Letters

RESEARCH LETTER

Distinct Relationships Between Visual and Auditory Perceptual Abnormalities and Conversion to Psychosis in a Clinical High-Risk Population

Hallucinations are a ubiquitous symptom experienced across psychotic disorders. This symptom, particularly in its auditory form, is widely thought to share a common substrate with other positive symptoms.[1] However, only unusual thought content and thought disorganization, not perceptual abnormalities (eg, hyperacusis, illusions, and momentary hallucinations), are associated with conversion to psychosis in clinical high-risk (CHR) populations,[2,3] despite the high incidence of perceptual abnormalities.[2]

Importantly, although the frequencies of auditory and visual perceptual abnormalities in CHR individuals are similar,[4] differences in the prevalence of auditory and visual hallucinations in full psychosis[5] may suggest distinct neurobiological substrates. Therefore, we hypothesized that auditory and visual perceptual abnormalities would have distinct clinical correlates in CHR individuals.

Methods | Participants were CHR outpatients, 13 to 30 years of age, seeking help at the Center of Prevention and Evaluation at the New York State Psychiatric Institute and were part of a longitudinal study approved by the institutional review board of the New York State Psychiatric Institute. Adults provided written informed consent; minors provided assent with written consent by a parent or legal guardian. All 203 participants met the criteria for the attenuated positive symptom syndrome defined in the Structured Interview for Psychosis-Risk Syndromes (SIPS; 57 converters, 144 nonconverters, and 2 unknown; **Table**).[6] Symptoms were not better explained by *DSM* disorders or current substance use. Participants were followed up every 3 months for up to 2 years. Conversion to psychosis was defined based on standard SIPS criteria.[6] Most converters (81%) had follow-up *DSM* diagnoses of schizophrenia or related disorders.

Using detailed vignettes and rater comments in the SIPS collected at enrollment (baseline), 2 independent, SIPS-certified raters (R.R.G. and G.B.) assigned perceptual-abnormality scores (ie, P4 scores), originally encompassing any abnormalities across sensory domains within the past month,[6] separately to auditory (denoted P4a, intraclass correlation coefficient $r = 0.98$) and visual experiences (denoted P4v, $r = 0.91$; **Figure**). Relationships to conversion were assessed via logistic regression and Cox proportional hazards regression. Statistical significance was set at $P \leq .05$.

Results | Consistent with previous research, the original global P4 scores were not associated with conversion status ($\beta = 0.01$, $P = .92$). However, when split into 2 variables, both P4a and P4v independently were associated with conversion status, although in opposite directions ($\beta_a = 0.25$, $P = .05$; $\beta_v = -0.44$,

Table. Demographic and Baseline Clinical Characteristics of Clinical High-Risk Individuals at Enrollment[a]

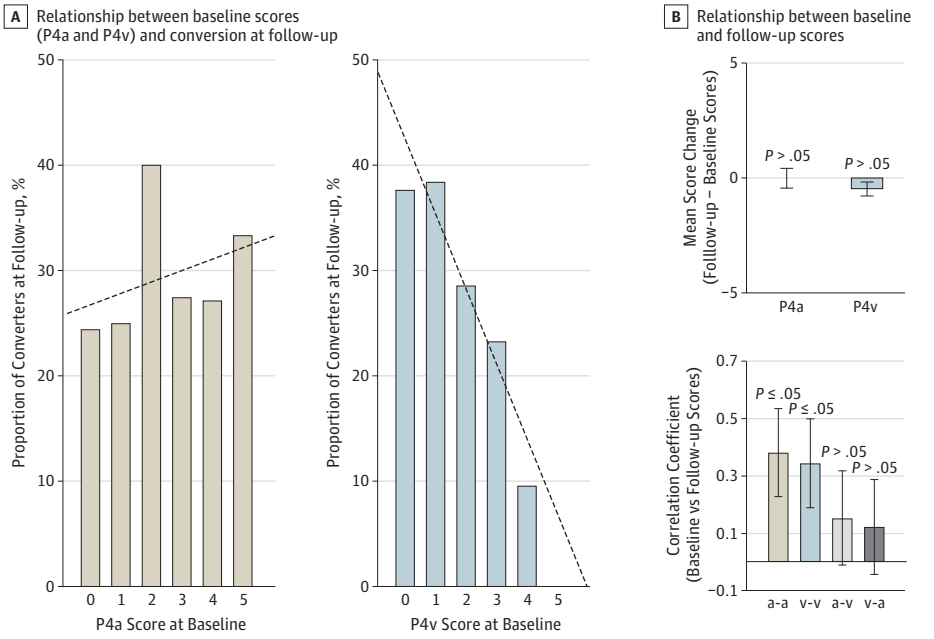
Characteristic	Nonconverters (n = 144)	Converters (n = 57)	*P* Value[b]
Age, mean (SD), y	20.15 (3.91)	20.09 (3.80)	.91
Female, No. (%)	45 (31.25)	9 (15.79)	.07
Hispanic, No. (%)	41 (28.47)	18 (31.58)	.68
Medication, No. (%)			
Any	43 (29.86)	15 (26.32)	.51
Antidepressants	20 (13.89)	6 (10.53)	.52
Antipsychotics	8 (5.56)	5 (8.77)	.40
Both drug types	15 (10.42)	4 (7.02)	.46
SIPS scores, mean (SD)			
Positive symptoms total, PT score	14.15 (3.97)	15.47 (3.94)	.03
Unusual thought content, P1 score	3.42 (1.04)	3.93 (1.03)	<.001
Suspiciousness, P3 score	3.33 (1.23)	3.40 (1.31)	.69
Grandiose ideas, P3 score	2.06 (1.57)	2.19 (1.65)	.59
Perceptual abnormalities, P4 score	2.82 (1.42)	2.84 (1.52)	.92
Disorganized communication, P5 score	2.53 (1.29)	3.10 (1.32)	.01
Negative symptoms total, NT score	16.00 (6.28)	18.91 (7.01)	.01
Disorganization symptoms total, DT score	9.37 (3.73)	10.88 (3.88)	.01
General symptoms total, GT score	11.49 (4.33)	11.74 (3.90)	.71
Global assessment of functioning score, mean (SD), GAF score	46.32 (7.17)	43.13 (5.89)	.004

Abbreviation: SIP, Structured Interview for Psychosis-Risk Syndromes.

[a] Certified SIPS raters assigned scores to 203 participants meeting criteria for both the SIPS attenuated positive symptoms syndrome and the *DSM-5* attenuated psychosis syndrome, based on the detailed vignettes and rater comments captured during the baseline interview. Conversion was defined based on the SIPS. Of the 57 converters, 46 (80.70%) received a *DSM* diagnosis of schizophrenia or related disorders (ie, nonaffective psychotic disorders).

[b] Corresponding to significant mean differences using the 2-sample *t* test for continuous data and significant relationships between conversion outcome and other categorical variables using the χ^2 test.

Figure. Longitudinal Relationship Between Baseline Severity of Auditory and Visual Perceptual Abnormalities and Clinical Outcomes at Follow-up



A, Relationship between auditory perceptual abnormalities (P4a scores in tan bar graphs) and visual perceptual abnormalities (P4v scores in blue bar graphs) at baseline and conversion to psychosis at follow-up. The dotted lines represent fitted regression lines. Note that 7% were not assigned any score because the raters did not have sufficient information to assign one; also note that no individuals were assigned the maximum P4v score of 5. B, Relationship between baseline and follow-up, postconversion scores among converters with available data for both time points only (n = 39). The top graph shows mean longitudinal changes in P4a and P4v scores, respectively. The bottom bar graph shows correlations (standardized β) between baseline (a for P4a scores; v for P4v scores) and follow-up, postconversion scores within (a-a, v-v) and between domains (a-v, v-a). Error bars indicate SEM.

P = .001; Figure, A). P4a scores were higher than P4v scores (P < .001; 67% vs 57% scored above 1, P < .001); P4a and P4v overlapped moderately (R^2 = 0.25; 48% scored above 1 for both). In addition, P4a, but not P4v, was associated with summed scores across P1 (unusual thought content), P2 (suspiciousness), P3 (grandiose ideas), and P5 (disorganized communication) (β_a = 0.37, P = .04; β_v = 0.14, P = .45; $\beta_a > \beta_v$, P = .01; see Table for item descriptions) cross-sectionally, indicating that auditory abnormalities are more strongly related to other attenuated positive symptoms than are visual abnormalities. Postconversion P4a and P4v scores remained stable relative to baseline and longitudinally correlated within, but not between, domains (Figure, B).

Similarly, survival analyses showed that global P4 scores did not predict days to conversion (β = 0.01, P = .95), while P4a and P4v were independent predictors in opposite directions (β_a = 0.19, P = .052; β_v = −0.37, P < .001). In an extended model controlling for known predictors of conversion (P scores other than P4, the NT [negative symptoms total] score, the DT [disorganization symptoms total] score, the GT [general symptoms total] score, the GAF [global assessment of functioning] score, and demographics), P4v was the single strongest (negative) independent predictor of days to conversion (β_v = −0.38, z = −3.36, P < .001); P4a, P1, P5, and NT scores were the only additional (positive) independent predictors that were at least marginally significant (1.64 < z < 2.11; P = .07, .04, .05, and .10, respectively) in this extended model.

Discussion | Visual perceptual abnormalities were strongly associated with a lower risk of conversion to psychosis, whereas auditory abnormalities were associated with a higher risk, along with P1 and P5 scores. In addition, our cross-sectional data support that core positive symptoms (including auditory, but not visual, abnormalities) may have a common substrate. Visual abnormalities in CHR populations may thus have distinct underlying substrates and may be associated with distinct clinical outcomes (eg, less severe or nonpsychotic disorders). Further research into the clinical value of concurrently measuring visual and auditory abnormalities and their corresponding neurobiological substrates is warranted.

Eugénie Lehembre-Shiah, BS
Wei Leong, MS
Gary Brucato, PhD
Anissa Abi-Dargham, MD
Jeffrey A. Lieberman, MD
Guillermo Horga, MD, PhD
Ragy R. Girgis, MD

Author Affiliations: New York State Psychiatric Institute, Department of Psychiatry, Columbia University, New York.

Corresponding Author: Guillermo Horga, MD, PhD, New York State Psychiatric Institute, Department of Psychiatry, Columbia University, 1051 Riverside Dr, Unit 31, New York, NY 10032 (horgag@nyspi.columbia.edu).

Published Online: November 16, 2016. doi:10.1001/jamapsychiatry.2016.3055

Author Contributions: Drs Horga and Girgis had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Mss Lehembre-Shiah and Leong contributed equally to this work. Drs Horga and Girgis also contributed equally to this work.
Concept and design: Lehembre-Shiah, Brucato, Abi-Dargham, Horga, Girgis.
Acquisition, analysis, or interpretation of data: Lehembre-Shiah, Leong, Brucato, Lieberman, Horga, Girgis.
Drafting of the manuscript: Lehembre-Shiah, Leong, Brucato, Horga, Girgis.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Leong, Brucato, Horga, Girgis.
Administrative, technical, or material support: Lehembre-Shiah, Leong, Abi-Dargham, Lieberman.

Conflict of Interest Disclosures: Dr Girgis receives research support from Otsuka, Forest, Bioadvantex, and Genentech. No other disclosures are reported.

Funding/Support: This project was supported by National Institute of Mental Health grants K23MH106746 (Dr Girgis), K23MH101637 (Dr Horga), and R01MH093398 and by the New York State Office of Mental Hygiene.

Role of the Funder/Sponsor: The sponsors had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

1. Fletcher PC, Frith CD. Perceiving is believing: a Bayesian approach to explaining the positive symptoms of schizophrenia. *Nat Rev Neurosci*. 2009;10(1):48-58.

2. Addington J, Liu L, Buchy L, et al. North American Prodrome Longitudinal Study (NAPLS 2): the prodromal symptoms. *J Nerv Ment Dis*. 2015;203(5):328-335.

3. Poe SL, Gill KE, Brucato G, Girgis RR. Parental age and attenuated thought disorder in a cohort at clinical high risk for psychosis. *Schizophr Res*. 2015;161(2-3):511-512.

4. Marshall C, Denny E, Cadenhead KS, et al. The content of attenuated psychotic symptoms in those at clinical high risk for psychosis. *Psychiatry Res*. 2014;219(3):506-512.

5. Waters F, Collerton D, Ffytche DH, et al. Visual hallucinations in the psychosis spectrum and comparative information from neurodegenerative disorders and eye disease. *Schizophr Bull*. 2014;40(4)(suppl 4):S233-S245.

6. Miller TJ, McGlashan TH, Rosen JL, et al. Prodromal assessment with the structured interview for prodromal syndromes and the scale of prodromal symptoms: predictive validity, interrater reliability, and training to reliability. *Schizophr Bull*. 2003;29(4):703-715.