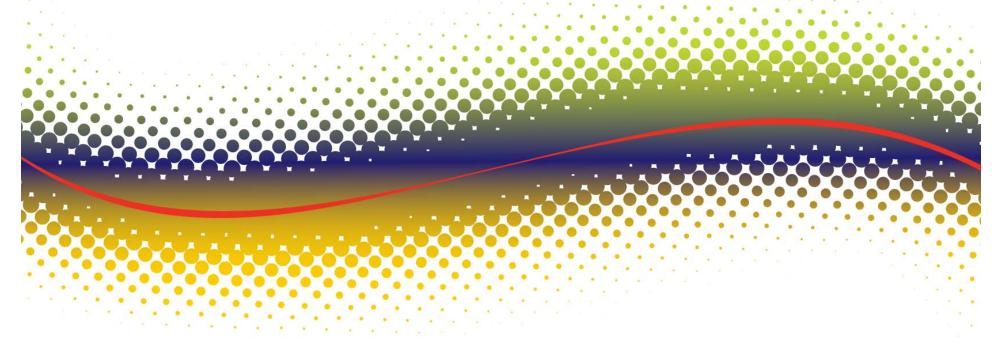




Building Language Resources Center for Autism Resear for Exploring Autism Spectrum Disorders

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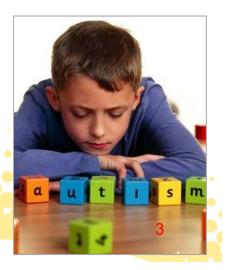


- Challenges
- Opportunities
- Prior research
- Current collaboration
- Future projects





- Brain-based disorder typically identified in early childhood 1.5% of U.S. children (CDC, 2016)
- Diagnostic criteria:
 - Impairments in social communication
 - Presence of repetitive behaviors or restricted patterns of interests
- "Spectrum" = mild to severe symptoms
- Significant public health cost
- Swift, accurate, early diagnosis is critical to improved outcomes
- Behaviorally defined: no brain scan or blood test
- Significant symptom overlap with other disorders
- Many children diagnosed late





PROBLEM:

sample heterogeneity +
small samples +
poor measurement =

non-reproducible scientific results





Opportunities



- Natural language interaction
 - Highly nuanced outward signal of internal brain activity
 - Fundamentally social
- Most children with ASD acquire language; nearly all vocalize
- Can HLT and Big Data methods help us identify ASD more reliably and understand it better?



Language in ASD



Variable vocalization throughout development:

- Differences evident in infancy
- Language delay as toddlers/preschoolers
- Difficulty being understood & understanding humor, sarcasm
- Conversational quirks
 - unusual word use
 - turn-taking
 - synchrony
 - accommodation

Real-life effects of pragmatic language problems:

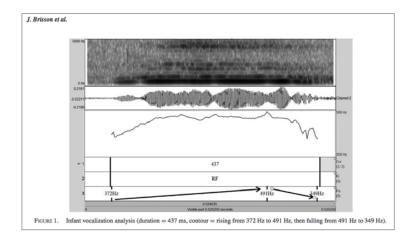
- Difficulty forming/maintaining friendships
- Increased risk of being bullied
- Difficulty with romantic relationships
- Difficulty maintaining employment

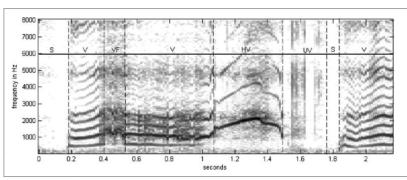
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Linguistic Data Consortium Early vocalization in ASD



- 4 mo: fewer complex pitch contours during cooing (Brisson et al., 2014)
- 6 mo: Higher and more variable F₀ in cries, poorer phonation (Orlandi et al., 2012; Sheinkopf et al., 2012)
- 9 mo: Fewer well-formed babble sounds (Paul et al., 2011)
- 12 mo: Less waveform modulation and more dysphonation in cries, compared to TD and DD (Esposito & Venuti, 2009)
- 16 mo: fewer responses to parent vocalizations, especially when directing to people (Cohen et al., 2013)
- 18 mo: Higher F₀ in cries, compared to TD and DD (Esposito & Venuti, 2010)





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ASD speech communication:

- Many small variations accumulate to create an odd impression
- Difficulty to determine what exactly differs
- Difficult to recognize





fast

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Characterizations



Too Flat Robotic _D slooow Stilted edanti \mathbf{O} Too quiet р Too Disorganize Sing-song "Little Too

Professor"







- The generalizations in the literature are mostly impressions (or stereotypes....)
 - There are few empirical studies
 - Sample sizes are generally very small
- In fact:
 - The ASD phenotype is very diverse in speech communication as in other ways
 - The truth is probably neither a point nor a "spectrum" but a complex multidimensional multimodal distribution in a space that we all live in
- We don't really know the dimensions of this space and figuring it out will take careful analysis of lots of data



Clinical Computational Linguistics



- Natural language:
 - Nuanced signal (marriage of cognitive and motoric systems)
 - Few practice effects
- Can automatically identify and extract features ("linguistic markers")
- Specific linguistic features associated with:
 - Depression
 - Dementia
 - PTSD
 - Schizophrenia





Prior Research



On average, individuals with ASD have been found to:

- Produce idiosyncratic or unusual words more often than typically developing peers (Ghaziuddin & Gerstein, 1996; Prud'hommeaux, Roark, Black, & Van Santen, 2011; Rouhizadeh, Prud'Hommeaux, Santen, & Sproat, 2015; Rouhizadeh, Prud'hommeaux, Roark, & van Santen, 2013; Volden & Lord, 1991)
- Repeat words or phrases more often than usual (echolalia; van Santen, Sproat, & Hill, 2013)
- Use filler words "um" and "uh" differently than matched peers (Irvine, Eigsti, & Fein, 2016)
- Wait longer before responding in the course of conversation (Heeman, Lunsford, Selfridge, Black, & Van Santen, 2010)
- Produce speech that differs on pitch variables; these can be used to classify samples as coming from children with ASD or not (Asgari, Bayestehtashk, & Shafran, 2013; Kiss, van Santen, Prud'hommeaux, & Black, 2012; Schuller et al., 2013)









Center for Autism Research (CAR)

- autism expertise
- data samples
- Linguistic Data Consortium (LDC)
 - corpus building methods
 - expertise in linguistics analysis

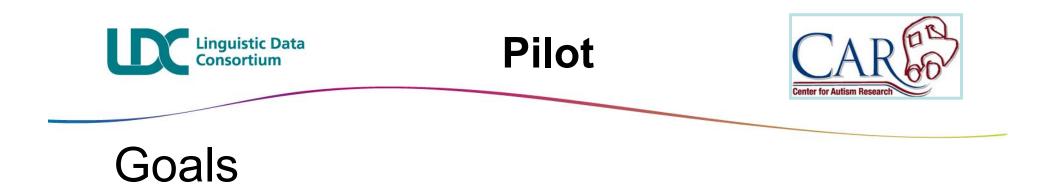


ADOS Pilot Project



 Process and analyze recorded language samples from Autism Diagnostic Observation Schedule ("ADOS"; Lord et al., 2012)

- Conversation and play-based assessment of autism symptoms
- Recorded for reliability and clinical supervision, coded on a scale, then filed away
- 600+ at CAR alone, thousands more across the U.S. and in Europe; never compiled
- Associated with rich metadata that includes family history, social, cognitive, and behavioral phenotype, genes, and neuroimaging



- Assess feasibility
- Identify and extract linguistic features
- Machine learning classification and/or discovery of relevant dimensions
- Correlate features with clinical phenotype

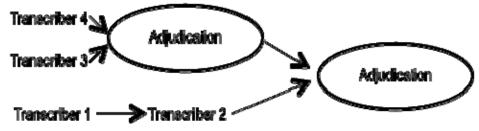




Transcription



- Time aligned, verbatim, orthographic transcripts
 (~20 minutes of conversation per interview, from ADOS Q&A segment)
- New transcription specification developed by LDC, (adapted from previous conversational transcription specifications)
- 4 transcribers and 2 adjudicators from LDC and CAR produced a "gold standard" transcript for analysis and for evaluation/training of future transcriptionists



- Simple comparison of word level identity between CAR's adjudicated transcripts and LDC's transcripts: 93.22% overlap on average, before a third adjudication resolved differences between the two
- Forced alignment of transcripts with audio



Participants



- Pilot sample
- N=100

- Mean age=10-11 years
- Primarily male
- 65 ASD, 18 TD,
 17 Non-ASD mixed clinical
- Average full scale IQ, verbal IQ, nonverbal IQ

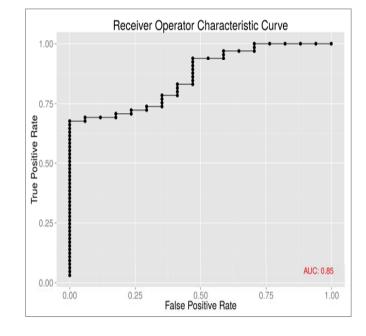


Preliminary Analyses



Bag-of-words classification:

- Correctly classified
 68% of ASD participants
 and 100% of TD participants
- Naïve Bayes, leave-one-out cross validation and weighted log-oddsratios calculated using the "informative Dirichlet prior" algorithm (Monroe et al., 2008)
- Receiver Operating Characteristic (ROC) analysis revealed good sensitivity and specificity; AUC=85%





Word Choice



- 20 most "ASD-like" words:
 - {nsv}, know, he, a, now ,no , uh, well, is, actually, mhm, w-, years, eh, right, first, year, once, saw, was
 - {nsv} stands for "non-speech vocalization", meaning sounds that with no lexical counterpart, such as imitative or expressive noise
 - "uh" appears in this list, as does "w-", a stuttering-like disfluency.
- 20 least "ASD-like" words:
 - like, um, and, hundred, so, basketball, something, dishes, go, york, or, if, them, {laugh}, wrong, be, pay, when, friends.

"um" appears, as does the word friends and laughter

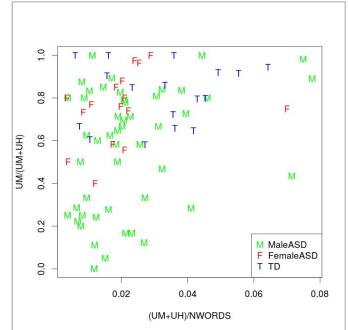
Fluency



 Rates of um production across the ASD and TD groups (um/(um+uh))

Linguistic Data

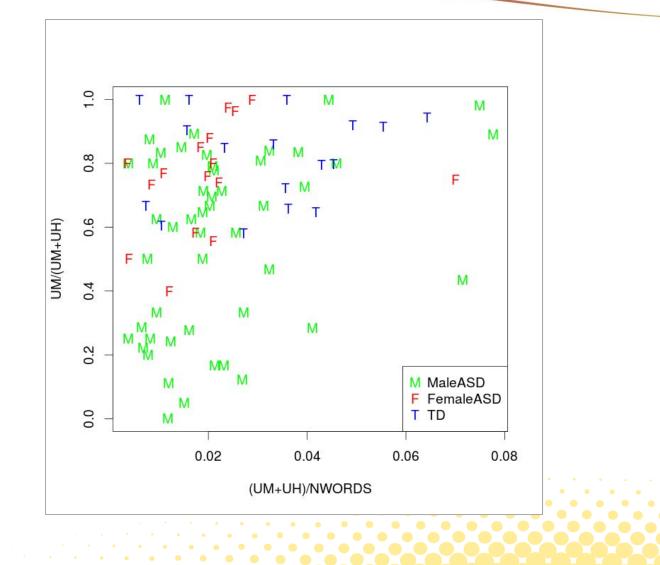
- ASD group produced UM during 61% of their filled pauses (CI: 54%-68%)
- TD group produced UM as 82% of their filled pauses (CI: 75%-88%)
- Minimum value for the TD group was 58.1%, and 23 of 65 participants in the ASD group fell below that value.







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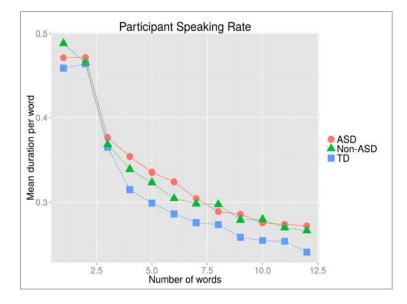
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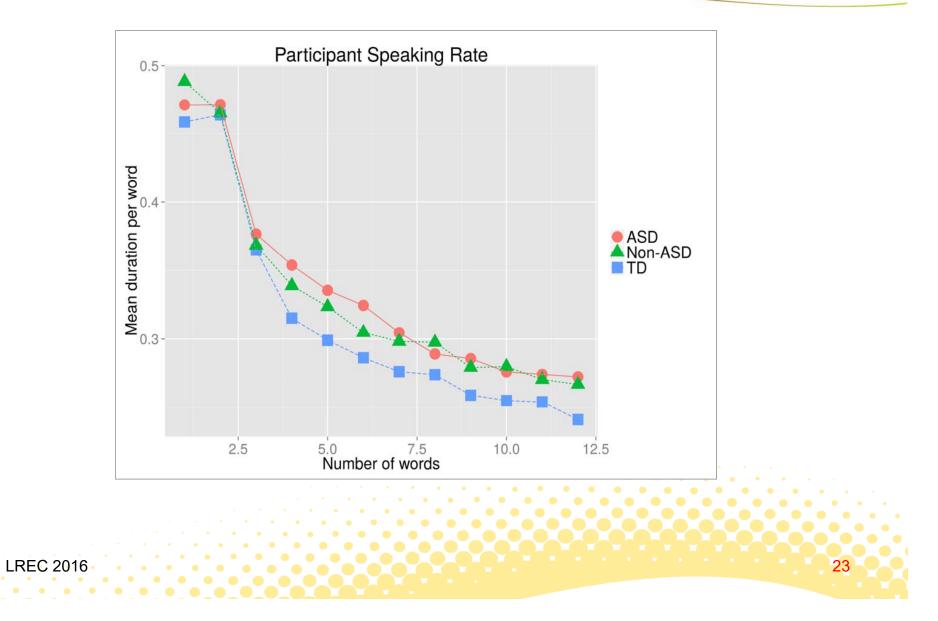


- Mean word duration as a function of phrase length
- TD participants spoke the fastest (overall mean word duration of 376 ms, CI 369-382, calculated from 6891 phrases)
- Followed by the non-ASD mixed clinical group (mean=395 ms; Cl 388-401, calculated from 6640 phrases)
- Followed by the ASD group with the slowest speaking rate (mean=402 ms; CI: 398-405, calculated from 24276 phrases)









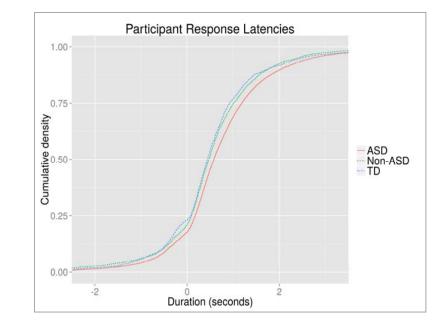


Latency to Respond



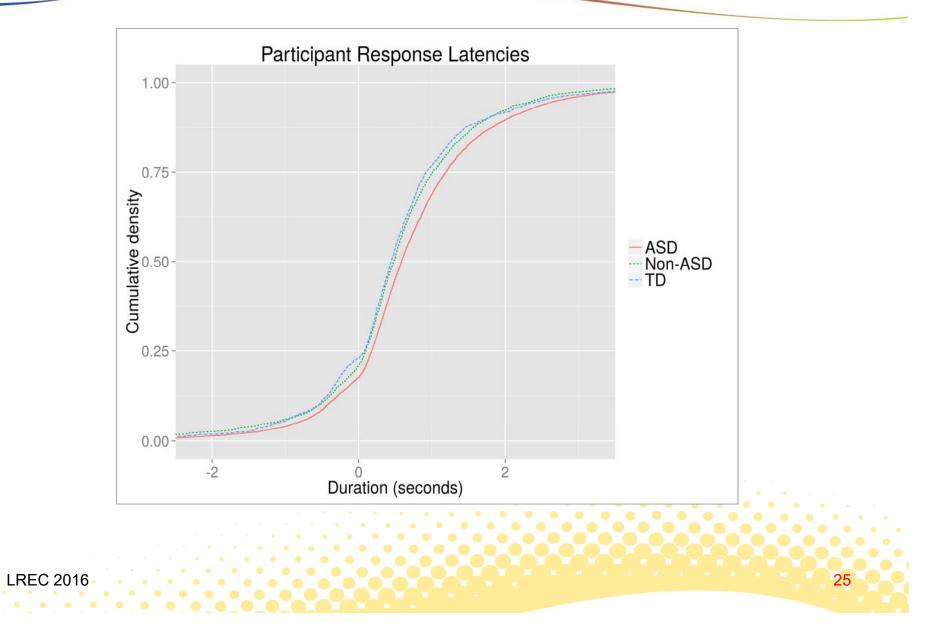
- Characterizes gap between speaker turns
- Too short = interrupting or speaking over a conversational partner
- Too long

 (awkward silences)
 interrupts smooth
 exchanges



 ASD somewhat slower than TD



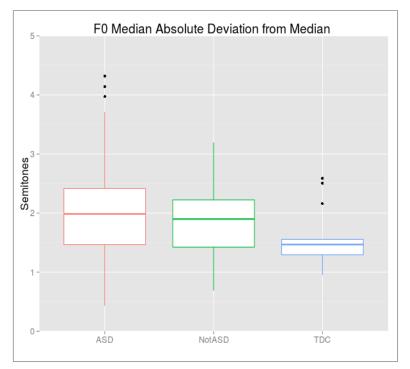




Fundamental Frequency

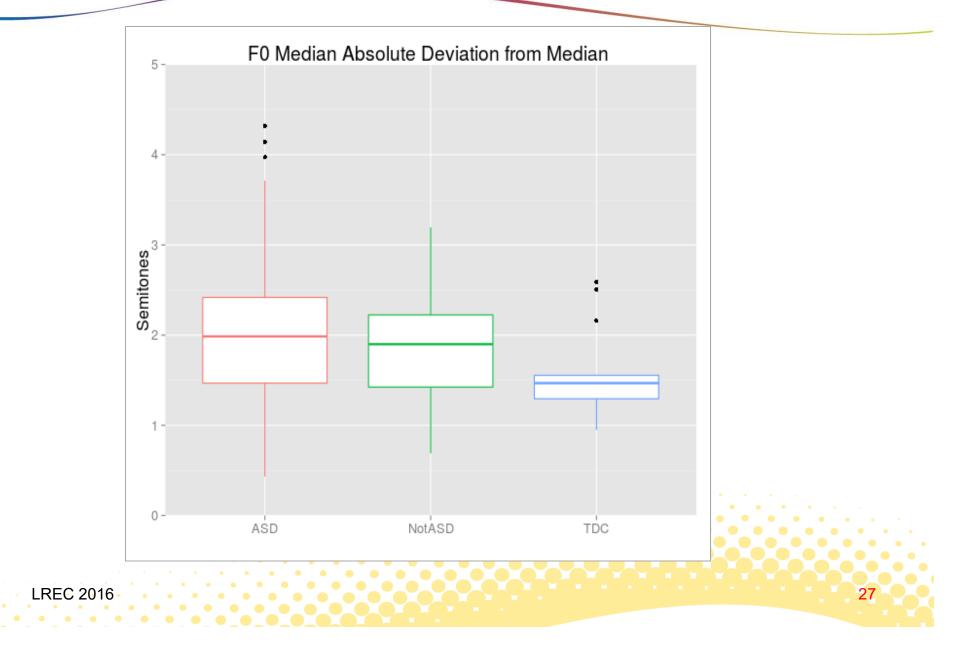


- Mean absolute deviation from the median (MAD)
 - Outlier-robust measure of dispersion in F0 distribution
 - Calculated in semitones relative to speaker's 5th percentile
- MAD values are both higher and more variable within the ASD and non-ASD mixed clinical group than the TD group
 - ASD: median: 1.99, IQR: 0.95
 - Non-ASD: median: 1.95, IQR: 0.80
 - TD: median: 1.47, IQR: 0.26











Next Steps



Expand sample sizes

- Improve classification metric
 - Focus on specificity (differentiate ASD from its cousins)
- Identify relevant dimensions of variation
- Hone HLT for pediatric clinical population
- Emerging collaborations include more ADOS evals with phenotypic data, neuroimaging, and genetics
 - Large body of shared data
 - Goal: gene-brain-behavior mapping

Enlarge age range

- Goal: downward extension to infancy
- Identify clusters of acoustic markers
- Chart growth to pinpoint critical points of divergence (targets for intervention)



PUBLICATION



- We have subject consent and IRB clearance for publication of anonymized transcripts and audio
- Larger ADOS sample from CAR in process
- Possible multi-site project (like ADNI) to pool very large collection of existing ADOS interviews processed and analyzed to the same standard

BUT

- New ADOS interviews require expensive, time-consuming in-person collection
- <u>NEED</u>: Scalable, inexpensive methods to collect natural language from large, diverse samples





Future Directions



Phone bank

- Inexpensive student worker asks ADOS questions
- Child and parent language samples, questionnaires, online IQ
- Nationally representative cohort
- Longitudinal samples

Computerized Social Affective Language Task (C-SALT)

- Self-contained laptop-based audio/video collection
- Records language and social affect in schools, clinics and homes
- Controlled recording is conducive to automated approaches (reduces need for transcription)

Combine data sources to improve predictive power:

 Motor, language, medical records, parent/teacher report, clinical judgment, performance tasks, imaging, genetics





CAR and LDC are eager to collaborate:

looking for novel analytic approaches and outside-the-box ideas!



Applications



Support clinical decision-making and improve access

- Low-cost, remote screening
- Direct behavioral observation: record in clinics, integrate into EHR
- Inform identification efforts and assist in differential diagnosis
- Identify behavioral markers → of underlying (treatable) pathobiology
 - Profiles of individual strengths and weaknesses link to biology = personalized treatment planning and improved outcomes
 - Granular assessment of response to intervention dense sampling

Give participants and families more information about themselves

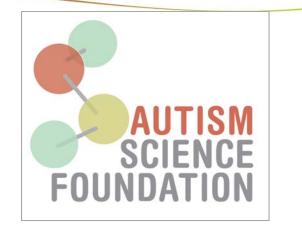
- Online feedback
- Monitor growth trajectories



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