Topological data analysis and hierarchical clusters for the assessment of psychosis in a community sample of children and adolescents: the Brazilian High Risk Cohort

Felipe C. Argolo, M.D.^{a,b}, Valdemir S. Souza, Pedro M. Pan, M.D., Ph.D.^a, Luisa von Nielander, M.D., MsC.^a, Lais Fonseca, M.D., MSC.^a, Giovanni Salum, M.D. Ph.D.^c, Luis Augusto Rohde, M.D., MSC.^c, Eurípedes Filho, M.D., MSC.^d, Ary Gadelha, M.D., MSC.^a, Jim van Os, M.D., Ph.D.^e, Rodrigo A. Bressan, M.D., Ph.D.^{a,b}

^a*Federal University of São Paulo, Brazil*

^b*King's College London, UK*

^c*Federal University of Porto Alegre, Brazil*

^d*University of São Paulo, Brazil*

^e*Maastricht University Medical Centre, Netherlands*

Abstract

The psychosis phenotype is generally associated with altered experience of salience associated with internal or external events, giving rise to experiences such as hallucinations or delusional ideation. Psychotic experiences (PEs) and traits vary in severity, frequency and functional impairment, and compose a wide behavioral range for the trait. Here, we examine how methodological expansions in psychometrics provide unique information about the internal structure and chronological transformations of PEs. We present the procedures of this paper in three steps: (1) validation of constructs using classical factor analysis; (2) evaluation derived from the data's topological structure; (3) assessment of longitudinal changes in magnitudes of PEs. A discussion follows, exposing methodological limitations and highlighting how this framework may benefit psychometrics and impact clinical practice.

Keywords: Psychosis, Psychotic Experiences, Factor analysis, Topological Data Analysis, Persistent homology, Hierarchical clustering

1. Introduction

The psychosis phenotype is generally associated with altered experience of salience associated with internal or external events, giving rise to experiences such as hallucinations or delusional ideation [1] [2]. Psychotic experiences (PEs) and traits vary in severity, frequency and functional impairment, and compose a wide behavioral range for the trait [3]. Here, we examine how methodological expansions in psychometrics provide unique information about the internal structure and chronological transformations of PEs.

PEs are common in the general population; in community youths from 9 to 12 years old, up to 17% reported at least one PE [4]. PEs are transient in approximately 80% of the subjects [5] and among those with persistent symptoms, only a minority develops actual psychotic disorders [3]. Considering the neurodevelopmental acquisition of behavior, investigation of

factors related to the emergence and persistence of PEs in youth can provide additional insights about typical and atypical development.

In order to capture subtleties of PEs, previous studies in community samples used a 20-item subset from the Community Assessment of Psychic Experience covering positive symptoms (CAPE-Pos). Exploratory and confirmatory factorial analysis yielded good fits for the CAPE-Pos, with standard approaches [6] assuming a hierarchical structure for the construct [7]. A meta-analysis of exploratory factorial analyses suggested a three-factor structure for CAPE-pos: perceptual anomalies/hallucinatory experiences, persecutory ideation, and bizarre experiences [8]. However, the total number of factors accepted is not settled, with reports of 3, 4 (most common) and 5 factors [6] [9] [10]. Although the psychosis prototype is familiar to psychiatry, its idiosyncratic definition and unknown boundaries challenge the assessment and proper analysis of data. Decades ago, Revelle [11] proposed distinct mathematical formulations, such as hierarchical clustering, for psychometrics; however, they remained in oblivion until mathematicians and data scientists revisited the subject [12]. These methods permit more precise inferences about latent traits, based on invariant characteristics, which are robust to coordinate changes and deformations. Therefore, its application in psychopathology may enhance the understanding of the psychosis phenotype.

It is thought that altered development in cognitive, cerebral and behavioural domains underlies the emergence of the psychosis trait in the general population. Longitudinal models, such as latent growth models, estimate developmental changes in magnitude of traits over time [13] [14]. We employ this method to investigate changes in PE latent traits over neurodevelopment. To this end, data from the Brazilian High Risk Cohort Study (BHRiCS) were used, a community sample of youths, at two time points: baseline and a 3-year follow-up. We present the procedures of this paper in three steps: (1) validation of constructs using classical factor analysis; (2) evaluation derived from the data's topological structure; (3) assessment of longitudinal changes in magnitudes of PEs. A discussion follows, exposing methodological limitations and highlighting how this framework may benefit the study of PE and impact clinical practice.

2. Methods

2.1. Sample

The BHRiCS is a cohort study designed to evaluate psychopathology in a school-based community sample of Brazilian children and adolescents, assessed in 57 public schools from São Paulo and Porto Alegre [15]. A sample of 9,937 students were initially screened and a total of 2,511 youths (6-12 years old, mean age at baseline 9.7 years, $SD = 1.92$; 53,1% male) were selected to participate, 958 randomly and 1553 with familial 'high-risk' status, based on the Family History Screen (FHS). Three years later, 2,010 subjects completed the first follow-up wave [16]. All parents or legal guardians provided signed consent, and children provided verbal assent if they were not able to read and write. The research protocol was approved by Institutional Review Board from the involved universities.

2.2. Questionnaire - Community Assessment of Psychic Experiences - Positive Symptoms (CAPE-pos)

Children and adolescents were interviewed using the Community Assessment of Psychic Experiences subscale of positive symptoms – CAPE-pos - [17] [18] at baseline (T0) and 3-year follow-up (T1).

The subscale of positive symptoms (CAPE-pos), an instrument composed of 20 self-reported items, has good factorial validity and reliability to assess PEs [8] [16]. In this study, trained psychologists assessed self-reported PE using CAPE-pos. The scale was designed to assess lifetime PE, with sub-items addressing frequency and impact evaluated on four-point likert scales [18]. In the present analysis, we used self-report yes/no answers for each item. A meta-analytic (n=9) mean reliability coefficient suggests good values for the scale (0.84 ± 0.10). CAPE-pos was a reliable PE assessment scale for developmental samples [8].

CAPE Positive

Relative frequency of positive responses (Baseline / Wave 1)

1. Believe in the power of witchcraft, voodoo or the occult (32.6% / 36.2%)
2. Things in magazines or on TV were written especially for you (10.3% / 10.1%)
3. Some people are not what they seem to be (54.1% / 49.0%)
4. Being persecuted in some way (29.5% / 16.5%)
5. People seem to drop hints about you or say things with a double meaning (14.4% / 9.3%)
6. Conspiracy against you (20.3 % / 7.7%)
7. Destined to be someone very important (30.5% / 19.6%)
8. You are a very special or Unusual person (24.1% / 12.3%)
9. Communicate telepathically (11.7% / 6.6%)
10. Electrical devices such as computers can influence the way you think (16.6% / 14.2%)
11. People look at you oddly because of your appearance (22.3% / 17.6%)
12. Thoughts in your head are being taken away from you (5.4% / 1.9%)
13. Thoughts in your head are not your own (6.6% / 2.4%)
14. Thoughts so vivid that you were worried other people would hear them (9.7% / 4.2%)
15. Hear your own thoughts being echoed back to you (22.0% / 9.2%)
16. Under the control of some force or power other than yourself (5.3% / 2.0%)
17. Hear voices when you are alone (26.4% / 14.5%)
18. Hear voices talking to each other when you are alone (8.3% / 3.1%)
19. A double has taken the place of a family member, friend or acquaintance (2.1% / 1.1%)
20. See objects, people or animals that other people cannot see (14.7% / 9.7%)

3. Statistical analysis

3.1. Exploratory and Confirmatory Factorial Analysis

Initially, we used Confirmatory Factorial Analysis (CFA) to test uniqueness of the trait measured by the instrument. Bifactor models are preferred to test if scores reflect a single latent source [19] [20]. This framework performs Exploratory Factorial Analysis (EFA),

followed by oblique rotation (oblimin) of factors and Schmid-Leiman (S-L) transformation to obtain one common factor [21], confirmed by CFA. The procedure was applied to each measure at each timepoint (CAPE T0, CAPE T1) to evaluate scales individually, as usually reported in previous studies [22]. We selected the number of 1st order factors by comparing the Bayes Information Criterion (BIC) of the models within the range suggested by previous studies on CAPE-pos (between 3 and 5).

3.2. Hierarchical clustering

Following the Revelle’s proposal [11], we illustrate how hierarchical clustering can add to factor analysis in psychometrics. The use of ultrametric spaces to address sparse and high-dimensional data has recently been revisited with new tools [12]. This method groups items hierarchically in a dendrogram, a b-ary tree, in which cuts at different heights define clusters. We performed hierarchical clustering using single-linkage (nearest neighbor), complete linkage (farthest neighbor) and Ward’s method. Compared to structural equation modeling, this approach does not rely on linear mapping to lower dimensions to express hierarchies.

Figure 1: Persistence

We used asymmetric distances (Jaccard distance: intersection over union) in a pairwise manner - com binação C(20,2) - to the 20 items for each observation (T0 and T1). The distance matrix reflects whether certain answers appear together (small distance) or separate (large distance). We chose asymmetrical distance, once two individuals reporting the same experience are likely more similar than two individuals denying the item. We verify the appearance of significant clusters under multistep-multiscale bootstrap resampling ($\alpha = 0.05$). Time-related changes in dendrograms are visually presented with connected tanglegrams. We also explore the factorial structure with information from topological properties. Specifically, we examine persistent homologies by tracking features (Betti numbers) under alpha shape filtration [23]. Previous works have linked the number of connected components in the objects (0th Betti number) to psychometric latent factors [12] [24]. Confidence intervals for significant components were estimated from Wasserstein distances, using bootstrapped diagrams drawn from data. The analyses compared samples at baseline and 3 years follow-up.

- a. Barcode and persistence diagrams suggesting four connected components at baseline (left) and follow-up (right): Largest four bottom bars in barcode diagram (top) and four points distant to the diagonal indicate consistent generators. Dashed line indicates bootstrap confidence interval (95%; 100 subsamples).

Figure 2: Dendrogram and others diagrams

- b. Tanglegram - Items emerging from close points in branches are hierarchically close.

3.3. Longitudinal evaluation - Latent Growth Model

Hierarchical SEM allowed the investigation of the psychotic trait using repeated measures. We used confirmatory factor analysis to model latent variables for methods. The following constraints were set: (1) the intercept parameter loaded equally in the unique trait of Psychosis at T0 and T1, representing the common mean; (2) the slope covariance parameter was constrained to zero at T0 and to one in T1, first order polynomial approximation as recommended in latent growth models; (3) Psychotic trait variables (T0 and T1) shared the same residual variance. From an inferential statistics point of view, this method is similar to a paired t-test when applied to two time points. We used this approach to estimate evolution/magnitude of change in psychosis, considering methods and latent variables.

3.4. Software and Sensitivity analysis

Mplus version 7.11, R base tools, packages lavaan (0.5-23.1097), psych (1.7.5), pvclust (2.0), dendextend (1.6.0), TDA (1.6), boot (1.3) and its dependencies were used for SEM, bifactorial models, hierarchical clustering, analysis of persistent homologies and bootstrapping of persistence diagrams. ([25] [26]. R version 3.4.3 [27] was used.

4. Results

4.1. Validity

Analyses with bifactorial models presented good fitness for CAPE measures at both time points according to squared errors ($RSMR \leq 0.08$ and $RMSEA \leq 0.06$; Table S1) and compared to null models (CFI and $TLI > 0.950$, Table S1). Values obtained for general factor saturation also reflected uniqueness of the trait (ω hierarch.: T0 = 0.74; T1 = 0.67). SEM resulted in significant common (intercept parameter) variance estimate ($\sigma=0.340$; $p < 0.001$) for the psychosis traits across time, which shows the invariance of the trait across both time points.

4.2. Factorial structure

Using bifactorial models, solutions with 4 subfactors were the most parsimonious according to BIC for baseline and follow-up ($BIC_{T0} = -427.32$; $BIC_{T1} = -564.46$) when compared to models of 3 or 5 subfactors. Tracking persistence homologies with alpha shape filtration also suggested 4 distinct and significantly connected components, as seen in persistence and barcode diagrams (Figure 1.a).

Some pairs of items remained significant across several methods of clustering ($p < 0.05$): subliminal messages and thought influence (Abnormal interpretation of external signals, Items 5 and 10); paranoia and auditory hallucinations when alone (Items 4 and 17); supernatural beliefs and suspiciousness about people’s nature/appearance (Odd beliefs, Items 1 and 3). Hierarchical clustering results resembled common traits found in the literature and bifactorial analysis: arbitrary cuts divide items related to paranoia and thought intrusion (items 12,13,16,19), close to auditory hallucinations (17, 20); telepathy, thought influence and hidden messages (items 2,5,9,10,14), superstitious beliefs (1-3) and grandiosity (items 7-8).

4.3. Longitudinal assessment

The latent growth model presented good fitness (RMSEA < 0.060 ; TFI and CFI > 0.950). SEM resulted in a significant common variance estimate ($\sigma=0.181$; Std. Err = 0.022; $p < 0.001$) for the psychosis traits. Each trait loaded in all items at the corresponding timepoint. The estimate for the slope variance parameter was significant for the model ($\sigma=0.305$; Std. Err = 0.046; $p < 0.001$), suggesting the existence of longitudinal differences within individuals.

The number of latent factors (four) was identical according to CFA and persistent homologies techniques, as seen in Figure 1.a. Figure 1.c compares dendrograms from TDA at both time-points, providing visualization of preserved symmetries: symptom grouping remained consistent across time points.

5. Discussion

We illustrate how topological features and hierarchical clustering deepen the standard CFA evaluation of latent traits in PE. Results from CAPE-pos data in our sample reinforce the uniqueness of the construct measured by the scale. Different mathematical approaches suggested four latent subfactors, consistent with the literature. Longitudinal evaluation supports the existence of longitudinal changes in overall levels within individuals.

5.1. Factorial structure and scale validity

CAPE-pos presented internal validity metrics with overall good fitness values according to classic metrics of squared errors and comparisons to null models (CFI/TLI). There are several studies investigating the scale’s underlying factor structure with bifactor models, with reports in literature ranging from 3 to 5 factors. While four factors is the most common result, a meta-analysis suggested a three factor structure as the best-fitting latent structure to the CAPE-pos ur analyses, bifactorial models with 4 first-order factors were optimal independent solutions according to the Bayesian Information Criterion. Persistent homologies under alpha shape filtration supports the existence of four subfactors, with barcode and persistence diagrams highlighting very distinct four connected components. This factor-solution seems to be the best fitting model to our sample of youth. Hierarchical clustering resulted in qualitatively similar groups of items for each factor when compared to structural equation modelling.

5.2. Neurodevelopment and Longitudinal assessment

The model considering two time-points also presented good fit to the data (Table S1). A significant slope estimate suggests that some variance within the psychosis trait is time-related for each individual. According to the neurodevelopmental hypothesis, the magnitude of changes in psychotic manifestation would be correlated with genetic vulnerability and environmental risk and protective factors[28].

Our results imply that there are probably different trajectory profiles in the population, with some individuals showing increasing PEs and others decreasing, as described in previous work [29]. Further studies may further clarify whether environmental risk factors, such as childhood adversity, interfere with this progression [16].

5.3. Methodological expansions

The combination of exploratory and confirmatory factor analysis in SEM comprise inductive assertions empirically based on the data and also provide a framework for hypothetic-deductive procedures [30]. In order to extract insights based on a richer set of geometrical objects, different methods can be examined. Revelle (1979) proposed that hierarchical clustering could address latent characteristics in different levels, while also being useful to overcome some side-effects of factor analysis, such as requiring large samples for reliable parameter estimates [11].

During the past years, data scientists have employed abstractions from mathematics to enhance analysis and understanding of several themes in genetics, neuroimaging, immunology and computer vision [31] [32]. These models, although sophisticated, are generally more intuitive to describe concepts, once they deal with conceived theoretical structures similar to the verified phenomena.

B-ary trees are metrically equivalent to discrete hyperbolic spaces. This methodological approaches were used in efficient embeddings of hierarchical data, such as recent state-of-the-art breakthroughs in natural language processing [33]. Ultrametricity is naturally related to high-dimensional data [34]. These properties, summed with recent advances on data processing procedures and computational power [12] make hierarchical trees promising to test hypotheses about psychopathological constructs. Topological features, such as homologies (Betti numbers), may also enhance our measures and the formulation of underlying constructs, uncovering pervasive characteristics. In other fields, these advances helped scientists in other fields, such as physics and chemistry [35] [36] [37]. Moreover, these features are adequate to cohort designs since they are naturally robust to coordinate changes and deformations.

5.4. Weakness and future directions

Even though we lost 19.9% of subjects at follow up, our attrition rate was in the acceptable range for a community-based study. In addition, incoming data from the third study phase will enhance our capacity to analyze trajectories with further measures. Noteworthy, CAPEpos is limited to positive symptoms, restraining our investigations to this domain. Further investigations should address negative, affective and cognitive domains of PEs, as these likely interact [38]. More importantly, in this report we focused on the psychometric output, rather than clinical and sociodemographic risk factors for PEs. Investigations testing which variables play important roles in shaping the phenotype during neurodevelopment are warranted.

5.5. Author's statement and funding

Authors declare to have no potential conflicts of interests. This work was funded by public grants: (1) Institutos Nacionais de Ciência e Tecnologia do CNPQ (números 573974/20080; 465550/2014-2); (2) FAPESP (números 2008/57896-8; 2014/50917-0; 2013/08531-5) and (3) European Research Council (Starting Grant (StG), LS7, ERC-2013-StG).

References

- [1] & Murray R. M. Howes, O. D. *Schizophrenia: An integrated sociodevelopmental-cognitive model. The Lancet*, 383(9929), 1677–1687. 2014. URL [https://doi.org/10.1016/S0140-6736\(13\)62036-X](https://doi.org/10.1016/S0140-6736(13)62036-X).
- [2] S. Kapur. *Psychosis as a state of aberrant salience: A framework linking biology, phenomenology, and pharmacology in schizophrenia. American Journal of Psychiatry*. 2003. URL <https://doi.org/10.1176/appi.ajp.160.1.13>.
- [3] & van Os J. Linscott, R. J. *An updated and conservative systematic review and meta-analysis of epidemiological evidence on psychotic experiences in children and adults: on the pathway from proneness to persistence to dimensional expression across mental disorders. Psychological Medicine*, 43(06), 1133–1149. 2013. URL <https://doi.org/10.1017/S0033291712001626>.
- [4] Cederlöf M. & Lichtenstein Kelleher, I. *Psychotic experiences as a predictor of the natural course of suicidal ideation: a Swedish cohort study. World Psychiatry*, 13(2), 184–188. 2014. URL <https://doi.org/10.1002/wps.20131>.
- [5] Kounali D. Cannon M. David A. S. Gunnell D. Heron J. ... Lewis G. Zammit, S. *Psychotic experiences and psychotic disorders at age 18 in relation to psychotic experiences at age 12 in a longitudinal population-based cohort study. American Journal of Psychiatry*, 170(7), 742–750. 2013. URL <https://doi.org/10.1176/appi.ajp.2013.12060768>.
- [6] Merikangas K. R. Moore T. M. Burstein M. Behr M. A. Satterthwaite T. D. ... Gur R. E. Calkins, M. E. *The Philadelphia Neurodevelopmental Cohort: Constructing a deep phenotyping collaborative*. 2015. URL <https://doi.org/10.1111/jcpp.12416>.
- [7] & Murray R. M. Howes, O. D. *Dopamine and the aberrant salience hypothesis of schizophrenia. World Psychiatry: Official Journal of the World Psychiatric Association (WPA)*, 15(1), 3–4. 2016. URL <https://doi.org/10.1002/wps.20276>.
- [8] & Touloupoulou T. Mark, W. *Psychometric Properties of “Community Assessment of Psychic Experiences”: Review and Meta-analyses. Schizophrenia Bulletin*, 42(1), 34–44. 2016. URL <https://doi.org/10.1093/schbul/sbv088>.
- [9] Houts R. M. Belsky D. W. Goldman-Mellor S. J. Harrington H. Israel S. ... Moffitt T. E. Caspi, A. *The p Factor: One General Psychopathology Factor in the Structure of Psychiatric Disorders?* 2014. URL <https://doi.org/10.1177/2167702613497473>.
- [10] Muchomba F. M. Gill K. E.-Ben-David S. Walder D. J. Malaspina D. Corcoran C. M. DeVolder, J. E. *The analysis of bridging constructs with hierarchical clustering methods: An application to identity. Journal of Research in Personality*, 70, 93–106. 2017. URL <https://doi.org/10.1016/j.jrp.2017.06.005>.

- [11] W. Revelle. *Hierarchical cluster analysis and the internal structure of tests*. *Multivariate Behavioral Research*, 14(1), 57–74. 2012. URL <https://doi.org/10.1207/s15327906mbr14014>.
- [12] Schwartz S. J. Lisa Amodeo A.-Feaster-D. J. Steinley D. L. Meca A. & Picariello S. Farrelly, Colleen M. *The analysis of bridging constructs with hierarchical clustering methods: An application to identity*. *Journal of Research in Personality*, 70, 93–106. 2017. URL <https://doi.org/10.1016/j.jrp.2017.06.005>.
- [13] Grubaugh A. L. Allen J. G.-Mahoney-J. Oldham J. M. Fowler J. C. ... Frueh B. C. Clapp, J. D. *Modeling trajectory of depressive symptoms among psychiatric inpatients: A latent growth curve approach*. *Journal of Clinical Psychiatry*, 74(5), 492–499. 2013. URL <https://doi.org/10.4088/JCP.12m07842>.
- [14] & Tisak J. Meredith, W. *Latent curve analysis*. *Psychometrika*, 55(1), 107–122. 1990. URL <https://doi.org/10.1007/BF02294746>.
- [15] Gadelha A. Pan P. M. Moriyama-T. S. Graeff-Martins A. S. Tamanaha A. C. ... Rohde L. A. Salum, G. A. *High risk cohort study for psychiatric disorders in childhood: rationale, design, methods and preliminary results*. *International Journal of Methods in Psychiatric Research*, 24(1), 58–73. 2015. URL <https://doi.org/10.1002/mpr.1459>.
- [16] Murray R. M. & Fisher H. L. Trotta, A. *The impact of childhood adversity on the persistence of psychotic symptoms: a systematic review and meta-analysis*. *Psychol Med*, 45(12), 2481–2498. 2015. URL <https://doi.org/10.1017/s0033291715000574>.
- [17] Achenbach T. M. Dumenci L. Rescorla-L. A. Almqvist-F. Weintraub S. ... Verhulst F. C Ivanova, M. Y. *Testing the 8-Syndrome Structure of the Child Behavior Checklist in 30 Societies*. *Journal of Clinical Child & Adolescent Psychology*, 36(3), 405–417. 2007. URL <https://doi.org/10.1080/15374410701444363>.
- [18] Bak M. Hanssen M. van Os J.-& Krabbendam L. Konings, M. *Validity and reliability of the CAPE: a self-report instrument for the measurement of psychotic experiences in the general population*. *Acta Psychiatrica Scandinavica*, 114(1), 55–61. 2006. URL <https://doi.org/10.1111/j.1600-0447.2005.00741.x>.
- [19] & Åberg-Bengtsson L. Gustafsson, J.-E. *Unidimensionality and interpretability of psychological instruments*. In *Measuring psychological constructs: Advances in model-based approaches*. (pp. 97–121). 2010. URL <https://doi.org/10.1037/12074-005>.
- [20] S. P. Reise. *The Rediscovery of Bifactor Measurement Models*. *Multivariate Behavioral Research*, 47(5), 667–696. 2017. URL <https://doi.org/10.1080/00273171.2012.715555>.
- [21] Revelle W.-Yovel I. & Li-W. Zinbarg, R. E. *Psychotic experiences and psychotic disorders at age 18 in relation to psychotic experiences at age 12 in a longitudinal population-based cohort study*. *American Journal of Psychiatry*, 170(7), 742–750. 2005. URL <https://doi.org/10.1007/s11336-003-0974-7>.

- [22] Eaton Kim, Hyunsik. *The hierarchical structure of common mental disorders: Connecting multiple levels of comorbidity, bifactor models, and predictive validity. Journal of Abnormal Psychology*, 124(4), 1064–1078. 2015. URL <https://doi.org/10.1037/abn0000113>.
- [23] Fasy B. Lecci-F. Rinaldo A. Singh-A. & Wasserman-L. Balakrishnan, S. *Statistical Inference For Persistent Homology. ArXiv Preprint ArXiv: ...*, 1–41. 2013. URL <http://arxiv.org/abs/1303.7117v15Cn><http://arxiv.org/abs/1303.7117>.
- [24] Lecci F.-Rinaldo A. Wasserman L.-Balakrishnan S. & Singh A. Fasy, B. T. *Symptom trajectories and psychosis onset in a clinical high-risk cohort: The relevance of subthreshold thought disorder. Schizophrenia Research*, 159(2), 278–283. 2014. URL <https://doi.org/10.1016/j.schres.2014.08.008>.
- [25] A. A. Beaujean. *Latent Variable Modeling Using R: a step-by-step guide*. 2014. URL <https://doi.org/10.1145/1859204.1859227>.
- [26] T. Brown. *Latent Variable Modeling Using R: a step-by-step guide*. 2015. URL <https://doi.org/10.1680/geot.8.B.012>.
- [27] R Development Core Team. *R Development Core Team. R: A Language and Environment for Statistical Computing*. 2017. URL <http://www.mendeley.com/research/r-language-environment-statistical-computing-96%52>:
- [28] O'Donovan M. C. Thapar A. & Craddock N. Owen, M. J. *Neurodevelopmental hypothesis of schizophrenia. British Journal of Psychiatry*. 2011. URL <https://doi.org/10.1192/bjp.bp.110.084384>.
- [29] Van Winkel R. Raaijmakers Q. A. W. Ormel J. Verhulst F. C. Reijneveld S. A. ... Vollebergh W. A. M. Wigman, J. T. W. *Evidence for a persistent, environment-dependent and deteriorating subtype of subclinical psychotic experiences: A 6-year longitudinal general population study. Psychological Medicine*, 41(11), 2317–2329. 2011. URL <https://doi.org/10.1017/S0033291711000304>.
- [30] J. Pearl. *Interpretation and identification of causal mediation. Psychological Methods*, 19(4), 459–481. 2014. URL <https://doi.org/10.1037/a0036434>.
- [31] Hahm J. Lee H. Kang E. Kang H. & Lee D. S. Kim, Heejung. *Psychotic experiences as a predictor of the natural course of suicidal ideation: a Swedish cohort study. World Psychiatry*, 13(2), 184–188. 2015. URL <https://doi.org/10.1002/wps.20131>.
- [32] Huntsman D. G. Nielsen T. O. Yorida E. Peacock M. Cheang M. C. U. ... Gilks C. B. Makretsov, N. A. *Hierarchical clustering analysis of tissue microarray immunostaining data identifies prognostically significant groups of breast carcinoma. Clinical Cancer Research*, 10(18 I), 6143–6151. 2004. URL <https://doi.org/10.1158/1078-0432.CCR-04-0429>.
- [33] & Kiela D. Nickel, M. *Poincare Embeddings for Learning Hierarchical Representations*. 2017. URL <http://arxiv.org/abs/1705.08039>.

- [34] F. Murtagh. *The remarkable simplicity of very high dimensional data: Application of model-based clustering. Journal of Classification*, 26(3), 249–277. 2009. URL <https://doi.org/10.1007/s00357-009-9037-9>.
- [35] Carlsson G. & Rabadan R. Chan, J. M. *Topology of viral evolution. Proceedings of the National Academy of Sciences*, 110(46), 18566–18571. 2013. URL <https://doi.org/10.1073/pnas.1313480110>.
- [36] Levine A. J. & Carlsson G. Nicolau, M. *Topology based data analysis identifies a subgroup of breast cancers with a unique mutational profile and excellent survival. Proceedings of the National Academy of Sciences*, 108(17), 7265–7270. 2011. URL <https://doi.org/10.1073/pnas.1102826108>.
- [37] & Vegter G. Rote, G. *Computational topology: An introduction. In Effective Computational Geometry for Curves and Surfaces (pp. 277–312)*. 2006. URL https://doi.org/10.1007/978-3-540-33259-6_7.
- [38] Guloksuz S. ten Have M. de Graaf R. van Dorsselaer S. Gunther N. . . . van Os J. Pries, L.-K. *Evidence That Environmental and Familial Risks for Psychosis Additively Impact a Multidimensional Subthreshold Psychosis Syndrome. Schizophrenia Bulletin*. 2018. URL <https://doi.org/10.1093/schbul/sby051>.

Supplementary Material

Table S1 – Goodness of fit measures for models

Model	CFI/TLI	RMSEA (95% CI)	RMSR
CAPE			
Time 0	0.986/0.982	0.023 (0.020 – 0.027)	0.057
Time 1	0.990/0.987	0.015 (0.010 – 0.020)	0.065
Two time-points (Latent Growth Model)	0.960/0.957	0.022 (0.020 – 0.023)	0.080

CAPE: Community Assessment of Psychic Experience; CBCL: Child Behavior Checklist; CFI: Comparative Fit Index; TLI: Tucker -Lewis Index; RMSEA: Root Mean Square Error of Approximation; RMSR: Root Mean Square of the Residuals.

Figure 3: Performance statistics for CFA models