



THE CHICKEN OR THE EGG?

DO <u>NEGATIVE SYMPTOMS</u> CAUSE <u>COGNITIVE IMPAIRMENTS</u> OR DO <u>COGNITIVE IMPAIRMENTS</u> CAUSE <u>NEGATIVE</u> SYMPTOMS?

INTRODUCTION

- Cognitive deficits and negative symptoms (NS) are core to psychotic disorder they are consistently demonstrated to be related ^{1,2}
- However, do cognitive deficits lead to NS, do NS lead to cognitive deficits or is the relationship bidirectional?
- Understanding the NS- cognition relationship is important in understanding psychotic disorders and has treatment implications

RESULTS Psychotic disorder Age NOS 10% Brief psychotic disorder 1% 23.6 Female 27% Schizoaffective SD = 5.1Schizophrenia disorder 20% 53% Hospitalizations Male 73% Schizophreniform 1.9 16% SD = 2.0Year Year Baseline B estimates presented ** p=0.00 * p < 0.05COG 1 0.73*** COG 2 0.91*** **Global NS** -1.59** -1.59** $X^{2}(5) = 6.43$ -0.98*** -1.43** p=0.27CFI= 1.00 NS 2 NS 1 NS 3 BIC =7337 RI **Pleasure** $X^{2}(5) = 7.46$ -0.53** -0.53** p=0.19and -0.39** CFI= 0.99 BIC =6239 MAP NS MAP NS MAP NS Motivation RI $X^{2}(5)=7.27$, p=0.20-0.93** CFI= 1.00 -1.06** -0.57** BIC = 6704EXP NS EXP NS EXP NS 0.9 z-score change in cognition predicts a clinically meaningful NS change ⁴

- Cognition significantly predicts NS in future timepoint
- Cognition significantly predicts future cognition

Across all cognition- NS models

• NS vary greatly between individuals, NS do not predict future NS

METHODS

DATA ACQUISITION



Recovery After Initial Schizophrenia Episode ³



N= 404 First episode Psychosis

STATISTICAL ANALYSIS

Random Intercept Cross Lagged Panel Model (in R)

Tests for potential bidirectional relations between variables across time (cross-lags)

Accounts for stable, between person differences in variables

RI

Equality constraints tested to determine whether relationship strengths between variables changed across time

Model with best fit selected (chi-square difference, BIC)

PANSS Negative Factor

(C)

Brief
Assessment
of
Cognition

Baseline 1 year 2 years

DISCUSSION



Cognitive deficits





Negative Symptoms

Cognitive deficits predict future NS, but NS do not predict future cognitive functioning.

CONCLUSION

- Cognitive deficits are implicated and contribute to NS severity 5,6
- Targeting cognition in early intervention could have benefits beyond cognitive improvements ⁷
- Strengths: cross lagged panel model allows for inferences of causality, robust results across NS dimensions and in sensitivity analyses
- Limitations: unable to account for other factors that might impact relationship
- Future directions: investigations in subgroups within psychosis and in other psychiatric populations

References 1. Au-Yeung, C. et al. (2023). The relationship between negative symptoms and MATRICS neurocognitive domains: A meta-analysis and systematic review. Progress in Neuro-Psychopharmacology and Biological Psychiatry, 127, 110833. 10.1016/j.pnpbp.2023.110833 2. Chavez-Baldini et al. (2023). The relationship between cognitive functioning and psychopathology in patients with psychiatric disorders: A transdiagnostic network analysis. Psychological Medicine, 53(2), 476. 10.1017/S0033291721001781 3. Kane, J. M. et al., (2016). Comprehensive Versus Usual Community Care for First-Episode Psychosis: 2-Year Outcomes From the NIMH RAISE Early Treatment Program. American Journal of Psychiatry, 173(4), 362–372. 10.1176/appi.aip.2015.15050632. 4. Czobor, P (2022). What Is the Minimum Clinically Important Change in Negative Symptoms of Schizophrenia? PANSS Based Post-hoc Analyses of a Phase III Clinical Trial. Frontiers in Psychiatry, 13, 816339. 10.3389/fpsyt.2022.816339. 5. Totzek, J et al. (2023). Longitudinal Inference of Multiscale Markers in Psychosis: From Hippocampal Centrality to Functional Outcome. Molecular Psychiatry, 1–10. 10.1038/s41380-024-02549-x 5 6. Makowski C al. Altered hippocampal centrality and dynamic anatomical covariance of intracortical microstructure in first episode psychosis. Hippocampus. 2020;30(10):1058-72. 10.1002/hipo.23215 7. Treen Calvo, D et al. (2018). Targeting recovery in first episode psychosis: The importance of neurocognition and premorbid adjustment in a 3-year longitudinal study. Schizophrenia Research, 195, 320–326. 10.1016/j.schres.2017.08.032

