**Longitudinal Trajectories of Psychosis Spectrum Symptoms in Community Youth: Findings from the Philadelphia Neurodevelopmental Cohort (PNC)**

Monica E. Calkins, Ellyn R. Butler, Tyler M. Moore, Kosha Ruparel, Bart Larsen, Daniel H. Wolf, Theodore D. Satterthwaite, Ruben C. Gur, and Raquel E. Gur

**Introduction**

Why psychosis is debilitating, and is thought to be exacerbated by poverty and trauma

What we know from cross-sectional and clinical high-risk samples

Longitudinal trajectories of psychosis symptoms in a community-based cohort not known

Important to characterize these trajectories to help inform the development of preventative interventions and improve functioning

We hypothesize that 1) PS-PS’s and OP-OP’s experience worse positive, negative, disorganized and general symptoms than TD-TD’s, with the gap widening across development for the PS-PS group; 2) PS-PS’s and OP-OP’s display worse general, social and role functioning than TD-TD’s, with PS-PS’s declining across development; and 3) block-level poverty indicators and the number of types of trauma exposures predict final PS status above and beyond diagnostic category at baseline.

**Methods**

Participants

Recruitment procedures:

A subsample (N=752) of PNC participants (N=9,498 youth, age 8-21) was invited for follow-up based on presence or absence of PS symptoms. Prospective assessments (mean interval=4.52 years) with the Structured Interview for Prodromal Syndromes (SIPS v. 4.0) included 2.8 visits on average (age range first=8-21.9; final=9.5-29.9). Youth were classified as PS-PS or TD-TD based on first-final visits. Not all participants completed the SIPS, GAF (Generalized Assessment of Functioning) and the Cornblatt’s Social and Role Functioning scales at every assessment (see Supplement for details).

Diagnostic labels

All participants were classified as TD, OP or PS at each clinical assessment. The first clinical assessment for every subject was conducted using the GOASSESS (), which is a lifetime screener for symptoms of the following disorders: generalized anxiety, separation anxiety, attention deficit hyperactivity, oppositional defiant, conduct, specific phobia, social anxiety, panic, agoraphobia, obsessive-compulsive, eating, depression, bipolar, psychosis, intermittent explosive, suicide, post-traumatic stress, and substance use. Participants that experience \_\_\_ symptoms of a disorder and experienced significant impairment were classified as having had the disorder.

All subsequent clinical assessments were performed using the \_\_\_ (CAPA) (), which assessed for lifetime symptoms at the second assessment, and symptoms over the past six months for every assessment after the second. Every clinical visit that utilized the CAPA assessed for symptoms of depression, mania and psychosis, while only some assessed for anxiety, \_\_\_, and \_\_\_.

Clinical dimensions

(descriptions of SIPS, GAF and social and role functioning)

Environment

The neighborhood environment was conceptualized as a latent variable of block group/neighborhood level characteristics, including the percent of residents who were in poverty, had finished high school, and who were employed (Moore et al., 2015). Trauma was quantified as the number of unique types of threatening experiences an individual was exposed to, including natural disasters, family violence, physical and sexual abuse, threatened with a weapon, bad accident, witnessed violence and witnessed dead body.

envSES -> percent married, percent in poverty, median family income, percent high school plus, population density, percent employed, percent vacant lots and percent female

number of types of trauma -> natural disaster, family violence, physical abuse, sexual abuse, physically threatened, bad accident, witness violence, witness dead body

Statistics

Longitudinal trajectories of prodromal symptoms by diagnostic group were modeled using generalized additive mixed models (GAMMs) as implemented in *gamm4* (Wood, Scheipl, & Wood, 2017). A cubic regression basis set with four equally spaced knots was utilized, and coefficients for the basis functions were penalized to avoid overfitting of nonlinear age trajectories. P-values were adjusted across GAMMs using false discovery rate correction (Benjamini & Hochberg, 1995), and 95% confidence intervals were generated for the splines by taking random samples from the posterior distributions. All models included main effects for diagnostic group (reference group was TD-TD), a spline of age, diagnostic group-by-spline-of-age interactions, and a random intercept per subject:

Where *i* indexes subject and . Sensitivity models controlling for demographic variables can be found in the Supplement. Finally, logistic regression was used to predict final PS status with baseline diagnoses (i.e., TD, OP, and PS), and environment and trauma variables. P-values were adjusted across logistic regression models using false discovery rate correction. All code can be found in <https://github.com/PennBBL/pncLongitudinalPsychosis>.

**Results**

Across development, PS-PS youth were higher than TD-TD on all SIPS domains (p’s<0.01), which, except for negative and disorganized symptoms, followed differing developmental trajectories (see Table 2 and Figures 2-3). The PS-PS’s displayed a nonlinear trajectory of positive symptoms; severity slowly increased until the early 20’s, then briefly plateaued before increasing in the late 20’s. The PS-PS’s exhibited increasing disorganized and general symptoms, and consistently lower and declining global functioning than TD-TD’s across development.

Prediction models demonstrated that, controlling for baseline diagnosis, both the number of types of trauma experienced and neighborhood poverty were associated with an increased likelihood of being PS at the final time point (see Table 3 and Figure 4). Exploratory interactions with baseline diagnosis were not significant. Sensitivity analyses controlling for baseline age, sex and race did not substantially alter the results. Note that…

**Table 1**. Demographics for full sample

**Table 2**. Generalized additive mixed models for psychosis spectrum and functioning domains



Note: All estimates for diagnoses are with respect to the reference group, TD-TD. Positive, Negative, Disorganized and General are subscales of the SIPS. Social and Role are scales from Cornblatt’s measure of social and role functioning. GAF=General Assessment of Functioning; TD=Typically Developing; OP=Other Psychopathology; PS=Psychosis Spectrum. This table was produced using the *sjPlot* package (Lüdecke & Lüdecke, 2015).

**Table 3**. Models predicting final psychosis spectrum status

**Figure 1**. Comorbidities at baseline



Note: F=Female, M=Male, ano=anorexia, bul=bulimia, man=mania, add=attention deficit disorder, con=conduct, odd=oppositional defiant, dep=depression, gad=generalized anxiety, ocd=obsessive-compulsive, pan=panic, ptd=post-traumatic stress, sep=separation anxiety, soc=social anxiety, agr=agoraphobia, phb=phobia, and psy=psychosis.

**Figure 2**. Non-linear age trajectories for psychosis spectrum domains by diagnoses



**Figure 3**. Non-linear age trajectories for functioning by diagnoses



**Figure 4**. Baseline trauma and neighborhood environment predict final psychosis spectrum status

**Discussion**

There are two major limitations of the clinical assessments: 1) the first and second assessments asked about lifetime symptoms, and 2) not all clinical visits assessed for every symptom domain. Given the overlap in the time period assessed during the first and second visits, it is possible that someone who came in during their first visit had recently experienced severity psychosis symptoms, which subsequently remitted soon after the first visit, but would still be classified as PS during the second visit because they had experienced clinically significant psychosis symptoms during their lifetime. Due to the inconsistent coverage of symptom domains across assessments, it is also possible that someone could have come in for a clinical visit and only been assessed for depression, mania and psychosis, not met criteria for any of those disorders, and therefore been classified as TD, all the while meeting criteria for an anxiety disorder.

**References**

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**Supplement**

Table S1. Demographics for subsample that completed the SIPS

Table S2. Demographics for subsample that completed the GAF

Table S3. Demographics for subsample that completed Cornblatt’s Social and Role Functioning scales

Table S4. Demographics for subsample that completed the trauma assessment

Table S5. Sensitivity analyses generalized additive mixed models