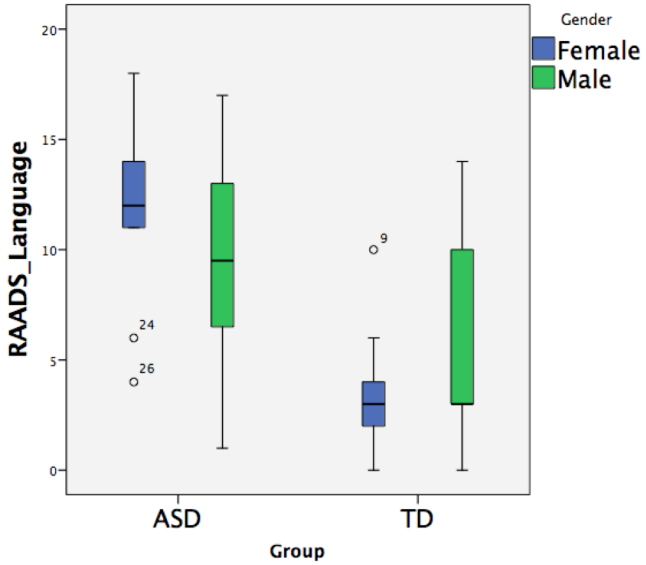
AQ Scores

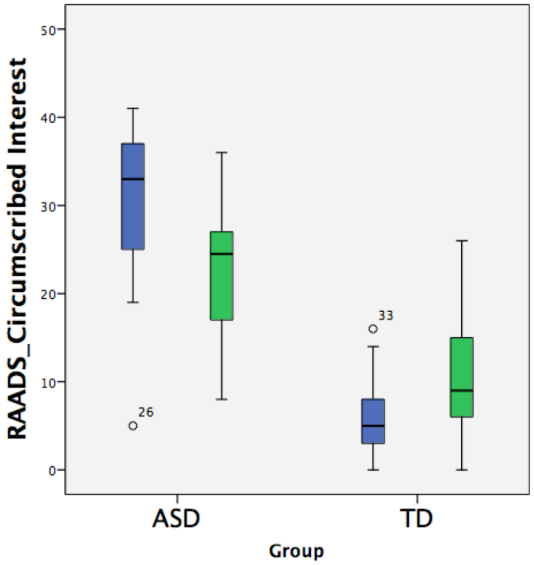


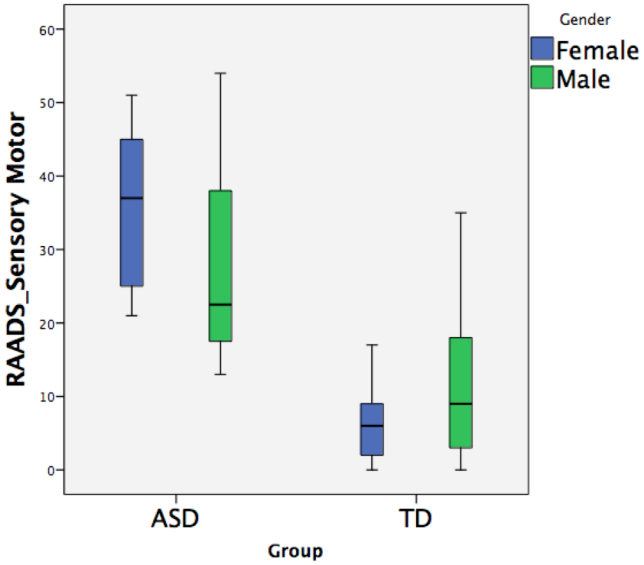
RAADS Scores





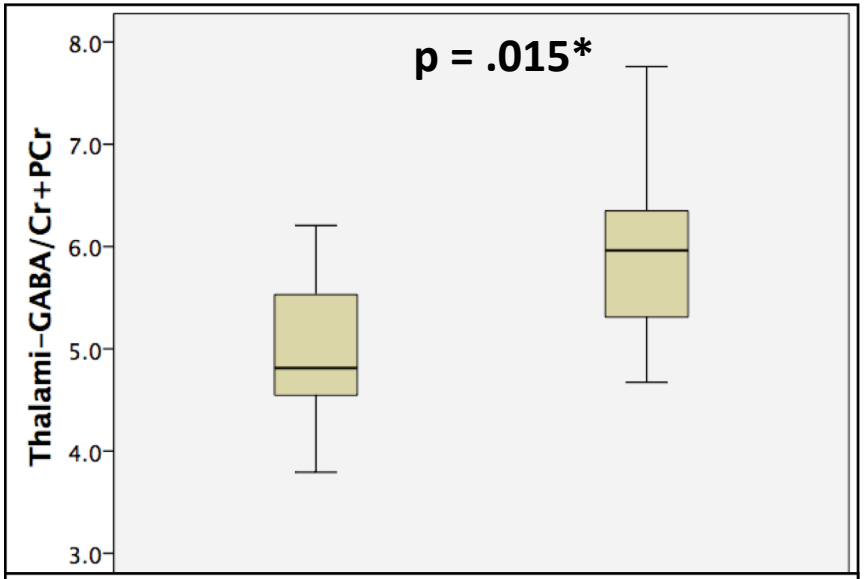


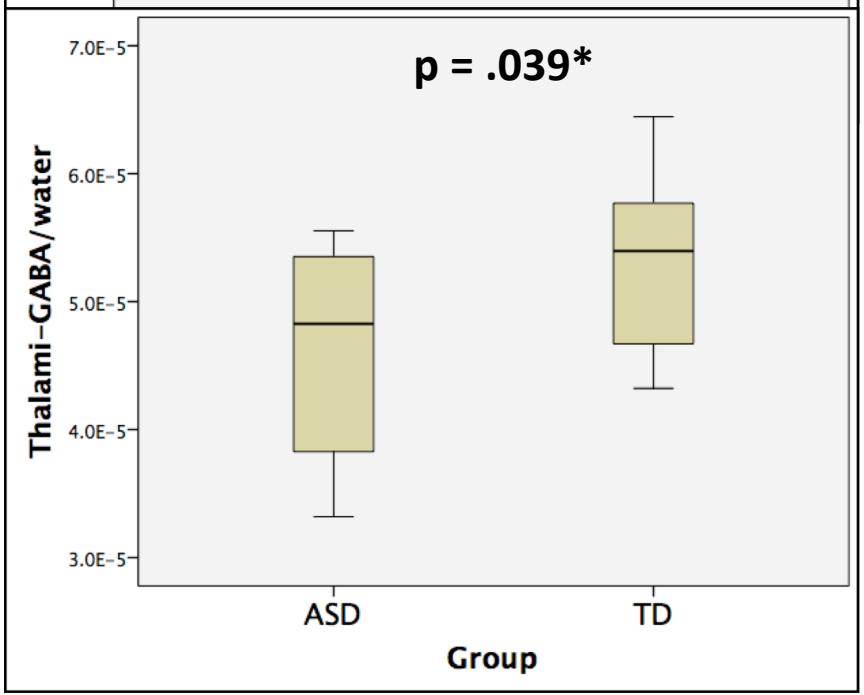




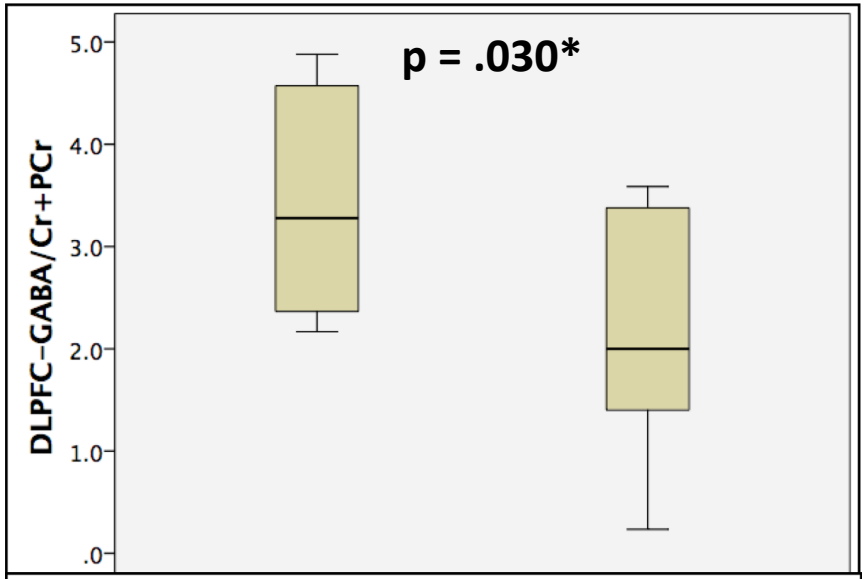
Aim 1: GABA levels in Male Participants

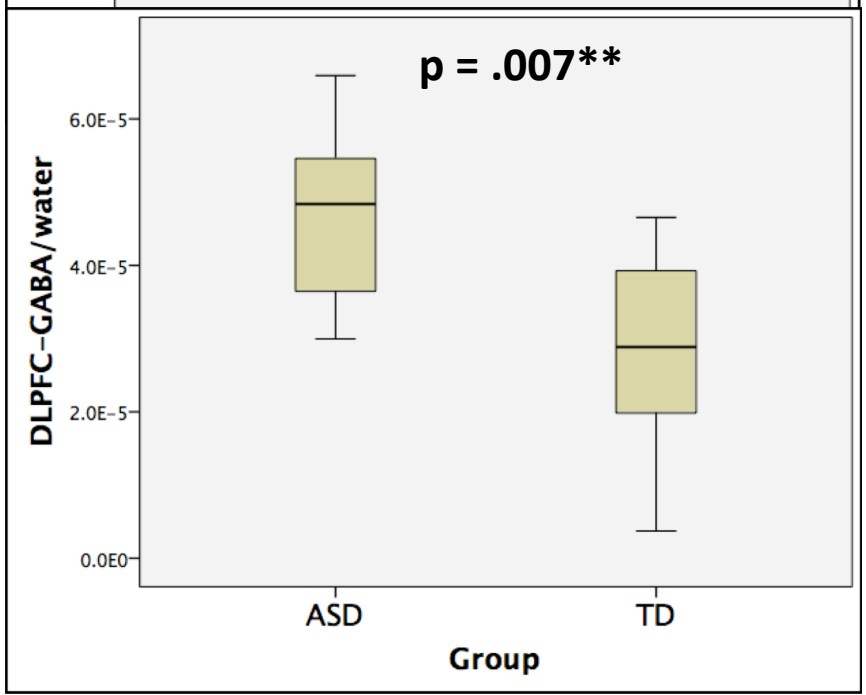
Thalami: TD > ASD





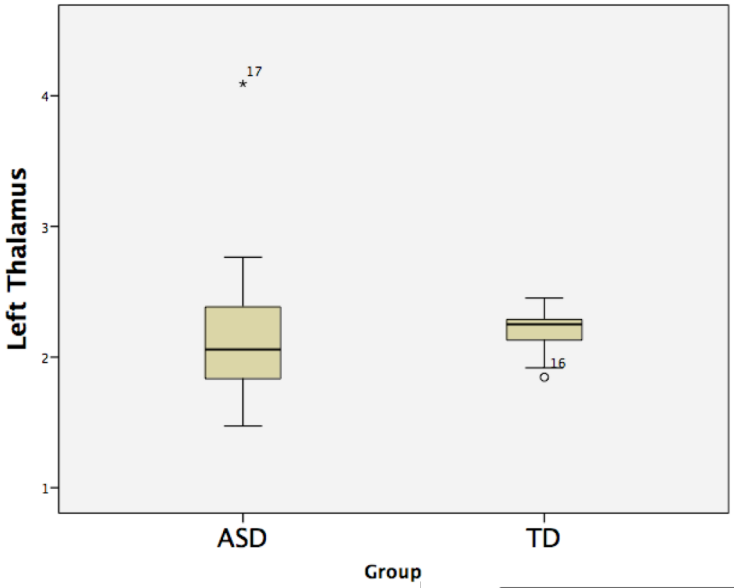
Left DLPFC: ASD > TD

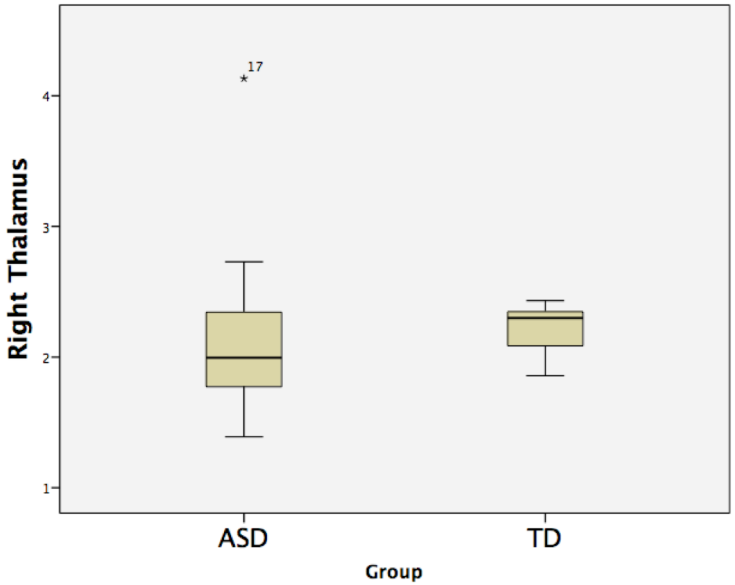


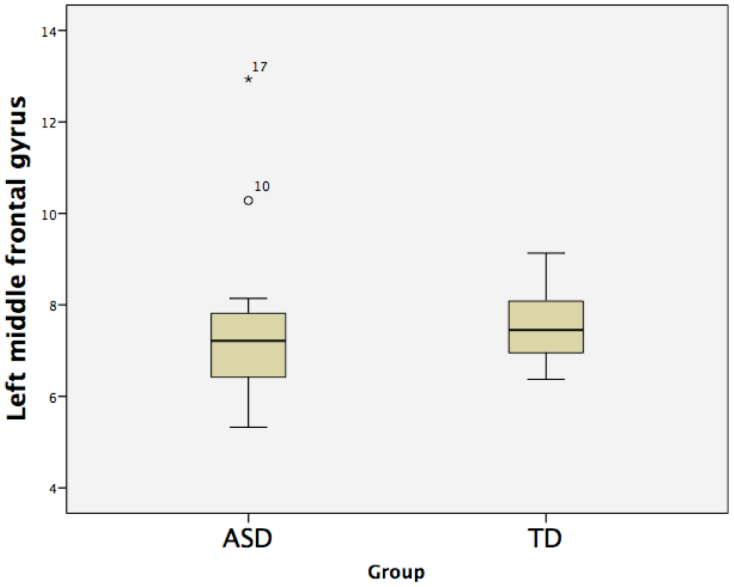


Aim 2: $GABA_A$ Receptor Binding Potential

- Lack of Group differences in BP_{ND}'s of all voxels of interest

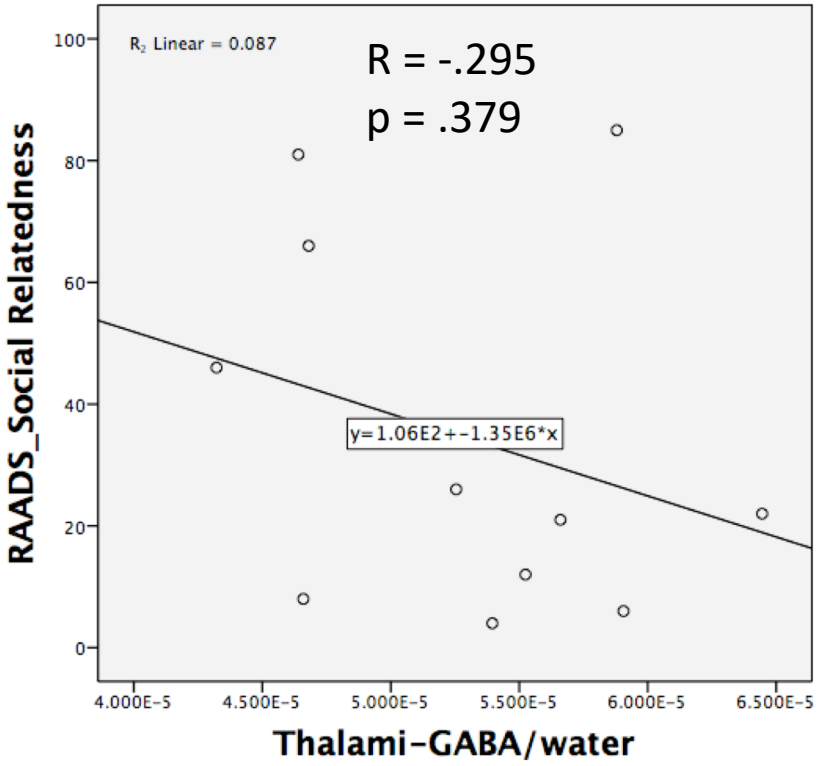


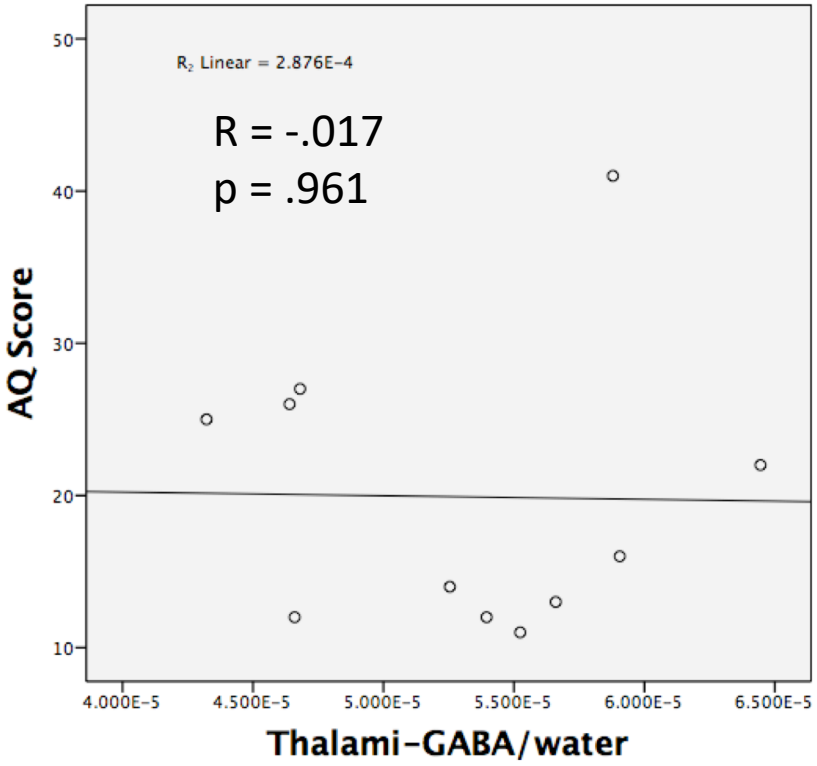




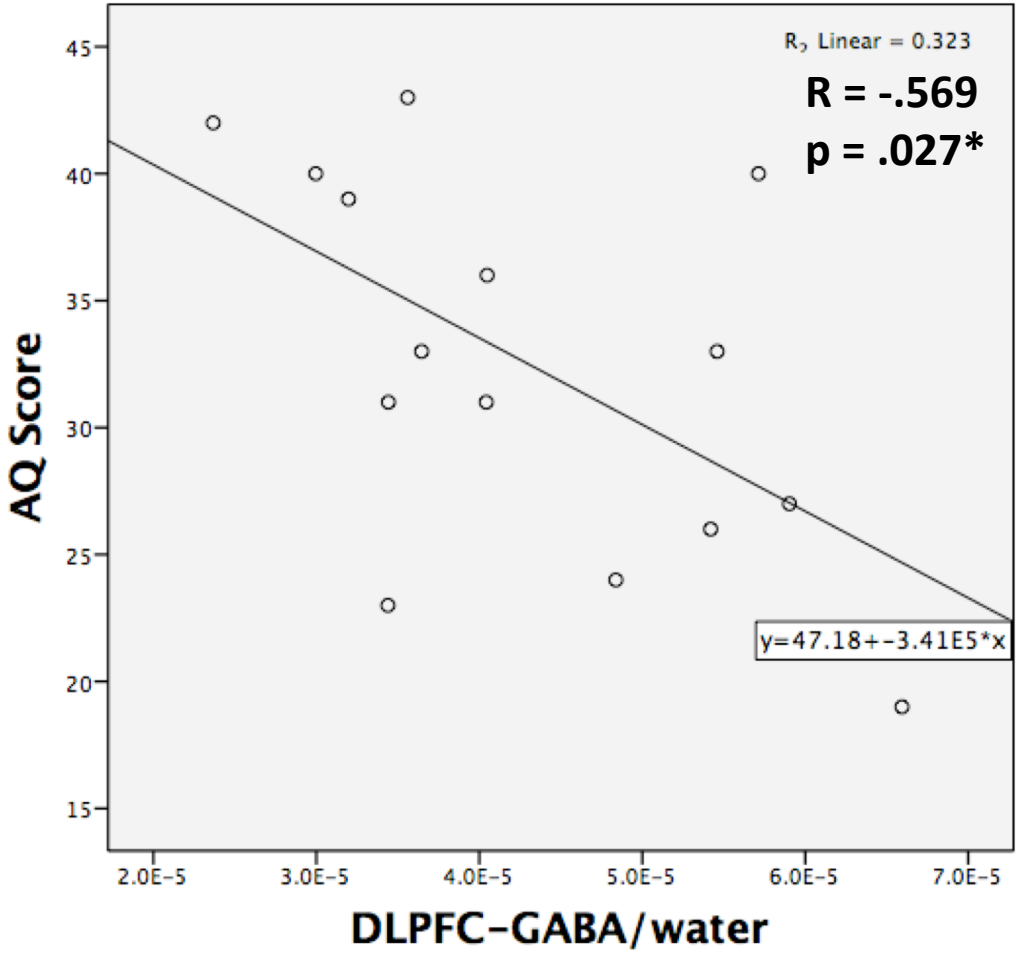
Aim 3: Correlations between GABA levels and Primary Social Functioning Measures – TD Participants ONLY

- No significant correlations

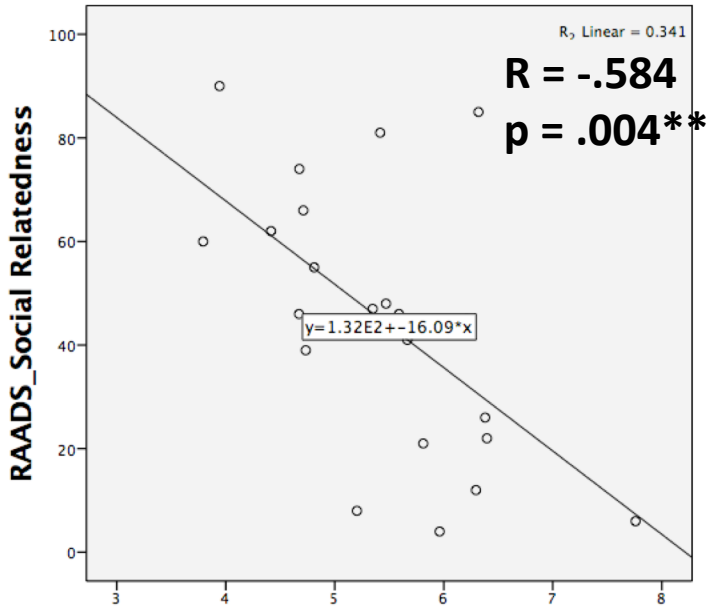


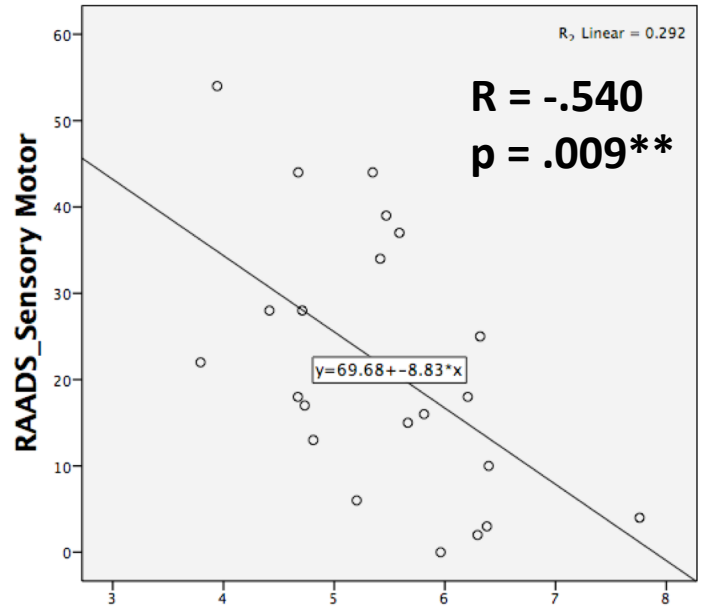


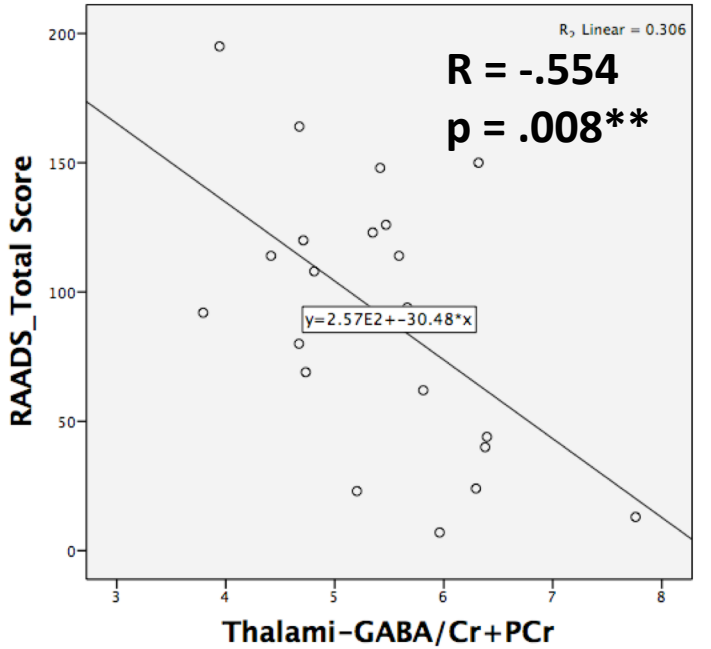
Aim 3: Correlations between GABA levels and Primary Social Functioning Measures – ASD Participants ONLY

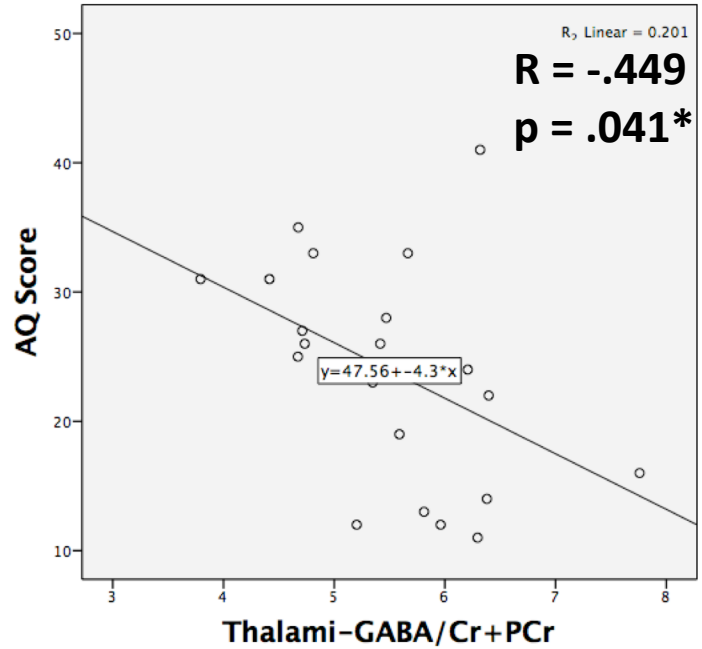


Aim 3: Correlations between GABA Levels and Primary Social Functioning Measures – MALE Participants ONLY

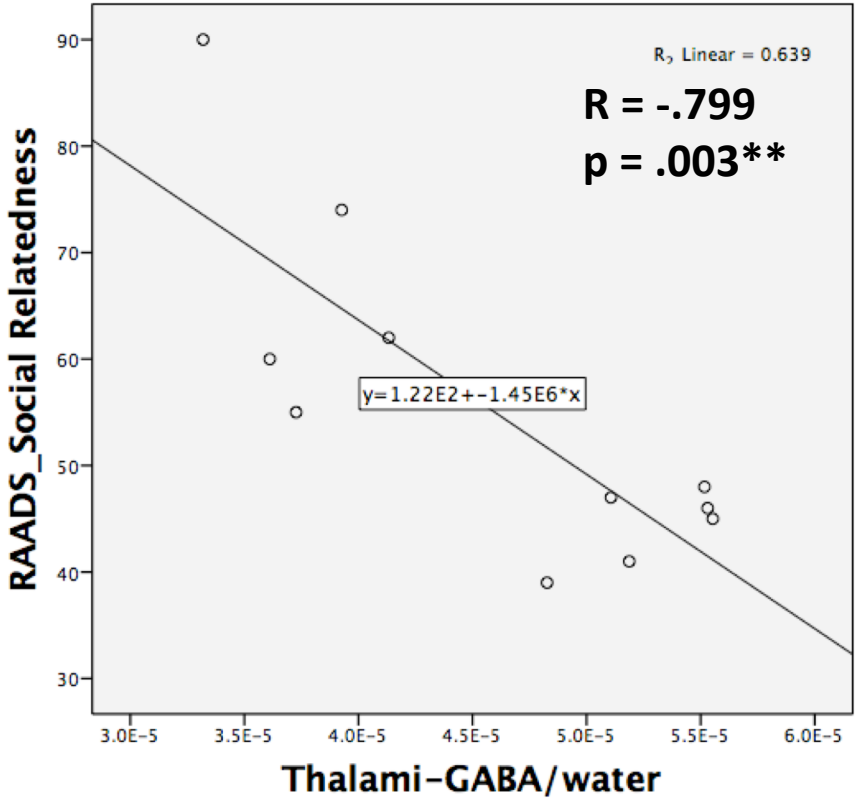


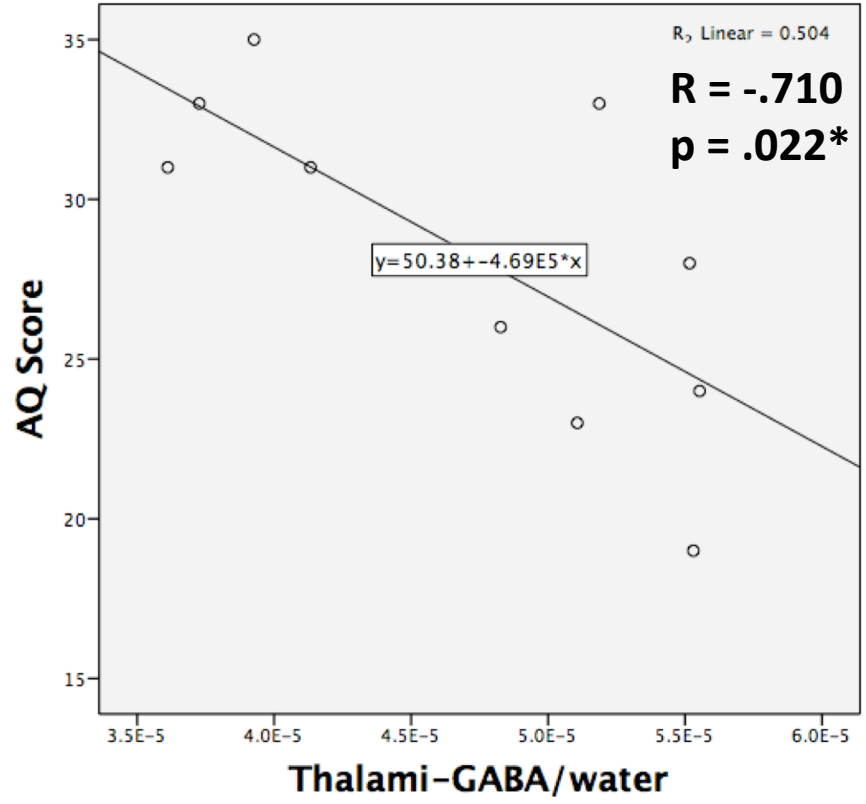






Aim 3: Correlations between GABA levels and Primary Social Functioning Measures – Male ASD Participants ONLY





CONCLUSIONS / DISCUSSIONS

Summary

- Region-specific differences in GABA levels between ASD and TD
  - Thalami: TD > ASD
  - Left DLPFC: ASD > TD
- No apparent differences in $GABA_A$ receptor density between ASD and TD.
- Correlations between GABA levels and socio-communicative function
  - In Male ASD, lower GABA levels in the thalami correspond to more socio-communicative deficits
  - In TD controls, GABA levels in the thalami do not correlate with socio-communicative function

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