Tracking heterogeneity in the psychosis prodrome through variation in language production

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What is the prodrome?

- A period of time preceding the onset of a mental illness, including psychotic disorders such as schizophrenia
- Young adults at **clinical high risk** (**CHR**) for psychosis often experience attenuated symptoms signaling risk
  - Positive symptoms (hallucinations and delusions)
  - Negative symptoms (reduction in social functioning, apathy)
- As much as 1% of the population develops psychosis, but the CHR conversion rate can reach 35% (Cannon et al., 2008)
- Intervention in the prodrome may improve outcomes, but reliable biomarkers are needed (Dickerson, 2015)

Speech and psychosis

- Motor variability is a key risk predictor in CHR populations due to disruptions in cortico-cerebellar and basal ganglia pathways (Bernard and Mittal, 2014)
- Atypical prosody has been described in populations experiencing schizophrenia and at high risk (Rapcan et al., 2008; Sichlinger et al., under review)
- A goal of our team is to discover whether motor disruptions leave traces in the speech of CHR individuals

A challenge: Clinical variability

- Psychosis is multi-faceted, and clinical profiles in the high-risk period are heterogeneous (Fusar-Poli et al., 2016)
- Individuals may mainly have positive symptoms, negative symptoms, or a mix, along with cognitive impairments
- Trajectories also vary: ~65% of CHR youth do not convert to a psychosis diagnosis (Cannon et al., 2008), and individuals may improve or decline on shorter time scales
- This clinical heterogeneity presents a challenge for straightforward classification analyses (CHR vs. control)

Key questions

- With variation in both symptoms and outcomes, how can the CHR population be comprehensively described?
- Can heterogeneity in the speech signal be leverage to detects early signs of increasing risk to psychosis?
- Do outliers represent statistical noise, or do they signal meaningful departures in the clinical trajectory of outlying individuals? (Fischer-Baum 2013)

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Leverage: Investigating atypical data points within and across individuals

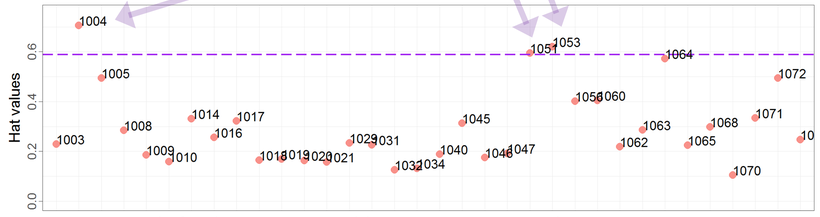
Leverage measures the distance between a given independent variable observation and other observations. High leverage data points have the potential to impact model estimates. One measure of leverage is the **hat value**, which assesses the change in the residual of a data point when it is included in the model vs. when it is held out. We'll use hat values to consider leverage from two different perspectives of "atypicality":

1. **"Population variation" approach:** is an individual atypical compared to their peers? Assessed via analyses which generate summary statistics of linguistic features to predict clinical status (control or CHR) of a single speaker.
2. **"Within-speaker" approach:** do a minority of atypical features cluster in an individual, even if their speech is not perceptibly unusual? Assessed via models of individual linguistic features (e.g. VOT, vowel duration) to look for clustering of high-leverage data points within speakers.

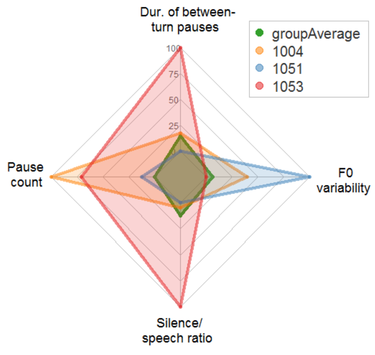
Leverage in population variation

Modeling clinical status as a function of linguistic variables

- Examples of predictors: F0 variability, silence/speech ratio, pause count
- Dependent variables: group (CHR or control), or symptom severity
- Each data point is an individual; **high hat values** (threshold: 2*average) = individuals who have an atypical relationship between a linguistic variable and clinical status, compared to the rest of the group

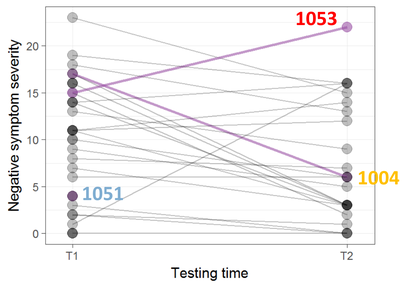


Plot from linear regression model: negativeScore ~ age + gender + turnPauseDur + gender:(F0var + pauseCount + silenceRatio + turnPauseDur) + age:(pauseCount + turnPauseDur)



Extreme feature values vary across "high-hat" individuals → not all show the same linguistic profile.

Do atypical individuals show distinct clinical trajectories?

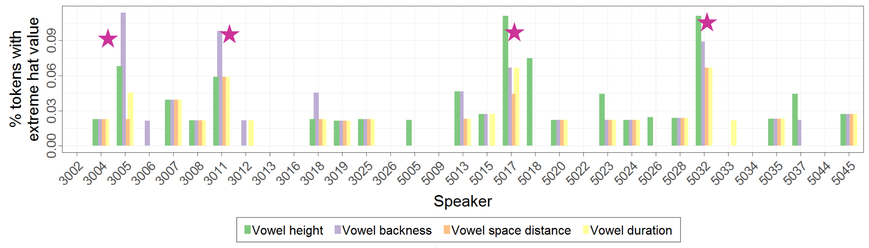


A small sample limits conclusions, but the speech patterns of speaker 1053 could be an early sign of more severe symptomology at time 2.

Leverage within speakers

Modeling single linguistic variables (e.g. VOT, vowel duration) as a function of clinical and demographic predictors. Each data point is a single measurement, and has an associated hat value.

Do atypical tokens (= high hat values) cluster within individuals?



Hat values extracted from four linear mixed effects regression models.
*Sample model structure: vowelDuration ~ gender * group + (1 + group || word) + (1 | speaker)*

★- individuals with atypical vowel production?

Longitudinal data is still being collected in this sample. We hypothesize that a cluster of atypical features at baseline may signal a developing motor impairment that reveals greater vulnerability at a later time point.

Further considerations

Our approach is one exploratory avenue for detecting a subtle signal amidst individual variation. Several important considerations remain:

- **Interpreting variation:** Linguistic variables may be atypical in two directions (e.g. very high or very low F0 variability). Theoretically-guided predictions are crucial to contextualizing outlying values.
- **Alternative models of clinical status**: Our study sample may consist of at least three discrete groups - controls, CHR individuals who don't convert, and CHR who do. What (if any) is the best modeling approach to discovering these groups when analyzing speech data?

Bernard, J. A., & Mittal, V. A. (2014). Cerebellar-Motor Dysfunction in Schizophrenia and Psychosis-Risk: The Importance of Regional Cerebellar Analysis Approaches. Frontiers in Psychiatry, 5, 1–14. **Cannon, T. D., Cadenhead, K., Cornblatt, B., Woods, S. W., Addington, J., Walker, E., ... & Heinssen, R. (2008).** Prediction of psychosis in youth at high clinical risk: a multisite longitudinal study in North America. Archives of General Psychiatry, 65(1), 28-37. **Dickerson, F. (Ed.) (2015)**. Early detection and intervention for people with psychosis. [Special issue.] Journal of Mental and Nervous Disease, 203, (5), 307-399. **Fischer-Baum, S. (2013).** Making sense of deviance: Identifying dissociating cases within the case series approach. Cognitive neuropsychology, 30(7-8), 597-617. **Fusar-Poli, P., Cappucciati, M., Borgwardt, S., Woods, S. W., Addington, J., Nelson, B., ... & Simon, A. E. (2016).** Heterogeneity of psychosis risk within individuals at clinical high risk: a meta-analytical stratification. JAMA psychiatry, 73(2), 113-120. **Rapcan, V., D'Arcy, S., Yeap, S., Afzal, N., Thakore, J., & Reilly, R. B. (2010).** Acoustic and temporal analysis of speech: A potential biomarker for schizophrenia. Medical Engineering and Physics, 32(9), 1074–1079 **Sichlinger, L., Cibelli, E., Goldrick, M., & Mittal, V.** Clinical correlates of aberrant conversational turn-taking in youth at clinical high-risk for psychosis. Under review.