SDSU Toddler MRI Project
Emerging Results

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Autism Spectrum Disorder (ASD)

- Prevalence: 1/54 (CDC, 2020)
- 5 years: median age of diagnosis in U.S.
Background

- Autism Spectrum Disorder = disorder of *brain development*
  - Brain markers are needed to
    -- understand the brain bases of ASD (basic science)
  -- improve diagnosis / enhance early detection
  -- develop *targeted* treatments
Autism and Brain Development Early in Life

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Human Brain Development
Neural Connections for Different Functions Develop Sequentially

- Sensory Pathways (Vision, Hearing)
- Language
- Higher Cognitive Function

-8 -7 -6 -5 -4 -3 -2 -1 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19

- Neurulation
- Neuronal Proliferation
- Neuronal Differentiation
- Neuronal Migration

- Synapse Formation
- Programmed Cell Death
- Synaptic Pruning
- Myelination
**SDSU Toddler MRI Project Aims**

**In search of early brain markers of ASD:**

**Aim:** to identify **early** brain markers of ASD that can guide diagnostic and intervention strategies

*Q: How do the organization and function of neural circuits in autism differ from the patterns observed in typical development?*
**SDSU Toddler MRI Project: Toddler Evaluations**

- ASD screening
  - M-CHAT
- Developmental Evaluation
  - Mullen Scales of Early Learning
  - Vineland-II
- ASD symptoms
  - ADOS-2
  - SCQ
  - ADI-R (for children > 36 months)
- Other Behavioral Concerns
  - CBCL

- Young children are recruited from many sites, including RCHSD ADI, DEC, Speech, and other developmental services
  
  *Dr. Themba Carr (RCHSD ADI) is a Co-Investigator*
  
  *Dr. Mikaela Kinnear (DEC) is a Co-Investigator*
SDSU Toddler MRI Project: Preparations for MRI

My Trip to Take a Picture of My Brain

Created By
Tamae Sugui & Sarah Reynolds
at the SDSU Center for Autism

A good brain picture takes a long time, so I will stay asleep when I go into the Space Machine. The scientists put headphones on my ears while I am asleep because the machine makes noise.

WHAT TO EXPECT AT AN MRI SCAN

Parent Guide

- Cube_T2.wav
- HCP_DTI.wav
- HCP_EPI_fMRI.wav
- localizer.wav
- MPRAGE_PROMO.wav
- SE_topup.wav
SDSU Toddler MRI Project: Bedtime Scans...
SDSU Toddler MRI Project: Bedtime Scans…
<table>
<thead>
<tr>
<th></th>
<th>ASD (n = 81)</th>
<th>TD (n = 47)</th>
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<tr>
<td></td>
<td>Mean ± SD (Min - Max)</td>
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</tr>
<tr>
<td>Age at 1st Visit (months)</td>
<td>34.2 ± 12.7 (17 - 63)</td>
<td>29.3 ± 15.1 (15 - 64)</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>63/18 (78%/22%)</td>
<td>25/22 (53%/47%)</td>
</tr>
<tr>
<td>Gestational Age at Birth (weeks)</td>
<td>38.9 ± 2.2 (34 - 43)</td>
<td>39.7 ± 1.1 (37 - 42)</td>
</tr>
<tr>
<td>SCQ</td>
<td>15.9 ± 7.4 (3 - 35)</td>
<td>4.7 ± 3.2 (0 - 11)</td>
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<tr>
<td>ADOS-2</td>
<td></td>
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<tr>
<td>Toddler Module, Total</td>
<td>16.4 ± 5.5 (7 - 25)</td>
<td>--</td>
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<tr>
<td>Module 1, Total</td>
<td>15.4 ± 5.7 (7 - 26)</td>
<td>--</td>
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<tr>
<td>Module 1, Comparison Score</td>
<td>6.0 ± 2.0 (3 - 10)</td>
<td>--</td>
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<tr>
<td>Module 2, Total</td>
<td>12.7 ± 4.2 (8 - 16)</td>
<td>--</td>
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<tr>
<td>Module 2, Comparison Score</td>
<td>5.3 ± 1.8 (2 - 9)</td>
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SDSU Toddler MRI Project: First Results

Delayed development (behaviorally) across multiple domains:

Mullen Scales of Early Learning

Vineland Adaptive Behavior Scales

ASD    TD
SDSU Toddler MRI Project: First Results

**Observed Associations:** ASD symptoms are associated with language skills

expressive language, age-equivalent scores

ados-2 total by mullen el ae

ados-2 total by mullen rl ae

r = -0.61

r = -0.66

N_{ASD}=75
SDSU Toddler MRI Project: First Results

Weaker relationship between age and language skills in ASD

- Mullen EL AE by Child's Age, ASD
  - $r = 0.61$

- Mullen EL AE by Child's Age, TD
  - $r = 0.90$

- Mullen RL AE by Child's Age, ASD
  - $r = 0.60$

- Mullen RL AE by Child's Age, TD
  - $r = 0.88$

$N_{ASD} = 75, N_{TD} = 46$
Autism and Brain Development Early in Life

**Early Signs of Autism**

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**Human Brain Development**

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FIRST YEAR

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Gao et al. (2015)
Autism and Brain Development Early in Life

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**Human Brain Development**

Neural Connections for Different Functions Develop Sequentially

![Graph showing human brain development stages](image)

Gao et al. (2015)
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Gao et al. (2015)
SDSU Toddler MRI Project: First Results

Most functional networks are detected in ~18-45 months old children

Figure from Chen et al. 2020 *JCPP*
SDSU Toddler MRI Project: First Results

Disrupted connectivity in sensory brain circuits

Chen et al. (2020)
SDSU Toddler MRI Project: First Results

Associations with autism symptoms

Chen et al. (2020)
SDSU Toddler MRI Project: First Results

Delayed brain network maturation

Chen et al. (2020)
SDSU Toddler MRI Project: First Results

Summary of the neuroimaging findings thus far

• Atypical connectivity patterns of the sensory networks in ASD
  – Greater connectivity (= reduced differentiation) between visual and motor regions is associated with greater autism symptoms
  – Differential age trajectory of between-network connectivity suggests delayed network maturation

• Implications
  – May be related to sensory processing abnormalities in ASD
  – Sensory processing difficulties can have downstream effect on problems in language and social skills
**SDSU Toddler MRI Project**

**Socioeconomic Status (SES) and Development in ASD**

- SES = Multifactorial construct characterizing individuals’ access to material and social resources (Adler & Newman, 2002)

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<tr>
<th>Economic Stability</th>
<th>Neighborhood and Physical Environment</th>
<th>Education</th>
<th>Food</th>
<th>Community and Social Context</th>
<th>Health Care System</th>
</tr>
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<tbody>
<tr>
<td>Employment</td>
<td>Housing</td>
<td>Literacy</td>
<td>Hunger</td>
<td>Social Integration</td>
<td>Health Coverage</td>
</tr>
<tr>
<td>Income</td>
<td>Transportation</td>
<td>Language</td>
<td>Access to Healthy Options</td>
<td>Provider Availability</td>
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<tr>
<td>Expenses</td>
<td>Safety</td>
<td>Early Childhood Education</td>
<td>Support Systems</td>
<td>Provide Linguistic and Cultural Competency</td>
<td></td>
</tr>
<tr>
<td>Debt</td>
<td>Parks</td>
<td>Education</td>
<td>Social Integration</td>
<td>Quality of Care</td>
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<tr>
<td>Medical Bills</td>
<td>Playgrounds</td>
<td>Vocational Training</td>
<td>Community Engagement</td>
<td></td>
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<tr>
<td>Support</td>
<td>Walkability</td>
<td>Higher Education</td>
<td>Discrimination</td>
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<td></td>
<td>Zip Code/Geography</td>
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<td>Stress</td>
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Artiga et al., 2020
Socioeconomic Status (SES) and Development: Background

Mean number of spoken words:
Vocabulary (CDI)

Fernald et al. 2013
*Dev Sci*
Hanson et al. (2013)
Early associations between SES and developmental skills are not immutable or determinative, especially in early childhood
SES and ASD: Background

• Low SES associated with later age of diagnosis (Dickerson et al., 2016)

• Low SES → Reduced access to early intervention

• Low SES associated with higher rates of comorbid intellectual disability (Delobel-Ayoub et al., 2015)
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Distribution of SES variables in our Sample

a) b) c)

- **Mean Parental Education Level**
- **Income:Needs Ratio**
- **Median Income (Postal Code) x 10^4**

- **TD**
- **ASD**
- **Combined Sample**
Geographic Distribution of Participants

San Diego County | SDSU Center for Autism: Participant Distribution

Toddler Clients
Instances
0
1
2
3 - 4
5 - 6
7 - 8

Map By: Christian Mejia
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Associations between SES variables and (Pre)-Language Skills in early childhood

a) MSEL EL T-score vs. Vineland RL v-score
b) MSEL EL T-score vs. Vineland RL v-score
c) INR by Exp. Lang. (Mullen)
d) MSEL EL T-score vs. Vineland RL v-score
e) MSEL EL T-score vs. Vineland RL v-score

MEL: Maternal Education Level
INR: Income-to-needs ratio

Olson et al. (2019)
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Associations between SES variables and Parental Stress

Caregiver Stress by Income-to-Needs Ratio
Neural Correlates of Language: Background

- Language in the brain:
  - Perisylvian regions
    - Temporal and inferior frontal cortices
  - Broca’s Area: speech production
  - Wernicke’s Area: receptive language / comprehension

- Increasingly left-lateralized throughout development (Berl et al., 2014)

Dickerson, 2019
Preliminary Results:
Associations between SES variables and Functional Connectivity in Language Regions

Herringshaw et al. (2016)
Both ASD and low SES pose vulnerabilities for language emergence and development.

Lower SES children are largely understudied in the context of ASD developmental and neuroimaging research.

Plasticity in neurodevelopment → Promising window for early intervention.
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Future Directions

• Longitudinal follow-ups
• Exploring co-occurring symptoms
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Questions?