Why Develop Language Resources for Autism?

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3rd International Symposium on Linguistic Diversity, Language Resources and Clinical Research

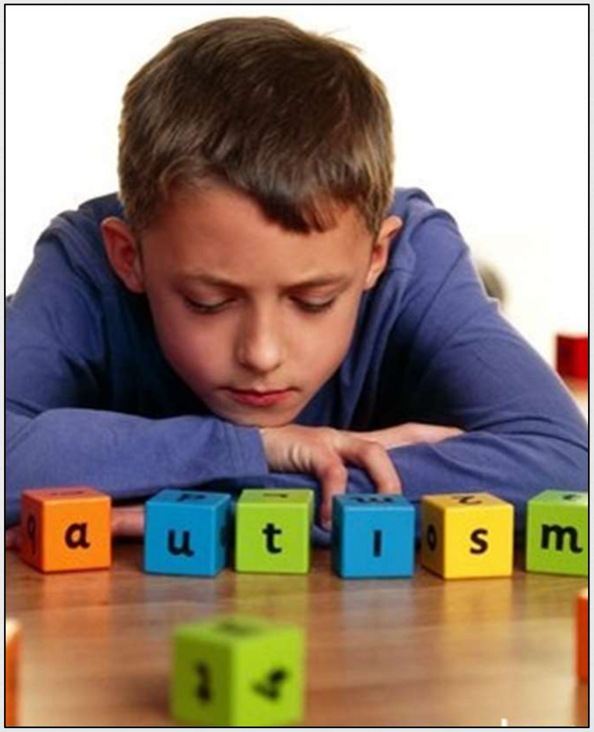
November 10, 2020

Penn Medicine

Children's Hospital of Philadelphia
RESEARCH INSTITUTE

Today's talk

- Autism Spectrum Disorder (ASD)
  - Overview
  - Why we need large shared resources
- A new kind of measurement
- Example results



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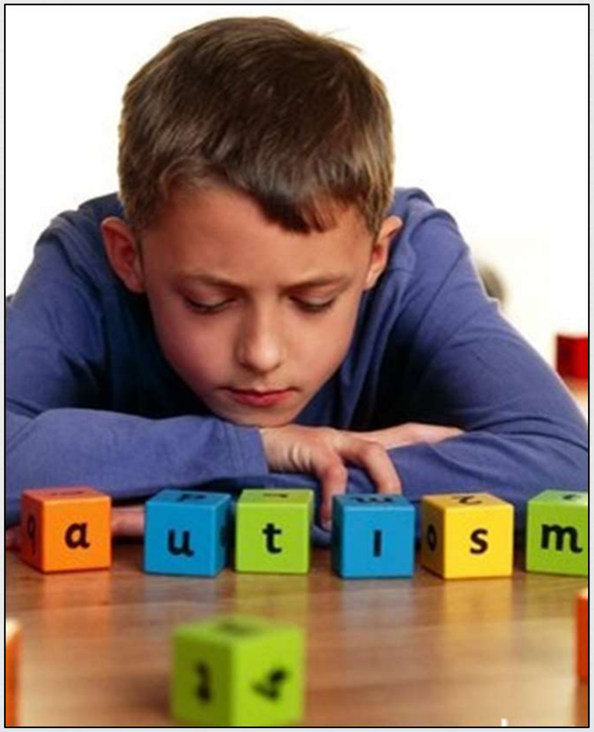
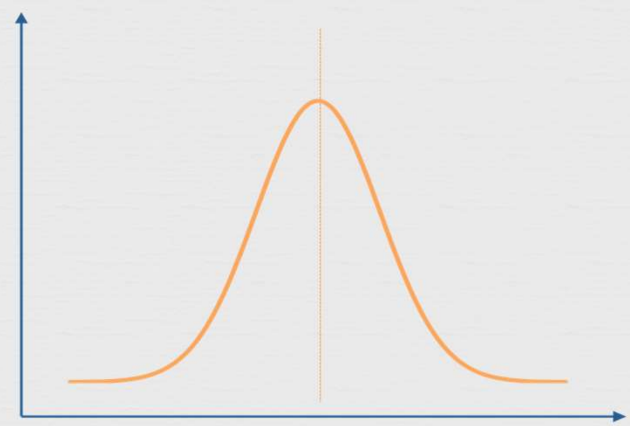


What is autism?

- Neurodevelopmental condition

- Behaviorally defined
  - Diagnosed using ***behavior only***
  - No genetic test
  - No brain scan



- Symptom severity lies on a continuum - <u>A</u>utism <u>S</u>pectrum <u>D</u>isorder

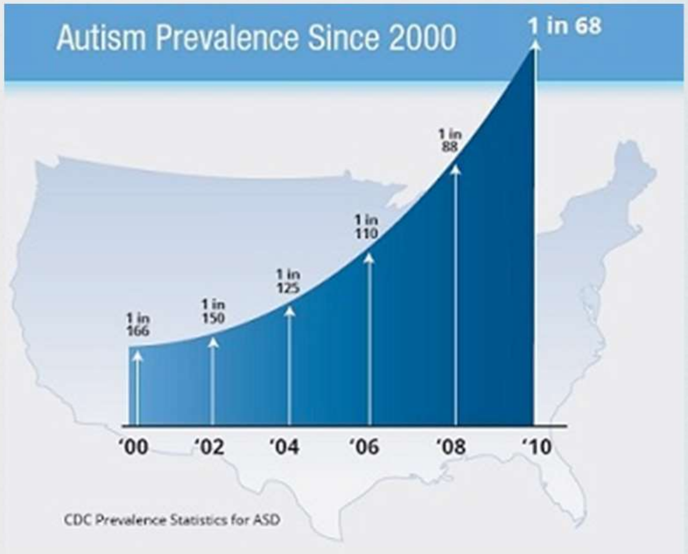
Core features

- **Impaired social communication**
- **Repetitive behaviors and restricted interests**
  - Present since early childhood
  - Interferes with everyday functioning

Who has autism?

- Estimated prevalence approximately 1-1.5%
  - 1 in 54 U.S. school children (CDC, 2020)

- ~4:1 boy:girl ratio
  - Traditionally thought to vary with IQ



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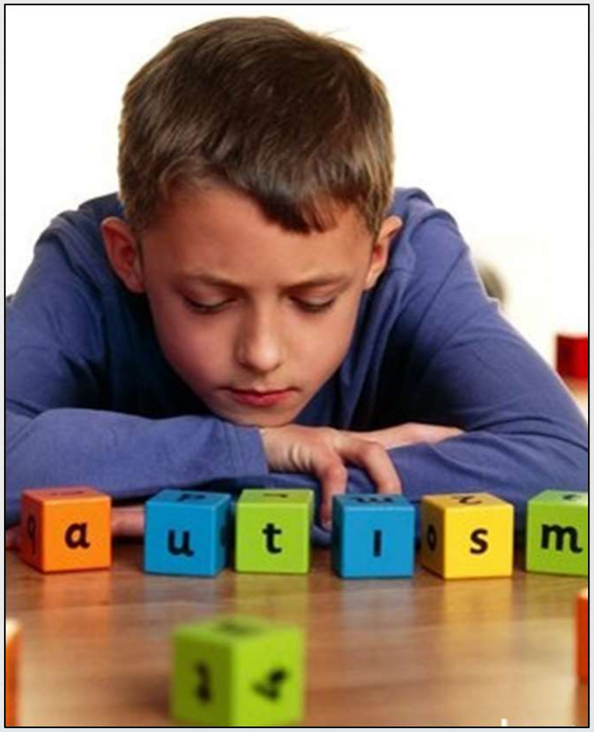
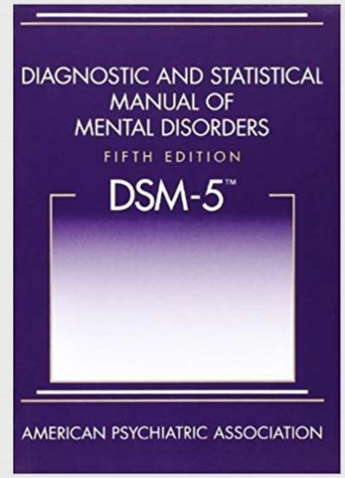


Why do we need large shared resources?
1. **Diagnosis is expensive and difficult**

- "Gold Standard" in the U.S. – expert clinician consensus
  - Autism Diagnostic Observation Schedule (ADOS)

- Based on <u>observable behavior</u> using <u>human judgment</u>

- <u>Problem</u>: imperfect agreement (kappa = .69)



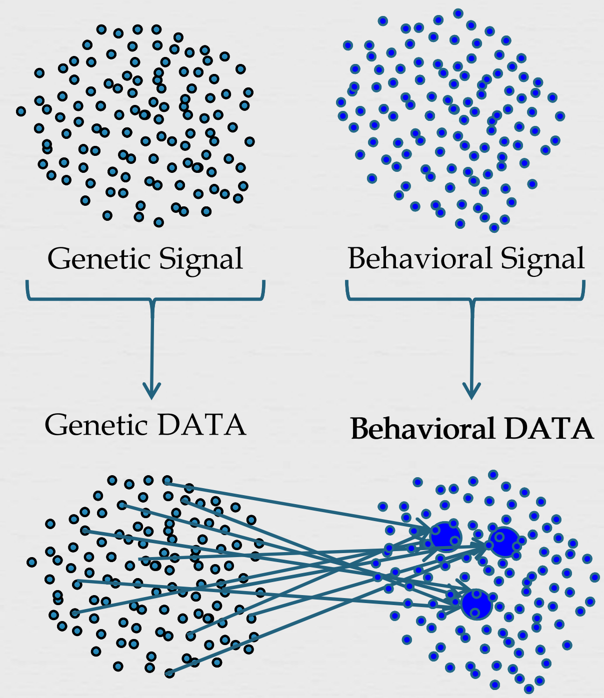
Why do we need large shared resources?
2. **Extreme phenotypic heterogeneity**

- **Heterogeneity**
  - Symptoms vary *between* individuals
  - Symptoms vary *within an individual* over the course of a lifetime
  - …and sometimes over the course of a day, or an hour!

- **Common co-occurring conditions -** ASD rarely occurs alone
  - Seizures, anxiety, ADHD, OCD, Tourette syndrome, language disorders, learning disorders, intellectual disability

Why do we need large shared resources?
3. Insufficiently granular measurement

- Current diagnosis and characterization methods are:
  - Expensive – small samples
  - Complicated, time-consuming
  - Rely on human judgment of behavior



- Mismatch
  - Rich genetic or imaging data maps to restricted yes/no dx category

- Need: highly quantifiable, fine-grained signal that is robust to practice effects

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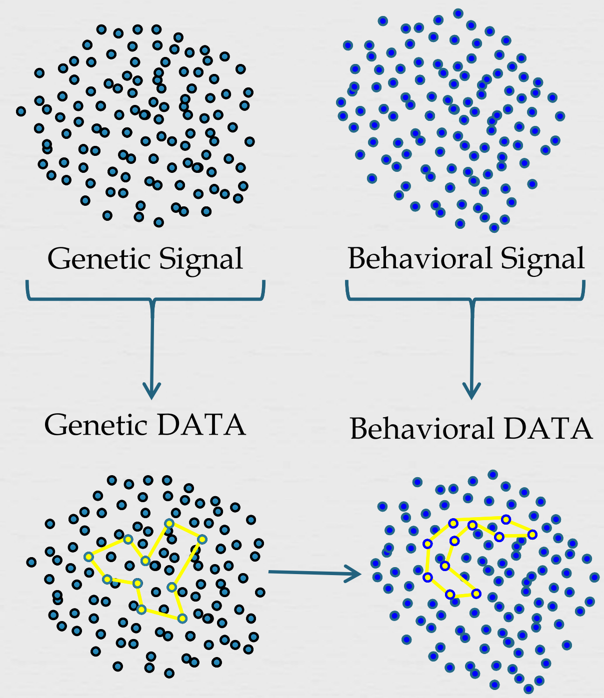

Behavioral heterogeneity + small samples + poor measurement =

less-reproducible scientific results
suboptimal evidence base for interventions
worse outcomes

How to quantify autism?

- Autism manifests in the context of live social interaction (2 people)

- **Need:** High-dimensional, scalable method to capture time-synced human signals from interacting partners

- *Result: Precise behavioral characterization of two interacting systems*

Quantifying social interaction

- Turn social interaction into *numbers*
- What you **do** (motor) and what you **say** (language)
  - <u>Motor</u>: computer vision
  - <u>Language</u>: computational linguistics

Analyzing the vocal signal: Challenges

- Language is highly <u>multivariate</u> (acoustics, words, grammar, conversational dynamics)

- "Normal" <u>changes across development</u> and sometimes <u>across cultures</u>

- Neurodevelopmental/psychiatric conditions have <u>different profiles</u>
  - *Opportunity* to create personalized profiles with different treatment indications

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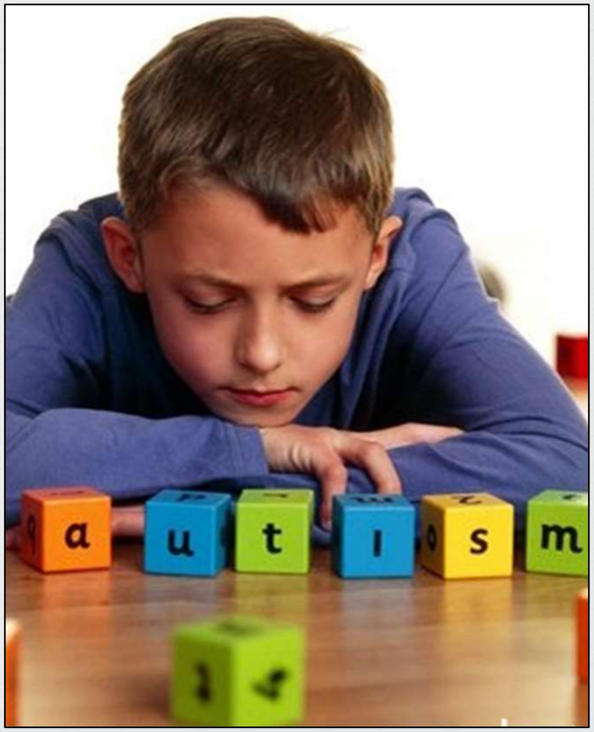


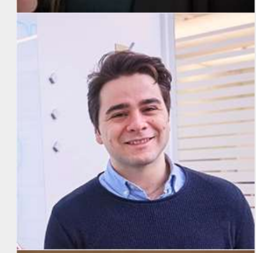
Dyadic biosensor

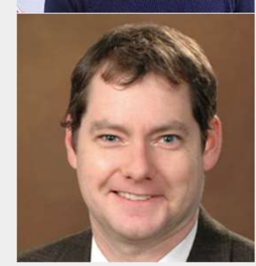
U.S. patent pending, J. Parish-Morris (Co-Inventor)

Keith Bartley

Bob Schultz

- Multi-channel directional microphones for automated analyses
- Video, audio, heart rate, skin conductance, accelerometers
- "Shovel ready" for machine learning





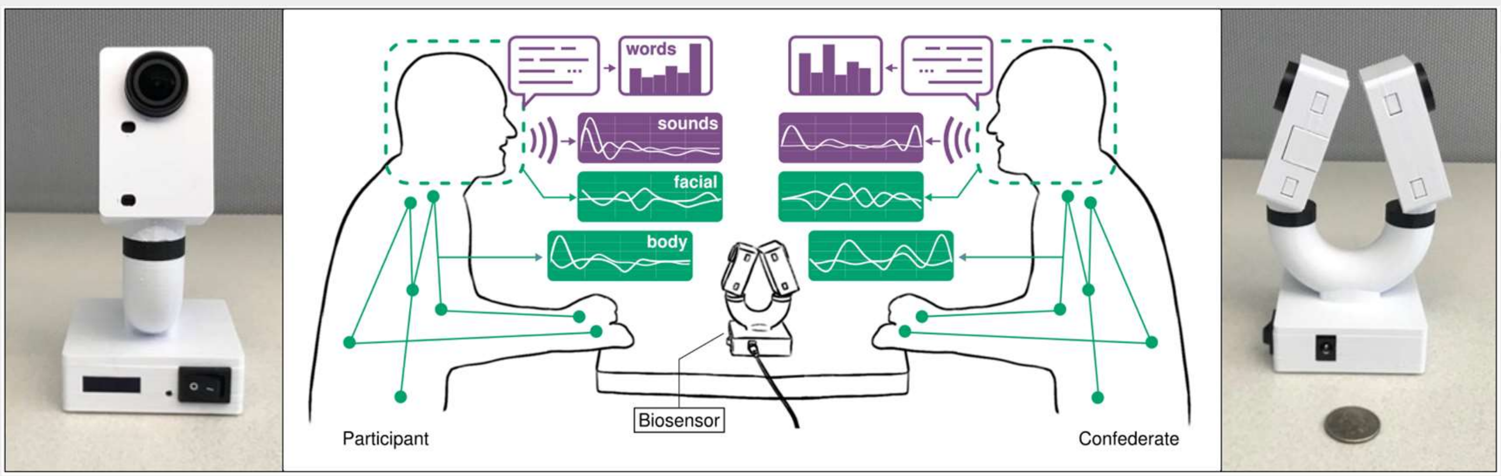


Fig.1 The Biosensor captures everything participants say and do with perfect synchronization.

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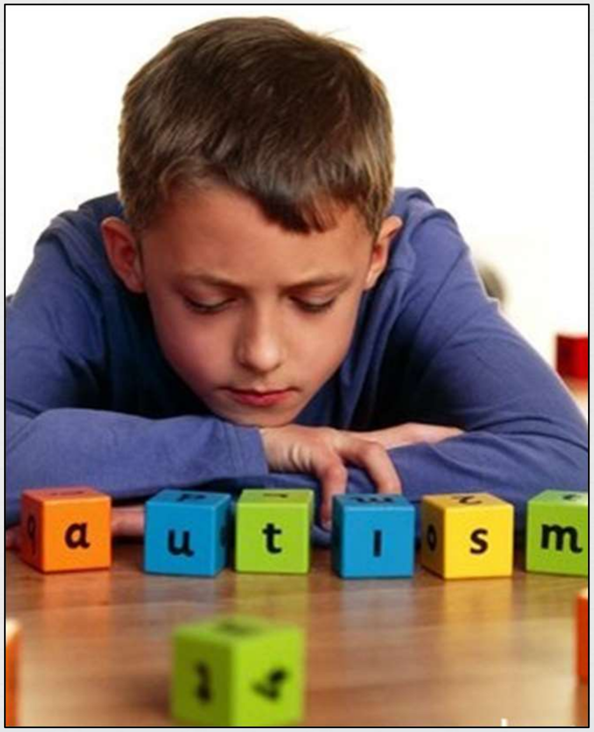


Example Study

Goal: Quantify restricted/repetitive behavior during naturalistic conversation using *computational linguistics* and *computer vision*

Compare behavioral diversity/entropy in adults with and without ASD in the domains of:

1. Language
2. Oral-motor movement

Participants

- Forty-four consenting adults, all native English speakers
  - Autism Spectrum Disorder (ASD): N=17
  - Typically developing (TD): N=27
- Diagnosed using according to DSM-5 criteria, informed by the Autism Diagnostic Observation Schedule – 2nd Edition[1]

Variable	ASD Mean (SD)	TD Mean (SD)	Statistics	p-value
Age (years)	26.9 (7.3)	28.1 (8.4)	W = 234	0.923
Sex (Male, Female)	15, 2	23, 4	χ^2: 0.08	0.774
Full-Scale IQ	102.1 (19.8)	111.7 (9.5)	W = 157	0.080
Verbal IQ	112.6 (22.1)	112.4 (11.2)	W = 215	0.736
ADOS Total	13.1 (3.0)	1.1 (0.9)	W = 442	< 2e-8*
ADOS Social Affect	9.8 (2.3)	1.0 (0.9)	W = 442	< 1e-8*
ADOS RRB	3.3 (1.5)	0.1 (0.3)	W = 441	< 1e-9*

1. Lord, C., Rutter, M., DiLavore, P. C., Risi, S., Gotham, K., & Bishop, S. (2012). Autism diagnostic observation schedule–Second edition (ADOS-2). *Los Angeles: Western Psychological Services*.

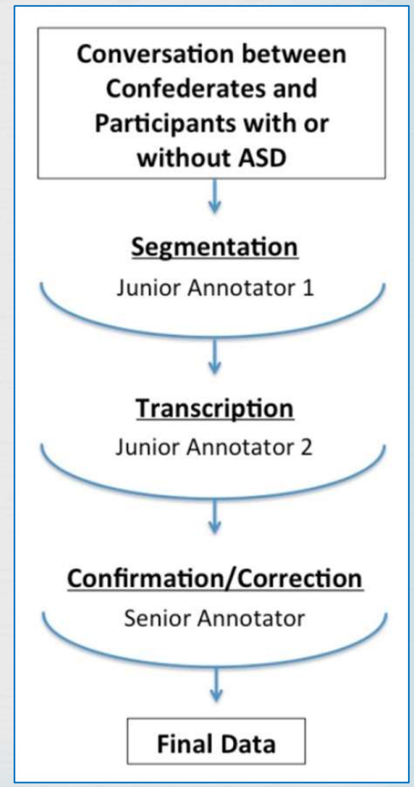
Paradigm

- Contextual Assessment of Social Skills (CASS)[1]
- 3-minute semi-structured assessment of conversational ability designed to mimic real-life first-time encounters
  - Framed as "getting to know each other"; no specific prompts provided
- CASS confederates:
  - 10 undergraduate students or BA-level research assistants
  - Trained to speak for no more than 50% of the time
  - Wait 10s to initiate the conversation; wait 5s before re-initiating conversation after pauses

1. Ratto, A. B., Turner-Brown, L., Rupp, B. M., Mesibov, G. B., & Penn, D. L. (2011). Development of the contextual assessment of social skills (CASS): A role play measure of social skill for individuals with high-functioning autism. *Journal of autism and developmental disorders*, *41*(9), 1277-1286.

Lexical pipeline

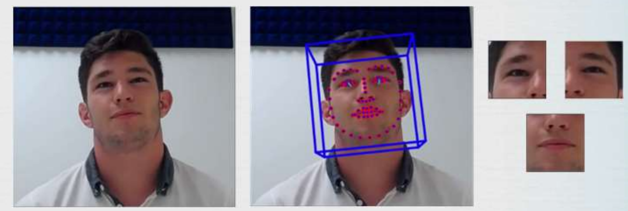
- Verbatim, orthographic, time-aligned transcription of utterances by participant and confederate
- Reliable, blinded annotators using Xtrans[1]
- All spoken words included, no stemming, stopwords remain
  - Diversity includes morphological differences like "want" and "wanted"
- Total word count and entropy calculated per speaker using qdap[2]

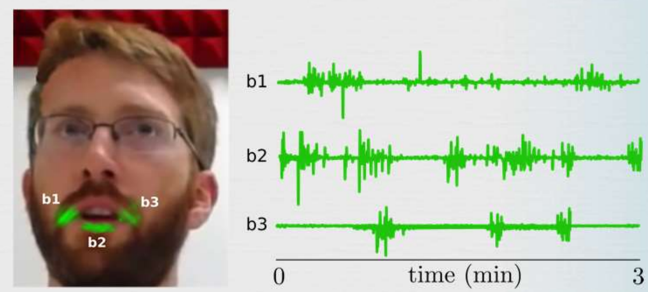


1. Glenn, M. L., Strassel, S. M., & Lee, H. (2009). XTrans: A speech annotation and transcription tool. In *Tenth Annual Conference of the International Speech Communication Association*.
2. Rinker, T. W. (2017). qdap: Quantitative Discourse Analysis Package. 2.3.0. Buffalo, New York. http://github.com/trinker/qdap

Oral-motor pipeline

- 3 steps: Face detection, face registration, and movement quantification
- Detection and localization of landmarks (eyes, lip corners, nose etc.)
  - Publicly available tool (OpenFace)[1]
- Registration
  - Part-based registration[2]
  - Video stabilization to eliminate jitter
- Quantification
  - Facial Bases method[3]
  - 60 mouth bases
  - Normalized the total activation count of each basis by the maximum count observed for the same basis of confederates





1. Baltrušaitis, T., Zadeh, A., Lim, Y.C. & Morency, L.P.(2018). OpenFace 2.0: Facial Behavior Analysis Toolkit, *IEEE International Conference on Automatic Face and Gesture Recognition.*
2. Sariyanidi, E., Gunes, H., & Cavallaro, A. (2015). Automatic analysis of facial affect: A survey of registration, representation, and recognition. *IEEE transactions on pattern analysis and machine intelligence*, *37*(6), 1113-1133.
3. Sariyanidi, E., Gunes, H., & Cavallaro, A. (2017). Learning bases of activity for facial expression recognition. *IEEE Transactions on Image Processing*, *26*(4), 1965-1978.

Statistical approach

- Entropy: the amount of information a data modality carries
- Shannon entropy[1] where *b* is the base of the logarithm (*b*=2; our measure of entropy is in bits)

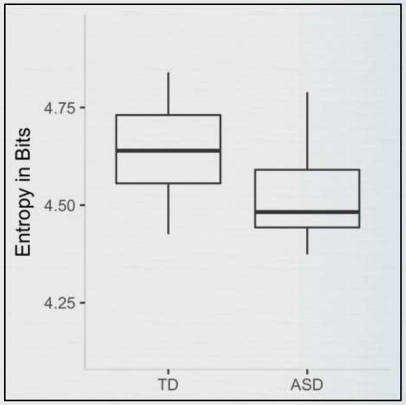
$$H = -\sum_{i=1}^{n} p(x_i) \log_b p(x_i)$$

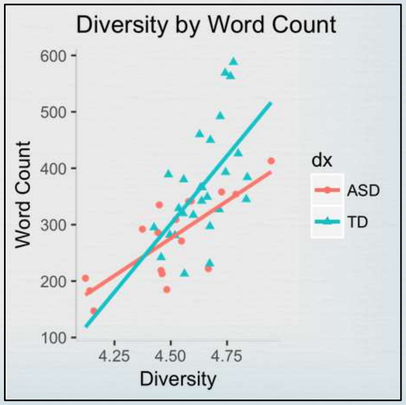
  - **High entropy** is expected when participants make a rich set of facial expressions and produce a variety of words while speaking
  - **Low entropy** is expected when participants generate a restricted set of mouth movements and produce repetitive speech patterns
- Tests:
  - Wilcoxon rank sum tests with continuity correction; exploratory correlation analyses
  - Linear mixed models (lme4) or simple linear models in R
    - ✓ Random effects of confederate identity and fixed effects of sex, age, and IQ checked for significance; excluded when non-significant
    - ✓ Facial analyses included speaking length and head motion as covariates

1. Cover, T. M., & Thomas, J. A. (2012). *Elements of information theory*. John Wiley & Sons.

Results: Lexical entropy

- Reduced entropy in participants with ASD as compared to TD participants, $t(42)=2.85$, $p=0.007$, Cohen's $d=0.82$
  - The effect of diagnosis on entropy was significant after accounting for age, IQ, and gender, $t(39)=3.25$, $p=0.002$
  - Diversity of confederate language did not differ by participant diagnosis, $t(35.26)=0.17$, $p=0.86$
- There was a (neurotypical) association between word count and entropy[1,2]
  - A second model tested the interactive effect of word count and diagnosis on participant lexical diversity
- The slope of the relationship between word count and diversity was greater in the TD group than the ASD group, interaction $t=-3.51$, $p=0.001$*

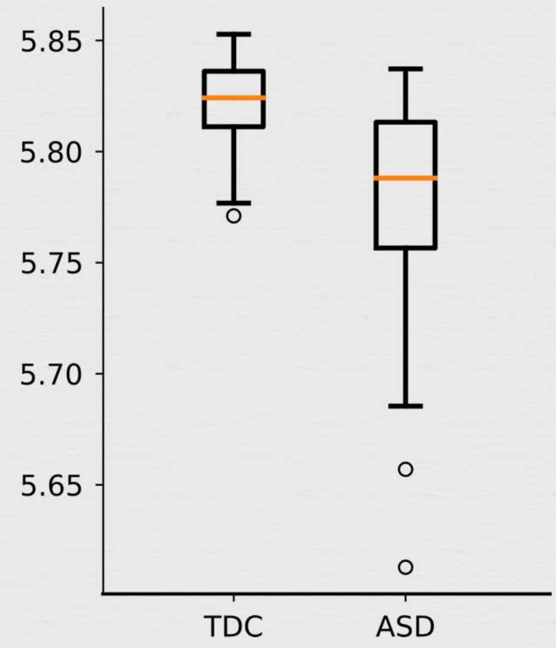




1. Shannon, C. E. (1951). Prediction and entropy of printed English. *Bell Labs Technical Journal*, *30*(1), 50-64.
2. Witten, I. H., & Bell, T. C. (1990). Source models for natural language text. *International Journal of Man-Machine Studies*, *32*(5), 545-579.

Results: Oral-motor entropy

- Reduced mouth movement diversity in the ASD group as compared to the TD group (Cohen's d=1.0, t=-2.73, p=0.009)
  - Model included head movement and speech length as covariates
  - Difference remained significant when age, sex, and IQ were included as covariates (Cohen's d=1.0, t=-2.52, p=0.016)
  - No covariates contributed significantly to the model



Discussion

- **Take home:** Reduced behavioral diversity, across domains, captures an underlying dimension of restriction and repetition that distinguishes autistic adults from typical controls

- Restriction in mouth movement (motor) not driven by restriction in words produced (cognitive) – uncorrelated – contributing unique variance

Future Research

- **Build** a large, shared resource of ASD conversations at LDC to accelerate the pace of discovery
- **Test** real-world effects of subtle linguistic differences in ASD (e.g., likelihood of referral, peer friendships)
- **Explore** linguistic markers of complex phenotypes (e.g., depression, ASD + anxiety, ASD + depression or ADHD)
- **Develop** targeted social communication interventions that are *personalized* for the unique challenges faced by a given individual


THANK
YOU

Acknowledgements

- Participants and families
- CAR clinicians, students, and staff

- Key collaborators:
  - Bob Schultz, Director of CAR
  - Mark Liberman & Chris Cieri & Sunghye Cho, LDC @ Upenn
  - Clare Harrop, UNC Psychiatry
  - Joe Donaher, CHOP Center for Childhood Communication
  - Ani Nenkova, UPenn Computer & Information Science
  - Ted Brodkin, UPenn Psychiatry
  - Jami Young, CHOP PolicyLab

- Funding sources
  - Autism Science Foundation
  - McMorris Family Foundation
  - NIMH R01, NIDCD R03, Roche Ltd, CHOP RI, EAC