

## Introduction

- Large language models:
  - Excellent discriminatory capabilities (patients vs. controls) [1]
  - BUT not yet used to quantify or understand the most prominent language atypicality in schizophrenia - positive thought disorder (disorganized speech)
- Positive thought disorder: Clinical assessment
  - Relies on relationships between individual words (local context) at the expense of broader discourse coherence (global context) [2]
  - Rating scales: subjective & time-consuming
- Aim: To objectively and automatically characterize influence of global vs. local context on each word in natural speech samples**
  - To what extent does lexical predictability rely on global vs. local context in patients vs. controls?
  - Does the degree of selective dependence on local vs. global context specifically predict the severity of positive thought disorder?

## Design

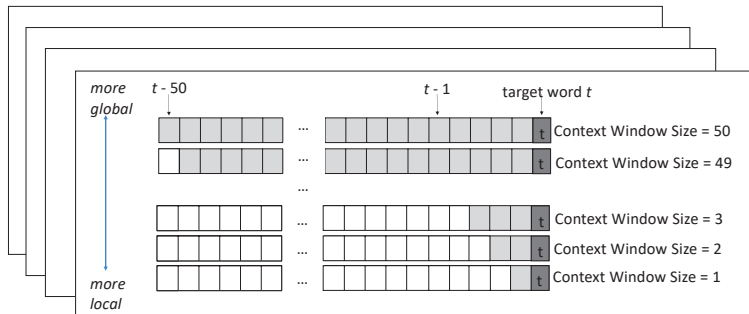
	Patients	Controls
N	70	36
Age	22.24(SD = 4.37)	21.52(SD = 3.32)
Sex	F: 14; M: 56; NB: 0	F: 12; M: 24; NB: 0
Mean Utterance Length (words)	72.80 (SD = 51.74)	94.60 (SD = 56.76)
PANSS-8 Total <sup>a</sup>	25.48 (SD = 6.86)	8.00 (SD = 0.00)
TLI Total <sup>b</sup>	1.56 (SD = 1.38)	0.30 (SD = 0.40)
TLI Disorganization <sup>b</sup>	1.00 (SD = 1.21)	0.16 (SD = 0.26)
TLI Impoverishment <sup>b</sup>	0.56 (SD = 0.70)	0.14 (SD = 0.25)

<sup>a</sup>Positive and Negative Syndrome Scale [3]; <sup>b</sup>Thought and Language Index [4]

• Domain-general cognitive function: Assessed using Semantic Fluency, Digit-Symbol Substitution, and the Trail Making Test (Part B)

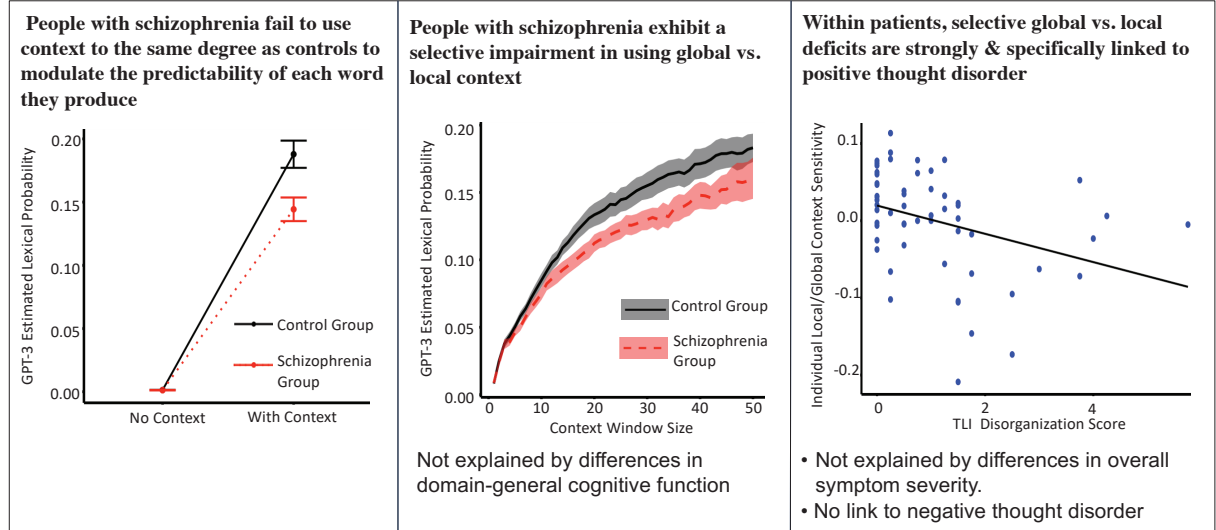
• Participants described 3 pictures for ~ 1 minute each → speech transcribed

• Used GPT-3 to extract the log probability of each word while manipulating the amount of context the model had access to:



## Results

Log probability: Dependent variable in a series of linear mixed effects analyses



## Discussion

- Global-vs.-local log probability selectively predicts positive thought disorder in first-episode schizophrenia
  - Sensitive linguistic biomarker for fast, automated, objective quantification of language disorganization
  - Facilitation of early detection of illness, symptom monitoring, prediction of outcome, trajectory of thought disorder over time
  - May detect more subtle, subclinical atypicalities in communication that impair psychosocial functioning
- Bridges clinical characterizations of thought disorder to neurocognitive evidence for selective deficits in the processing of global vs. local information in language comprehension
- Consistent with hierarchical generative models of psychosis [4]
  - Uncertainty over global representations, represented over longer time-scales at the highest levels of the cortical hierarchy → weaker predictions propagated down to lower cortical levels, → reduced suppression of lexical prediction error

**Future Directions: Beyond GPT, which lacks the feedback connections that drive healthy language processing in the brain**

- Predictive coding [5-7]: Biologically plausible
  - Will allow us to explicitly simulate the effects of perturbed feedback on global vs. local lexical predictability

## REFERENCES

- Corcoran, C. M., Mittal, V. A., Bearden, C. E., Gur, R. E., Hitzzenko, K., Bilgrami, Z., ... & Wolff, P. (2020). *Schizophrenia research*, 226, 158-166.
- Bleuler, E. (1911/1950).
- Kay, S. R., Fiszbein, A., & Opler, L. A. (1987). *Schizophrenia bulletin*, 13(2), 261-276.
- Liddle, P. F., Ngan, E. T., Caissie, S. L., ... & Weg, R. (2002). *The British Journal of Psychiatry*, 181(4), 326-330.
- Brown, M., & Kuperberg, G. R. (2015). *Frontiers in Human Neuroscience*, 9, 643.
- Rao, R. P., & Ballard, D. H. (1999). *Nat Neurosci*, 2(1), 79-87.
- Friston, K. (2005). *Philos Trans R Soc Lond B Biol Sci*, 360(1456), 815-836.
- Nour Eddine, S., Brothers, T., Wang, L., Spratling, M., & Kuperberg, G. R. (under review). *BioRxiv*.

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