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Evidence of phenotypes indexing cognitive resilience and vulnerability in the early course of mood and psychosis spectrum illness; mapping the latent structure, characteristics, and longitudinal stability of cognitive heterogeneity

Tamsyn E Van Rheenen [a,b,*], Elysha Ringin [a], Denny Meyer [b], Kelly Allott [c,w], Julian Wenzel [d], Rachel Upthegrove [e,f], Alexandra Stainton [c,w], Raimo K.R. Salokangas [g], Stephan Ruhrmann [d], Marlene Rosen [d], Eva Meisenzahl [h], Eleonora Maggioni [i,j], Theresa Lichtenstein [d], Rebekka Lencer [k,l], Joseph Kambeitz [d], Udo Dannlowski [k,y,z,aa], Dominic B. Dwyer [c], Katie Chisholm [m], Stefan Borgwardt [l], Carolina Bonivento [n], Alessandro Bertolino [o], Linda Antonucci [o], Nikolaos Koutsouleris [p,q], Paolo Brambilla [j,r], Christos Pantelis [a,s,t,u], Lana Kambeitz-Ilankovic [d,v], Stephen J. Wood [b,c,x], the PRONIA Consortium

[a] Department of Psychiatry, Faculty of Medicine Dentistry and Health Sciences, University of Melbourne, Melbourne, Australia
[b] Centre for Mental Health and Brain Sciences, School of Health Sciences, Swinburne University, Melbourne, Australia
[c] Orygen, Melbourne, Australia
[d] Department of Psychiatry and Psychotherapy, Faculty of Medicine and University Hospital, University of Cologne, Cologne, Germany
[e] Department of Psychiatry, University of Oxford, England
[f] Institute for Mental Health, University of Birmingham, England
[g] University of Turku, Department of Psychiatry, Finland
[h] Department of Psychiatry and Psychotherapy, Medical Faculty, Heinrich-Heine University, Düsseldorf, Germany
[i] Department of Electronics, Information and Bioengineering, Politecnico di Milano, Milan, Italy
[j] Department of Neurosciences and Mental Health, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy
[k] Institute for Translational Psychiatry, University of Münster, Münster, Germany
[l] Department of Psychiatry and Psychotherapy, University of Lübeck, Germany
[m] School of Psychology, University of Sussex, Brighton, UK
[n] Scientific Institute IRCCS "Eugenio Medea", Pasian di Prato, Ud, Italy
[o] Department of Translational Biomedicine and Neuroscience, University of Bari Aldo Moro, Bari, Italy
[p] Department of Psychiatry and Psychotherapy, Ludwig Maximilian University of Munich, Munich, Germany
[q] Department of Psychosis Studies, King's College, London, UK
[r] Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy
[s] Florey Institute of Neuroscience and Mental Health, University of Melbourne, Parkville, VIC, Australia
[t] Monash Institute of Pharmaceutical Sciences (MIPS), Monash University, Parkville, Victoria, Australia
[u] Western Centre for Health Research & Education, University of Melbourne & Western Health, Sunshine Hospital, Furlong Road, St Albans, Victoria, Australia
[v] Department of Psychology and Educational Sciences, Ludwig-Maximilian-University, Munich, Germany
[w] Centre for Youth Mental Health, University of Melbourne, Melbourne, Victoria, Australia
[x] School of Psychology, University of Birmingham, England
[y] Department of Psychiatry, Medical School and University Medical Center OWL, Protestant Hospital of the Bethel Foundation, Bielefeld University
[z] German Center for Mental Health (DZPG), Site Jena Magdeburg Halle, Germany
[aa] Center for Intervention and Research on Adaptive and Maladaptive Brain Circuits Underlying Mental Health (C-I-R-C), Site Jena Magdeburg Halle, Germany

* Address correspondence to: Tamsyn Van Rheenen, Department of Psychiatry, Faculty of Medicine Dentistry and Health Sciences, University of Melbourne, Melbourne, Australia.
E-mail address: tamsyn.van@unimelb.edu.au (T.E. Van Rheenen).

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ABSTRACT

The latent structure and longitudinal stability of cognitive heterogeneity during the early course of mood and psychosis spectrum illness has not been well-studied. We determined the presence, stability and characteristics of latent cognitive profiles underlying a transdiagnostic sample of individuals at high risk for psychosis (CHR) or with a recent onset of psychosis (ROP) or depression (ROD). The sample comprised 666 CHR, ROP or ROD individuals. Latent Profile Analysis identified transdiagnostic cognitive profiles in baseline and 11-month follow up data. Latent Transition Analysis established the stability of these profiles and their transition probabilities. Profiles were characterised across several clinical factors and those indexing functioning, neurodevelopment, stress exposure, and physical/brain health.

A 3-profile model was most optimal at both timepoints, with profile equivalence metrics indicating a low likelihood of transition between them, and thus, temporal stability. The profiles were labelled 'Average Cognition', Moderately Impaired', 'Severely Impaired', with all diagnoses represented in each. No changes in cognition were observed for any profile over the follow-up despite clinical symptom improvement. The Severely Impaired profile had the lowest premorbid adjustment, brain and cognitive reserve, and the highest levels of functional impairment. A higher number and burden of recent stressful life events were reported in the Average Cognition profile. The findings suggest that stable transdiagnostic latent cognitive profiles are observable even at very early stages of manifest mood and psychotic illness. The Severely Impaired profile appears to map to indices of abnormal neurodevelopment, while the Average Cognition profile appears to represent a more stress-resilient phenotype.

1. Introduction

Accumulating evidence suggests that cognitive impairment is an outcome-shaping transdiagnostic feature of psychopathology, highlighting that diagnostic categories alone are insufficient for capturing clinically relevant cognitive differences compared to the norm (Abramovitch et al., 2021; Carruthers et al., 2021; Correa-Ghisays et al., 2022; Lewandowski et al., 2024; Van Rheenen et al., 2016; Van Rheenen et al., 2020b). Within this transdiagnostic framework, the burden of cognitive impairment is particularly pronounced for mood and psychotic disorders (Abramovitch et al., 2021), and this burden is closely linked with functional disability (Bowie et al., 2010).

At the same time, schizophrenia, bipolar disorder, and major depression each exhibit substantial person-to-person heterogeneity in the presence and magnitude of cognitive impairment (Carruthers et al., 2019a; Karantonis et al., 2020; Van Rheenen and Rossell, 2016; Van Rheenen et al., 2017); and data-driven clustering methods have been increasingly used to parse this cognitive heterogeneity (Carruthers et al., 2021; Guo et al., 2023; Russo et al., 2017; Van Rheenen et al., 2017; Wenzel et al., 2024). These methods have resulted in the identification of latent subgroups, or profiles, often in a 3-profile structure that comprises patients with relatively intact or severely impaired cognition bordering those with mild-moderate cognitive decrements (Carruthers et al., 2019b; Carruthers et al., 2021; Green et al., 2020; Martin et al., 2020; Pu et al., 2018).

These cognitive profiles have been shown to cut across diagnostic boundaries (Crouse et al., 2020; Van Rheenen et al., 2017), map onto differences in psychosocial functioning (Carruthers et al., 2021; Crouse et al., 2020; Green et al., 2020; Wenzel et al., 2021), and have distinguishing biobehavioural characteristics (Czepielewski et al., 2016; Karantonis et al., 2021b; Lewandowski et al., 2019; Pu et al., 2018; Van Rheenen et al., 2018; Vicent-Gil et al., 2021; Wenzel et al., 2024). And while the evidence mapping these profiles to *unique* patterns of brain morphology is generally weak (Karantonis et al., 2022), some research has found meaningful profile differentiation in terms of functional imaging (Lewandowski et al., 2018b), demographic (Lewandowski et al., 2014) and broader cognitive features (Karantonis et al., 2020; Van Rheenen and Rossell, 2016; Van Rheenen et al., 2017), as well as genetic (Russo et al., 2017) and genomic factors (Gurvich et al., 2023) that are relevant to developmental/aging pathways. Collectively, these data raise the possibility that cognitive profiles on the mood and psychosis spectrum index disparate cognitive trajectories influenced by dissociable factors.

Although cognitive profiles have been repeatedly found in adults with established illness (Green et al., 2020; Karantonis et al., 2022; Martin et al., 2020), preliminary work has also identified them earlier in the illness course (Crouse et al., 2020; Crouse et al., 2018; Reser et al., 2015; Wenzel et al., 2024; Wenzel et al., 2021). These profiles may thus have potential for transdiagnostic outcome-based risk stratification, but their prognostic utility remains unclear given the near-complete absence of longitudinal studies specifically examining the stability of cognitive profile membership over time, and the nature and predictors of within-profile cognitive change and between-profile transition. Moreover, most prior studies have examined cognitive profiles within single diagnoses, leaving questions open not only about how cognitive profiles emerge and evolve over time, but also about comparability when disorders are considered together. Longitudinal transdiagnostic cognitive studies during the early course of mood and psychotic illness are critically needed to address these gaps.

In this study we examined the latent structure of cognitive heterogeneity, its temporal stability, and its correlates, in a transdiagnostic sample of individuals at clinical high risk (CHR) for psychosis and those with a recent onset of psychosis (ROP) or depression (ROD). We used data from the Personalized Prognostic Tools for Early Psychosis Management (PRONIA) project, to which participants were *a)* recruited in either a high-risk state or within 2-years of their initial symptom onset; *b)* deeply phenotyped across several factors; *and c)* tracked over 11-months of the early stage of illness that is typically characterized by increased psychological distress and risk for relapse and suicidality (e.g., Brown et al., 2020; Dutta et al., 2010; Tan et al., 2014). The dataset therefore provided a unique opportunity to examine the presence of latent cognitive profiles, probability of profile membership permanency, extent of within-profile cognitive change, and the factors associated with cognitive profile membership and/or transition.

Factors considered mechanistically relevant, and hypothesised a priori to contribute to individual differences in cognitive functioning, were used here to characterise emergent cognitive profiles across several interrelated domains. Within this thematic framework, sociodemographic and clinical factors captured broad illness context and severity, whereas physical and brain-health factors indexed cardiometabolic and inflammatory burden and compromised brain structure. Development and stress-relevant factors were included to reflect early neurodevelopmental vulnerability, stress exposure and reserve capacities that may buffer or exacerbate cognitive decline. Finally, functioning and auxiliary cognitive measures were examined as external validators to aid interpretation of the profiles. These thematic domains were selected based on their relevance to cognitive development and functioning across the lifespan, their association with cognition or cognitive profiles

in previous mood and psychosis spectrum disorder studies, and/or their relevance to mood and psychosis spectrum disorder phenomenology, risk, and resilience (for example, see: Amoretti et al., 2019; Amoretti et al., 2022; Bauer et al., 2014; Carruthers et al., 2021; Caruana et al., 2024; Karantonis et al., 2021a; Lupien et al., 2007; Ringin et al., 2021; Ringin et al., 2023; Ringin et al., 2024; Van Rheenen et al., 2020a; Van Rheenen et al., 2018; Wells et al., 2020). We reasoned that examining factors from these domains would inform theoretical models of the emergence, trajectories, and significance of the cognitive profiles, and thus, could be clinically informative for stratification, prognosis and intervention target selection. Consistent with prior work, we predicted that three latent cognitive profiles would emerge in the data and that their membership would remain stable over time.

2. Methods

2.1. Participants

The sample comprised 666 clinical participants from the PRONIA study (87.2 % NCaucasian; 46.5 % female; n=225 ROP, n=229 ROD, n=212 CHR - see supplementary material for diagnostic criteria). Included data were collected across nine EU sites between February 2014 and November 2017. The study was approved by the local ethics committee of each site, and written informed consent was provided by participants or their guardians. General inclusion criteria were i) aged between 15 and 40 years, and ii) sufficient knowledge of the local language. Exclusion criteria were i) a history of neurological or somatic disease affecting the brain, ii) head trauma with loss of consciousness (>5 min), iii) current or past alcohol or substance dependence (previous 6 months), iv) intellectual disability, v) >90 days of antipsychotic treatment in the previous year, or vi) contraindication to magnetic resonance imaging. Further exclusion criteria for each diagnostic group is given in the supplementary material.

2.2. Cognitive variables included in the latent profile analysis

To be consistent with previous cognitive profiling research in established transdiagnostic samples (Karantonis et al., 2020; Van Rheenen et al., 2017), we used processing speed (Trail Making Test-A, Digit Symbol Substitution Test), attention (Continuous Performance Task – Identical Pairs), working memory (Auditory Digit Span, Self-ordered Pointing Task), verbal learning (Rey Auditory Verbal Learning Test), visual learning (Rey-Osterreith Complex Figure Test), executive function (Trail Making Test-B) and fluency (semantic/category-based and phonetic/letter-based) domain scores in the profile analysis. Scores from each test were first z-standardised and relevant scores reversed to ensure higher scores represented better performance. These scores were standardised differently depending on the analyses they were used in. The z-scores of domains with multiple tests were then summed into composite scores for use in the profiling procedure described below. All scores were normally distributed within standard bounds for skewness and kurtosis (Kim, 2013). **Supplementary Table S1** and **S2** have further detail.

2.3. Profile characterisation

Factors from the following thematic domains were examined as correlates of cognitive profile membership: *Sociodemographic*: age and sex; *Clinical*: diagnostic group, age of onset, illness duration, medication use and class, and clinical symptoms measured by the Positive and Negative Syndrome Scale (PANSS: Kay et al., 1987), the Scale for the Assessment of Negative Symptoms (SANS: Andreasen, 1983) and the Beck Depression Inventory-II (BDI-II: Beck et al., 1996); *Physical/brain health*: smoking, alcohol use, body mass index (BMI), waist circumference, global cortical thickness and blood-based biomarkers (CRP, BDNF and TNFα); *Development/stress-relevant*: premorbid adjustment (Premorbid Adjustment Scale, PAS: Cannon-Spoor et al., 1982), childhood adversity (Childhood Trauma Questionnaire, CTQ: Bernstein and Fink, 1998), bullying (Bullying Scale for Adults, BSA: Haidl et al., 2020), recent life events (Cologne Chart of Life Events, CoLe, Betz et al., 2020), brain reserve capacity proxied by head size/intracranial volume (ICV), cognitive reserve capacity proxied by crystallised intelligence (WAIS Vocabulary subtest, Wechsler, 1997), and psychiatric hospitalisations, suicide attempts and obstetric complications (measured by self-report).

Functioning (Global Assessment of Functioning scale [GAF]: Hall, 1995), and *auxiliary cognitive variables* not included in the initial cognitive profiling procedure (general and fluid cognition proxied by *g* and the WAIS Matrix Reasoning subtest) were also examined for further insight into the profiles. The Supplementary Material has further details about the measures.

2.4. Statistical analysis

Latent Profile Analyses (LPA) and Latent Transition Analyses (LTA) - a repeated measures extension of LPA, were performed in Mplus version 8.0 (Muthén and Muthén, 2010). LPA (cross-sectional) and LTA (longitudinal) are model-based approaches that capture the latent structure of the data, and in the case of LTA, individual transitions between profiles over time. Unlike traditional clustering methods such as hierarchical clustering, these approaches enable estimation of probabilities for class membership, and for LTA, transition probabilities, to formally quantify stability and change in latent status. Transition probabilities specifically allow characterisation of the extent to which profiles are stable versus malleable and facilitate identification of distinct patterns of improvement and decline. Aside from attrition (accounted for by re-analysing only the participants with data available at both T0 and T1 for the LTA analyses described below), the data analysed was complete and no data was missing. All other analyses were completed using the Statistical Package for the Social Sciences (SPSS) Version 30.0 (IBM).

2.4.1. Latent profile identification

LPA was conducted using the Timepoint 0 (T0) and Timepoint 1 (T1; 9-months per protocol but 11-month average follow up) data separately, to identify cognitive profiles at each timepoint based on the seven cognitive domains.[1] At both timepoints, a profile varying diagonal variance-covariance matrix was selected given it is a more realistic model than the standard profile invariant diagonal matrix since each variable (cognitive domain scores standardised to the patient sample) can have a different amount of variation in each profile (Johnson, 2021). Profiles were added within the separate T0 and T1 models until an error appeared indicating poor model fit.

The optimal number of profiles at each timepoint was assessed using the following information; i) model fit indices; Akaike information criterion (AIC), Bayesian information criterion (BIC), sample-size adjusted Bayesian information criterion (ssaBIC), where lower values indicated better model fit, ii) the Lo-Mendel-Rubin Likelihood Ratio Test (LMR-LRT), where a significant p value indicates a model where *k*-1 profiles provides the better fit, iii) Entropy, or classification accuracy, where higher values reflect a more accurate profile selection, iv) profile size and v) profile discrimination based on cognitive performance.

The cognitive performance of each profile was compared using ANOVA, including diagnostic group as a fixed factor to identify potential interaction effects and validate the appropriateness of our transdiagnostic analytic approach. To aid the interpretation of each profile, and for visualisation purposes, the means and standard deviations of participants were standardised against that of a healthy control group

[1] The T0 LPA profiles were derived from larger sized samples compared to the T1 LPA profiles, due to attrition between the timepoints. Cognitive domain scores were standardised to the patient sample at each timepoint (n=666 at T0 and n=407 at T1).

(n=360 at T0 and n=271 at T1). The final T0 and T1 models were further evaluated with 10-fold cross-validation.

2.4.2. Profile stability and transition

LTA was used to assess profile equivalence and the likelihood of profile transition across T0 and T1 in the subsample of participants with data available at *both* timepoints (n=407).[2] Prior to this, an LPA was conducted on the T0 data of the subsample[3] to determine if the profile structure of the larger sample replicated, to inform the LTA model specifications. In a longitudinal context, profile equivalence implies the qualitative meaning and characteristics of the profiles at each timepoint are the same, which is a precondition for interpreting transition probabilities. To establish profile equivalence, two competing models were computed in the subsample data, one where the cognitive means of each profile calculated in the LTA were freely estimated (non-invariance model), and the other where the means were constrained to be equal at each timepoint (invariance model). The fit of the two models were then compared using the BIC and AIC (lower values indicating better fit) and a chi-square test. The profiles were considered equivalent if there was no decrease in model fit when the profile means were constrained to be equal. If profile equivalence (measurement invariance) was established, the transition probability matrix was examined to assess profile stability and the probability of participants in each profile at T0 transitioning to any other profile at T1.

2.4.3. Profile characterisation

Predictors of transition could not be examined given the negligible number of transitioners identified in the LTA, but factors associated with T0-latent profile membership were explored (**Table S3**). Separate sets of ANOVAs (with post-hoc Games-Howell tests to correct for pairwise multiple comparisons), chi square tests, and paired-sample *t*-tests were used to characterise and compare these profiles on two-types of outcomes: a) the sociodemographic, clinical, cognitive/functioning, physical/brain health, and development/stress-relevant factors also measured at T0 (analysis set 1 - cross-sectional); and b) the degree of across-timepoint change in the time-varying factors[4] or the frequency of events occurring following T0 (analysis set 2 – prospective). We did not apply formal correction for multiple testing across these outcomes due to the exploratory nature of this element of the study. The LPA-defined T0 profiles are reported for analysis set 1 given they were derived from the full sample, though we verified the results of these analyses in the T0 LTA-defined profiles derived from the subsample. For analysis set 2, the LTA-defined T0 profiles were used to allow for the removal of transitioners (determined based on the LTA profiles) to circumvent the confounding effect their inclusion would have on the results. Although the T0 profiles in these separate analyses sets were derived from distinct, albeit related, profiling procedures, they have ~90 % participant overlap and are near-identical.

3. Results

The sociodemographic, clinical and cognitive characteristics of the transdiagnostic clinical sample at T0 and T1 are presented in **Table S4,** the healthy control sample used for comparative visualisation purposes and profile interpretation in **Table S5**, and each diagnostic group (CHR, ROP, ROD) in **Table S6.**

3.1. Latent cognitive profiles

666 participants (225 ROP, 229 ROD, 212 CHR) were included in the LPA at T0 and 407 participants (131 ROP, 147 ROD, 129 CHR) were included at T1. The sample attrition rate was 38.9 %. At T0, those *without* cognitive data at follow-up had significantly poorer working memory ($F(2664) = 20.31$, $p < 0.001$), processing speed ($F(2664) = 10.19$, $p = 0.001$), visual learning ($F(2664) = 6.16$, $p = 0.013$), verbal learning ($F(2664) = 16.00$, $p < 0.001$), and executive function ($F(2664) = 6.31$, $p = 0.012$), general cognition ($F(1663) = 14.53$, $p < 0.001$) and fluid intelligence ($F(1661) = 12.09$, $p < 0.001$) than those with follow-up data, but no differences in clinical, functioning or other variables were evident **(Table S7)**.

LPA model fit statistics for both T0 (full sample) and T1 (subsample with follow-up data) are presented in **Table S8.** A 3-profile model was considered optimal at both timepoints, suggesting the latent profile structure at both timepoints was the same. All diagnoses were represented in each profile (**Fig. S1**). The profiles differed from each other in cognitive performance but there were no significant profile by diagnostic group interaction effects (**Table S9**), demonstrating the appropriateness of the transdiagnostic approach. Ten-fold cross validation showed high reliability of the 3-profile solution at both T0 and T1, with intraclass correlation coefficients of 0.991 (95 % CI; 0.989 – 0.992, $p < 0.001$), and 0.916 (95 % CI; 0.893 – 0.935, $p < 0.001$), respectively. Visual inspection of the profiles at both timepoints indicated that the shape and pattern of cognitive scores within the profiles was similar at T0 and T1. The profiles were labelled 'Average Cognition', Moderately Impaired', and 'Severely Impaired' based on their cognitive performance relative to healthy controls (Fig. 1 and **Table S10).** The average proportion of the full clinical sample in each profile across timepoints was: 38.8 % Average Cognition, 48.5 % Moderately Impaired, 12.7 % Severely Impaired (**Table S6** details the breakdown by timepoint).

3.2. Profile stability and transition

The prerequisite LPA in the T0 data of the subsample with follow-up data (used to inform the LTA) indicated that the 3-profile structure of the full sample was well replicated (**Table S11**). The subsequent LTA in the subsample revealed profile equivalence across the T0 and T1 timepoints, indicated by lower BIC and AIC values for the measurement invariance model compared to the non-invariance model, and a non-significant chi-square value (Table 1)**.** The transition probabilities for each profile are shown in Fig. 2 and **Table S12**. There was <5 % probability of transition in all profiles, indicating a high degree of stability. The probability of transitioning versus remaining in the same profile did not differ by diagnosis ($\chi^2 = 3.56$, $p = 0.169$).

3.3. Profile characterisation

3.3.1. Cognitive profile differences in factors measured at T0 (analysis set 1)

Characteristics of the cognitive profiles derived from the full sample LPA at T0 are reported in Table 2. There were no profile differences in age or sex. The proportion of CHR, ROP and ROD participants in each profile significantly differed (**Fig. S1**), with the highest proportion of ROPs in the Severely Impaired profile (65.0 %), of RODs in the Average Cognition profile (47.8 %), and a relatively even diagnostic split in the Moderately Impaired profile (34.2 % CHR, 34.5 % ROP, and 31.3 % ROD). The proportion of those who did not complete the T1 cognitive battery was highest in the Severely Impaired profile, followed by the Moderately Impaired and Average Cognition profiles (55.6 % vs 39.5 % vs 30.2 %). The descending order of symptom severity from the PANSS and the SANS total scores was: Severely Impaired > Moderately

[2] To determine profile transition probabilities, rather than using the profile memberships established in the initial LPA, the LTA requires re-calculation of the profiles to account for the cognitive performance at the other timepoint. Hence, the LTA was conducted on only the participants whose data was available at *both* T0 *and* T1 (n=407).

[3] This T0 LPA used cognitive domain scores standardised to the participant subsample with data available at both timepoints.

[4] Between-profile difference scores were calculated by subtracting the value of a given variable at T0 from the same variable at T1. These were then compared between profiles using ANOVA.

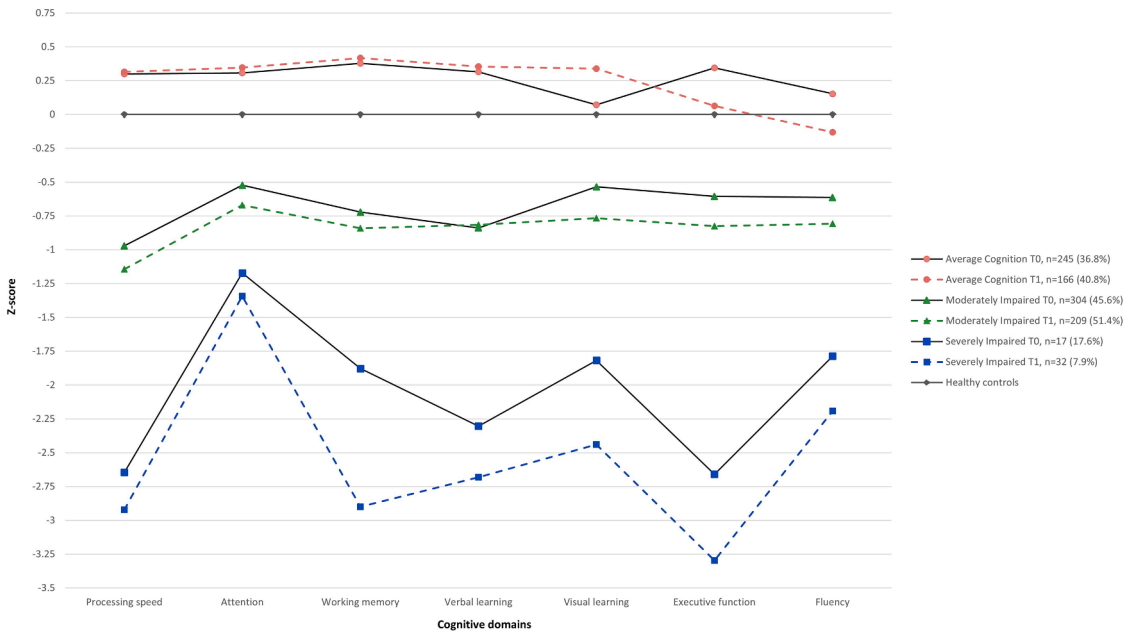

Fig. 1. Cognitive profiles derived from the clinical sample at T0 and T1. The T0 profiles were derived in the full sample (n= 666) while the T1 profiles were derived in the subsample with follow up data (n=407). Values reflect means and SDs. Note that scores are standardised to a healthy control sample, which was included in the study as a comparator group for visualisation and profile naming purposes only. Percentage in legend refers to the percentage of clinical participants in each profile *within* each timepoint.

Table 1
Fit indices for measurement invariance testing between Timepoint 0 (T0) and Timepoint 1 (T1).

Model	Free parameters	AIC	BIC	Loglikelihood	$\Delta\chi^{2a}$	*df*	*p*
Measurement invariance	50	14,010.56	14,211.01	-6955.28			
Measurement non-invariance	92	14,064.67	14,433.49	-6940.34	24.32	42	0.9868

Fit indices were generated from the Latent Transition Analysis (LTA) conducted on the participant subsample with data available at both T0 *and* T1 (n=407).The X2 difference test was conducted using the Satorra Bentler Scaled X2 test, which is specifically designed for models estimated with maximum likelihood estimation with robust standard errors (MLR). The degrees of freedom (df) and p value are associated with this test. A significant result suggests that measurement invariance does not hold, meaning the non-invariance model provides a better fit to the data, and the profiles should be interpreted separately. The test was performed to compare the measurement non-invariance model to the measurement invariance model, hence only one set of values are reported.

Impaired > Average Cognition. The Severely Impaired profile had significantly lower BDI-II scores and a higher psychotropic medication load, with more participants in this profile using sedatives/hypnotics/other anxiolytics and antidepressants than the Average Cognition profile. In turn, fewer in the Average Cognition profile used antipsychotics than the two impaired profiles.

General and fluid cognition differed significantly between all profiles with scores in the ascending order of Severely Impaired > Moderately Impaired > Average Cognition. The Severely Impaired profile had worse functioning, premorbid adjustment, and ICV (proxying brain reserve capacity) than the two other profiles, while the number and burden of recent life events at T0 was also rated lower. There were no differences in the proportion of participants in each profile self-reporting obstetric complications, suicide attempts or psychiatric hospitalisations prior to T0. However, crystallised intelligence (proxying cognitive reserve capacity) differed significantly between profiles, being lowest in the Severely Impaired profile, and highest in the Average Cognition profile.

The Severely Impaired profile encompassed more smokers than the Average Cognition profile but there were no significant profile differences in other physical/brain health measures. These profile characteristics mostly held for the T0 LTA profiles derived in the subsample with follow-up data, with only minor differences evident **(Table S13).**

3.3.2. Within- and between-group cognitive profile differences in time-varying factors over follow-up (analysis set 2)

Table S14 reports *within*-profile comparisons of the available T0 and T1 time-varying factors. Table 3 reports *between*-profile comparisons of the T1-T0 difference scores for these factors, and of other scores referencing events during the follow-up for which difference scores could not be calculated. Within all profiles, BMI slightly but significantly increased between T0 and T1, while SANS and PANSS scores significantly decreased. Waist circumference also significantly increased in the Moderate and Severely Impaired profiles, while executive function slightly worsened in the Average Cognition profile, as did attention in the Moderately Impaired profile. However, there were no significant between-profile differences in the *degree* of change in any of these factors. This contrasted significant BDI-II score decreases in the Average Cognition and Moderately Impaired profiles across timepoints which differed significantly in magnitude from the Severely Impaired profile, in whom no significant change from baseline effect was observed. The number and burden of life events occurring over the follow-up was also significantly higher in the Average Cognition and Moderately Impaired profiles than the Severely Impaired profile. No other within or between-profile differences over the follow-up were observed.

4. Discussion

This study represents one of the largest and most comprehensive

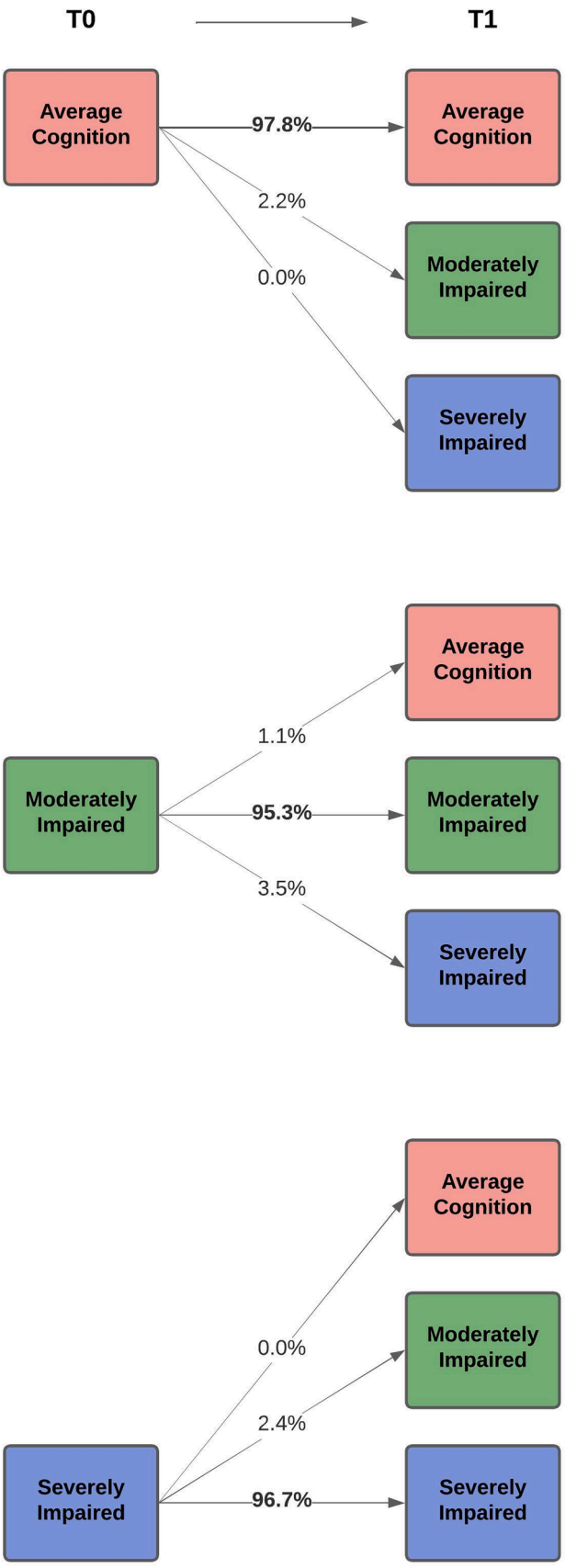

Fig. 2. Probability of transition between cognitive profiles at T0 and T1 for the subset of the sample with data at both timepoints (n=407).

characterisations of heterogeneity underlying the cognitive data of individuals on the mood and psychosis spectrum, and the only study to our knowledge, to have examined the stability of this heterogeneity during the early illness course. Consistent with previous work (Crouse et al., 2020; Crouse et al., 2018; Karantonis et al., 2020; Van Rheenen et al., 2017), we identified three robust cognitive profiles. One had average cognitive functioning with no particular weaknesses or strengths. The two others had cognitive performance that was, at minimum, half a standard deviation below that of healthy individuals, with the most severely impaired profile showing decrements of >1.75 standard deviations on most domains. Notably, the degree of impairment in these profiles was similar, if not more substantial, than that reported in a large, older, transdiagnostic sample with greater illness chronicity (Van Rheenen et al., 2017).

The profiles were transdiagnostic in composition, but differences in cognitive performance between them were not driven by a particular diagnostic group. There were also no diagnostic differences in the probability of transitioning versus remaining in the same profile. Importantly, all diagnoses were represented in all profiles, though there was a greater number of ROP participants in the Severely Impaired profile and a greater number of ROD participants in the Average Cognition profile. These proportion differences across profiles explain why traditional group-level analyses consistently show cognitive impairments to be of greater magnitude in primary psychotic versus primary mood disorders. However, ours, and other studies, suggest that such group-level analyses may be inadequate (Karantonis et al., 2020; Lewandowski et al., 2018a; Lewandowski et al., 2014; Van Rheenen et al., 2017), especially given that ROP participants were also represented in the Average Cognition profile, and ROD participants were represented in the Severely Impaired profile. The non-negligible inclusion of RODs in the two impaired profiles alongside the fact that CHR and ROP participants in the PRONIA study were allowed to currently or previously have depression, suggests that these profiles are unlikely to be driven solely by psychosis-specific factors. Likewise, cognitive impairments in ROD participants were less likely to be driven by comorbid psychosis features because this diagnostic group was 'purer' in the sense that participants within it could not also have met criteria for CHR or ROP. Rather, the observed cognitive heterogeneity suggests that participants with cognitive impairment may have other transdiagnostic vulnerability factors that may or may not interact with depression or psychosis for such impairments to manifest.

The latent three-profile structure identified in the full sample at T0 held via 10-fold cross-validation and in the subsample of participants with follow-up data (with >90 % cross-over in profile membership). The structure was also replicated in the subsample at T1, with profile equivalence metrics indicating temporal stability in the three profiles across time and in line with our hypothesis. Indeed, in the subsample, the likelihood of transitioning between profiles was low, with the average probability of patients remaining within the same profile across time being >95 %.

The profiles did not differ meaningfully on most measures of physical/brain health. However, the most severely impaired profile, whilst the smallest in size, had the highest psychotropic medication load and encompassed the largest proportion of antipsychotic users. This profile also had the highest PANSS/SANS scores but the lowest BDI-II scores, findings likely owed to the greater proportion of ROP patients (65 %) represented in this profile.[5] The Severely Impaired profile also had the lowest general cognition and fluid intelligence scores as well as the highest levels functional impairment, aligning to findings linking poor cognition to adverse psychosocial outcomes (Carruthers et al., 2021; Crouse et al., 2020). Crystalised intelligence scores were also lower in the Severely Impaired profile, as was ICV, consistent with evidence from

[5] See **Supplementary Table S6**, which shows significantly higher PANSS/SANS and lower BDI-II scores in the ROP group.

Table 2
Characterisation of Entire Timepoint 0 (T0) Sample Cognitive Profiles^.

Factor	Average Cognition (1)	Moderately Impaired (2)	Severely Impaired (3)	Profile Comparison	Effect size[#]	Significant post-hoc comparisons[*]
Inclusion at follow-up				χ^2 (2) = 21.50, $p < 0.001$ *	0.180	(1) v (2), (1) v (3), (2) v (3)
Included at follow-up (%)	171 (69.8)	184 (60.5)	52 (44.4)			
Attrition (%)	74 (30.2)	120 (39.5)	65 (55.6)			
Sociodemographic factors						
Age	24.57 ± 5.40	25.04 ± 6.01	25.17 ± 5.59	F (2662) = 0.62, p = 0.540	0.002	
Sex				χ^2 (2) = 4.34, p = 0.114	0.081	
Female (%)	125 (51.2)	136 (45.0)	47 (40.2)			
Male (%)	119 (48.8)	166 (55.0)	70 (59.8)			
Cognition and functioning						
General cognition (*g*)	0.94 ± 0.39	-0.13 ± 0.39	-1.61 ± 0.59	F (2662) = 1392.49, p < 0.001*	0.808	(1) v (2), (1) v (3), (2) v (3)
Fluid intelligence (WAIS matrix reasoning)	0.54 ± 0.61	-0.03 ± 0.87	-1.02 ± 1.15	F (2660) = 133.97, p < 0.001*	0.289	(1) v (2), (1) v (3), (2) v (3)
Functioning (GAF disability and impairment)	80.80 ± 7.68	79.31 ± 8.85	75.73 ± 9.44	F (2649) = 13.64, p < 0.001*	0.040	(1) v (3), (2) v (3)
Clinical factors						
Diagnostic group	84 (34.3)	104 (34.2)	24 (20.5)		0.252	(1) v (2), (1) v (3), (2) v (3)
CHR (%)	44 (18.0)	105 (34.5)	76 (65.0)	χ^2 (4) = 84.6, $p < 0.001$*		
ROP (%)	117 (47.8)	95 (31.3)	17 (14.5)			
ROD (%)						
Depressive symptoms (BDI-II)	24.92 ± 11.90	23.27 ± 12.43	19.70 ± 11.94	F (2603) = 6.33, p = 0.002*	0.021	(1) v (3), (2) v (3)
Positive, negative and general symptoms (PANSS)	53.13 ± 14.02	59.25 ± 19.13	69.01 ± 20.41	F (2630) = 30.65, p < 0.001*	0.089	(1) v (2), (1) v (3), (2) v (3)
Negative symptoms (SANS)	24.44 ± 20.52	30.45 ± 24.12	44.15 ± 28.52	F (2629) = 25.75, p < 0.001*	0.076	(1) v (2), (1) v (3), (2) v (3)
Age of illness onset (years)	23.83 ± 5.36	23.94 ± 6.05	24.18 ± 5.73	F (2584) = 0.14, p = 0.873	0.0005	
Illness duration (months)	8.52 ± 7.42	9.43 ± 13.94	8.87 ± 9.10	F (2584) = 0.41, p = 0.662	0.001	
Psychotropic medications (#)	1.05 ± 0.99	1.24 ± 1.21	1.62 ± 1.37	F (2636) = 8.87, p < 0.001*	0.027	(1) v (3), (2) v (3)
Hypnotics/sedatives/other anxiolytics use	36 (15.3)	63 (21.2)	30 (28.3)	χ^2 (2) = 8.09, p = 0.018*	0.113	(1) v (3)
Using (%)	200 (84.7)	234 (78.8)	76 (71.7)			
Not using (%)						
Antipsychotics	52 (22.0)	106 (35.7)	63 (59.4)	χ^2 (2) = 45.52, $p < 0.001$ *	0.267	(1) v (2), (1) v (3)
Using (%)	184 (78.0)	191 (64.3)	43 (40.6)			
Not using (%)						
Antidepressants						
Using (%)	123 (52.1)	114 (38.4)	33 (31.1)	χ^2 (2) = 16.61, $p < 0.001$ *	0.161	(1) v (3)
Not using (%)	113 (47.9)	183 (61.6)	73 (68.9)			
Development and stress-relevant factors						
Obstetric complications[@]		57 (19.1)			0.005	
Yes (%)	45 (18.7)	242 (80.9)	21 (18.8)	χ^2 (2) = 0.02, p = 0.993		
No (%)	196 (81.3)		91 (81.3)			
Head size (ICV, ml)	1546.68 ± 146.52	1546.15 ± 142.81	1485.00 ± 152.27	F (2624) = 6.69, p = 0.001*	0.021	(1) v (3), (2) v (3)
Crystallised intelligence (WAIS Vocabulary)	0.52 ± 0.73	-0.05 ± 0.84	-0.95 ± 1.11	F (2655) = 115.19, p < 0.001*	0.260	(1) v (2), (1) v (3), (2) v (3)
Premorbid Adjustment (PAS)	0.27 ± 0.12	0.30 ± 0.13	0.37 ± 013	F (2624) = 23.69, p < 0.001*	0.071	(1) v (3), (2) v (3)
Childhood Adversity (CTQ)	39.98 ± 13.19	41.11 ± 13.24	41.84 ± 14.46	F (2575) = 0.75, p = 0.472	0.003	
Bulling (BSA)	13.00 ± 9.88	13.45 ± 10.46	14.38 ± 10.82	F (2526) = 0.59, p = 0.553	0.0001	
[#] of recent life events (CoLE)[+]	4.07 ± 2.85	3.64 ± 2.86	2.89 ± 2.65	F (2643) = 6.65, p = 0.001*	0.020	(1) v (3), (2) v (3)
Burden of recent life events (CoLE)[+]	9.38 ± 7.35	8.38 ± 7.45	7.05 ± 7.43	F (2643) = 3.84, p = 0.022*	0.012	(1) v (3)
Previous psychiatric hospitalisation(s)		177 (59.4)	69 (63.3)	χ^2 (2) = 1.69, p = 0.429	0.051	
Yes (%)	134 (56.1)	121 (40.6)	40 (36.7)			
No (%)	105 (43.9)					
Psychiatric hospitalisations (#)	0.66 ± 0.69	0.82 ± 0.92	0.87 ± 0.87	F (2643) = 3.29, p = 0.038*	0.010	Not significant
Previous suicide attempt(s)	6 (2.5)	14 (4.7)	5 (4.5)	χ^2 (2) = 1.93, p = 0.381	0.055	
Yes (%)	234 (97.5)	281 (95.3)	107 (95.5)			
No (%)						
Physical and brain health factors						
Lifetime smoking	103 (42.7)	146 (48.8)	64 (56.6)		0.097	(1) v (3)
Smoker (%)	138 (57.3)	153 (51.2)	49 (43.4)	χ^2 (2) = 6.13, p = 0.047*		
Non-smoker (%)						

(*continued on next page*)

Table 2 (*continued*)

Factor	Average Cognition (1)	Moderately Impaired (2)	Severely Impaired (3)	Profile Comparison	Effect size[#]	Significant post-hoc comparisons[*]
Alcohol (units per week)	3.48 ± 6.09	4.06 ± 11.28	3.32 ± 9.02	F (2627) = 0.37, p = 0.689	0.001	
Body Mass Index (BMI)	23.76 ± 4.34	23.53 ± 4.72	23.98 ± 4.24	F (2616) = 0.45, p = 0.637	0.004	
Waist circumference (cm)	82.45 ± 11.99	80.63 ± 12.75	81.94 ± 14.06	F (2494) = 1.11, p = 0.330	0.004	
Blood based biomarkers CRP (mg/L)	0.98 ± 1.10	0.87 ± 0.92	1.11 ± 1.34	F (2387) = 1.25, p = 0.289	0.006	
TNFα (pg/mL)	1.86 ± 1.39	1.88 ± 1.36	1.98 ± 1.26	F (2410) = 0.17, p = 0.842	0.001	
BDNF (ng/mL)	23.89 ± 6.22	22.65 ± 7.60	24.28 ± 6.79	F (2410) = 1.99, p = 0.139	0.010	
Global CTh (mm^3)	2.96 ± 0.12	2.96 ± 0.12	2.95 ± 0.13	F (2625) = 0.30, p = 0.743	0.001	

Values reflect means and SDs unless otherwise stated. Note that generalised, fluid, and crystalised intelligence tests were auxiliary cognitive measures and were not included in the latent profile analysis used to derive the cognitive subgroups.

ˆProfiles were derived from the Latent Profile Analysis (LPA) conducted on the T0 data of the full sample (n=666).

[+] CoLE life events refer to those occuring in the 12 months preceeding T0.

[@] Obstetric complications were measured by asking participants if they had experienced any known infections or other complications during intrauterine (pregnancy) development or if there were complications during their birth

[#] Effect sizes reported are Eta-squared for one-way ANOVAs and Cramer's V for Chi-squared tests.

[*] Post-hoc comparisons completed for significant tests only. For one-way ANOVAs, Games Howell post hoc comparison was used. For chi-square, secondary chi-squares were run comparing each pairing of the profiles (average vs moderate, average vs severe, and moderate vs severe).

WAIS;Weschler Adult Intelligence Scale, GAF; Global Assessment of Functioing, CHR; Clincial High Risk for Psychosis, ROP; Recent Onset Psychosis, ROD; Recent Onset Depression, PANSS; Positive and Negative Syndrome Scale, SANS; Scale for the Assessment of Negative Symptoms, BDI; Beck Depression Inventory, CTQ; Childhood Trauma Questionnaire, PAS; Premorbid Adjustment Scale, BSA; Bullying Scale for Adults, CoLE; Cologne Life Events, BMI; Body Mass Index, ICV; Intracranial Volume, CTh; Cortical Thickness, CRP; C-Reactive Protein, TNFα; Tumor Necrosis Factor alpha, BDNF; Brain Derived Neurotrophic Factor; Severe; Severely Impaired profile, Moderate; Moderately Impaired profile, Average; Average Cognition profile.

older chronic samples (Burdick et al., 2014; Czepielewski et al., 2016; Karantonis et al., 2020; Van Rheenen et al., 2020a; Van Rheenen et al., 2018; Van Rheenen et al., 2017).

Crystalised intelligence is a developmental marker indexing premorbid cognition and *cognitive reserve* (Boyle et al., 2021; Oliveira et al., 2014; Van Rheenen et al., 2020a), while ICV reflects *brain reserve* and maximal attained head size given that it scales with early postnatal growth but remains stable from late childhood onwards (DeCarli et al., 2024; Farias et al., 2012; Gale et al., 2003; Van Loenhoud et al., 2018). In our data, evidence of lower cognitive and brain reserve alongside worse premorbid adjustment in the Severely Impaired profile, suggest that there are abnormalities in the developmental trajectory of individuals with severe cognitive impairment on the mood and psychosis spectrum.[6]

Lower cognitive and brain reserve have previously been implicated in worse cognitive and clinical outcomes in mood and psychotic disorders and are known predictors of cognitive decline in older people (Ayesa-Arriola et al., 2023; Camprodon-Boadas et al., 2024; Herrero et al., 2020; Mortimer et al., 2003; Van Rheenen et al., 2020a; Zahodne et al., 2015). Thus, the Severely Impaired profile may be especially vulnerable to exacerbated adverse cognitive (and perhaps clinical) outcomes in the *longer-term*. Indeed, a study of near-midlife mood and psychosis spectrum patients provided evidence of putatively premature cognitive ageing in only those displaying the most severe cognitive impairments compared to age-matched patients with moderate cognitive impairments and those with no cognitive impairments at all (Van Rheenen et al., 2017). That said, in our data, no substantial changes in cognition were observed for any of the profiles over the *short-term*. This was despite meaningful and equivalently sized improvements in psychosis and depressive symptoms (bar the Severely Impaired profile who saw no change in the latter) in *all* profiles over the follow-up. This divergent pattern, in the context of stability in profile membership over time, gives credence to the notion that the cognitive profiles identified in this, and previous work, are not merely reflections of current clinical symptomatology (Karantonis et al., 2020; Martin et al., 2020). Rather the profiles appear to be phenotypes reflecting stable cognitive traits in their own right.

The experience of childhood adversity, suicide attempts, psychiatric hospitalisations, and recent stressful life events was reported in all profiles. There were no between-profile differences in the former variables, but the number and perceived burden of life events reported by the Moderately Impaired and Average Cognition profiles was roughly equivalent and higher than the Severely Impaired profile at both timepoints. In the context of previous evidence showing that childhood adversity, life events, suicidality, and the cumulative toxicity of multiple clinical episodes all contribute to cognitive impairment (Aas et al., 2014; Burdick et al., 2014; Hasselbalch et al., 2013; Richard-Devantoy et al., 2014), these findings raise the possibility that the Average Cognition profile represents a more stress-resilient cognitive phenotype. Indeed, the preserved cognitive performance of this profile despite equivalent or greater stressor burden compared to the other profiles is consistent with a pattern of cognitive resilience. The Average Cognition profile also displayed the highest levels of crystallised intelligence - our proxy of cognitive reserve - which, consistent with contemporary frameworks describing cognitive reserve as a proposed mechanism of resilient outcomes (Stern et al., 2023), may support compensatory mechanisms (Barulli and Stern, 2013) that can buffer against the adverse cognitive effects of such stressors (for an example, see Fares-Otero et al., 2024).

A strength of this study is its characterisation of cognitive profiles using factors that speak to cognitive risk and resilience. This contrasts past work that has mainly compared profiles on clinical symptoms, functioning, and/or neural correlates that lack clear relevance to cognitive development/aging pathways. Nonetheless, our findings should be interpreted within the context of some limitations. First, the limited follow-up period (average of 11 months) may have impeded our

[6] It should be noted that the significance of the ICV effect reduced from p = .001 to p = .053 in the T0 re-analysis of the subsample with follow up data, though this was likely due to a reduction in power given the means, standard deviations and effect magnitude in the subsample were near identical to that of the full sample.

Table 3
Comparison of change (Timepoint 0 to Timepoint 1) between cognitive profiles[^].

		Average Cognition (1)	Moderately Impaired (2)	Severely Impaired (3)	Profile Comparison	Effect size[#]	Significant post-hoc comparisons[*]
Factor category	*T1-T0 difference scores*						
Cognition	Processing speed	-0.04 ± 0.62	0.03 ± 0.72	0.004 ± 0.92	F (2389) = 0.50, p = 0.607	0.003	
	Attention	0.01 ± 0.83	0.01 ± 0.59	-0.19 ± 0.69	F (2390) = 2.10, p = 0.124	0.011	
	Working memory	-0.02 ± 0.55	0.08 ± 0.71	-0.09 ± 0.77	F (2391) = 1.79, p = 0.168	0.009	
	Verbal learning	-0.01 ± 0.62	0.03 ± 0.81	0.11 ± 0.85	F (2391) = 0.46, p = 0.631	0.002	
	Visual learning	0.09 ± 0.77	-0.07 ± 0.86	0.08 ± 0.97	F (2391) = 1.89, p = 0.152	0.010	
	Executive function	-0.10 ± 0.59	0.11 ± 0.86	0.06 ± 1.28	F (2385) = 2.79, p = 0.062	0.014	
	Fluency	-0.02 ± 0.68	0.06 ± 0.68	0.01 ± 0.54	F (2391) = 0.55, p = 0.578	0.003	
	General cognition (*g*)	-0.02 ± 0.42	0.06 ± 0.53	-0.04 ± 0.67	F (2390) = 1.32, p = 0.270	0.007	
	Fluid intelligence (WAIS matrix-reasoning)	-0.001 ± 0.67	0.02 ± 0.86	0.08 ± 1.23	F (2385) = 0.20, p = 0.869	0.001	
Clinical factors	Positive, negative and general symptoms (PANSS)	-12.15 ± 14.00	-14.30 ± 16.98	-17.79 ± 17.26	F (2371) = 2.27, p = 0.105	0.012	
	Negative symptoms (SANS)	-8.58 ± 21.94	-12.56 ± 22.20	-8.05 ± 21.94	F (2371) = 1.87, p = 0.156	0.010	
	Depressive symptoms (BDI-II)	-11.41 ± 11.53	-9.08 ± 11.37	-3.39 ± 12.78	**F (2320) = 6.93, p = 0.001**[*]	0.041	(1) v (3), (2) v (3)
Developmental factors	Head size (ICV)	-1.04 ± 14.50	-0.95 ± 15.20	-4.43 ± 15.07	F (2, 340) = 0.86, p = 0.425	0.005	
	Crystallised intelligence (WAIS vocabulary)	0.01 ± 0.43	0.05 ± 0.48	0.005 ± 0.65	F (2382) = 0.13, p = 0.756	0.001	
Physical and brain health factors	BMI	0.59 ± 1.65	0.69 ± 2.02	1.14 ± 2.11	F (2341) = 1.37, p = 0.254	0.008	
	Waist circumference (cm)	2.02 ± 5.77	2.02 ± 5.52	4.63 ± 5.70	F (2277) = 2.87, p = 0.058	0.020	
	Global CTh (mm^3)	0.001 ± 0.05	-0.01 ± 0.05	-0.01 ± 0.05	F (2341) = 2.54, p = 0.080	0.015	
	Events occurring between T0 and T1[+]						
Stress-relevant factors	Psychiatric hospitalisation(s) since T0 Yes (%) No (%)	23 (14.6) 135 (85.4)	42 (23.0) 141 (77.0)	13 (28.3) 33 (71.7)	χ^2 (2) = 5.84, p = 0.054	0.123	
	Suicide attempt(s) since T0 Yes (%) No (%)	0 (0.0) 158 (100)	1 (0.55) 183 (99.5)	0 (0.0) 46 (100.0)	χ^2 (2) = 1.11, p = 0.574	0.054	
	# of life events since T0 (COLE)	2.13 ± 1.85	1.92 ± 1.72	1.26 ± 1.45	**F (2385) = 4.43, p = 0.013**[*]	0.022	(1) v (3), (2) v (3)
	Burden of life events since T0 (COLE)	3.30 ± 3.62	3.40 ± 3.48	1.91 ± 2.25	**F (2379) = 3.55, p = 0.030**[*]	0.018	(1) v (3), (2) v (3)

Values reflect means and SDs unless otherwise stated.

[+] Change from T0 difference scores were unable to be calculated for these variables

[^] The profiles were derived from the Latent Transition Analyses (LTA) conducted on the participant subsample with data available at both T0 *and* T1 (n=407).

[#] Effect sizes reported are Eta-squared for one-way ANOVAs and Cramer's V for Chi-squared.

[*] Games Howell Post-hoc comparisons were completed for significant tests only.

PANSS; Positive and Negative Syndrome Scale, SANS; Scale for the Assessment of Negative Symptoms, BDI; Beck Depression Inventory, CoLE; Cologne Life Events, BMI; Body Mass Index, ICV; Intracranial Volume, CTh; Cortical Thickness.

capacity to see cognitive change within the profiles, since noticeable cognitive deterioration, at least in the absence of acute CNS injury, typically occurs in a protracted manner (Harada et al., 2013). Second, since an initial pre-T0 cognitive assessment was not included in the PRONIA study, the general absence of cognitive deterioration observed across all profiles could potentially be attributed to prior 'practice' from the T0 cognitive assessment artificially inflating T1 performance when declines from T0 may have otherwise been seen. However, the use of alternative forms of the cognitive tests at T1, where available, would have mitigated this to some extent. Third, participants without follow-up data generally had worse cognition at T0, and the attrition rate in the Severely Impaired profile was >50 %. Thus, cognitive deterioration in the Severely Impaired profile may not have been detected since participants arguably most at-risk for such deterioration dropped out and could not be included in the prospective analyses. That said, it is unlikely that this attrition would have affected the *temporal stability of membership* to this profile, because upward movement (which could translate to profile transition) in cognitively impaired individuals in the absence of intervention is usually reflective of practice effects, rather than true improvement. Nonetheless, the stability of this subgroup should be interpreted with caution given that a substantial number of its cases were unobserved at T1.

Fourth, although crystallised intelligence has been consistently used as a proxy for cognitive reserve capacity in past research, it is singular measure that does not capture broader components of the cognitive reserve construct related to education, occupational attainment and engagement in cognitively stimulating activities (Amoretti et al., 2019). Similarly, ICV is most consistently used as a proxy for brain reserve (Van Loenhoud et al., 2018) but alternate operationalisations have also been proposed (Stern, 2009). Fifth, given the exploratory nature of the study,

we did not apply formal correction for multiple testing across the key factors used to characterise latent cognitive profiles. Although Type I error risk was controlled for post-hoc pairwise between-profile comparisons, findings from this part of the study should therefore be considered hypothesis-generating. Finally, only neurocognitive profiles were examined here, but future research would do well to examine whether similar latent profiles can be identified based on social cognitive measures.

In sum, our findings not only demonstrate that transdiagnostic cognitive profiles are observable at very early stages of manifest clinical symptoms, but also that membership of these latent profiles remains stable across the following year. Notably, the Severely Impaired profile appears to be at least partially borne from an abnormal developmental trajectory and may be vulnerable to especially poor outcomes. In contrast, the Average Cognition profile appears to represent a more resilient cognitive phenotype given data suggesting that it is not simply less susceptible than cognitively impaired profiles to cognition impairing-stressors or putatively neurotoxic clinical events such as hospitalisations or suicide attempts. Rather this profile appears to be better able to compensate for them, such that cognition within it is spared. A factor that may facilitate this compensation - cognitive reserve - could therefore represent an interventional target for which enhancement could help to mitigate or attenuate cognitive impairment in mood and psychotic disorders. Future longitudinal studies with lengthier follow-ups are needed to determine the extent to which the findings of this work hold in the longer-term. Nonetheless, our findings do suggest that cognitive profile membership may have prognostic utility for outcome-based risk stratification across mood and psychosis illness stages and the lifespan.

Author contributions

TVR conceptualised the research idea and wrote the original draft; ER performed the statistical analysis; DM advised on the statistical analysis; All authors contributed to the interpretation of results and reviewed and edited the manuscript.

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Declaration of competing interest

All authors declare they have no conflicts of interest.

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Supplementary materials

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References

Aas, M., Dazzan, P., Mondelli, V., Melle, I., Murray, R.M., Pariante, C.M., 2014. A systematic review of cognitive function in first-episode psychosis, including a discussion on childhood trauma, stress, and inflammation. Front. Psychiatry 4, 182.
Abramovitch, A., Short, T., Schweiger, A., 2021. The C Factor: cognitive dysfunction as a transdiagnostic dimension in psychopathology. Clin. Psychol. Rev. 86, 102007.
Amoretti, S., Cabrera, B., Torrent, C., Bonnín, C.d.M., Mezquida, G., Garriga, M., Jiménez, E., Martínez-Arán, A., Solé, B., Reinares, M., 2019. Cognitive reserve assessment scale in health (CRASH): its validity and reliability. J. Clin. Med. 8, 586.
Amoretti, S., Rabelo-da-Ponte, F.D., Garriga, M., Forte, M.F., Penades, R., Vieta, E., Parellada, E., Ramos-Quiroga, J.A., Gama, C.S., Verdolini, N., 2022. Obstetric complications and cognition in schizophrenia: a systematic review and meta-analysis. Psychol. Med. 52, 2874–2884.
Andreasen, N.A., 1983. Scale for the Assessment of Negative Symptoms. University of Iowa, Iowa City, Iowa.
Ayesa-Arriola, R., Miguel-Corredera, M., de la Foz, V.O.-G., Neergaard, K.D., Correa-Ghisays, P., Setién-Suero, E., Crespo-Facorro, B., 2023. Education and long-term outcomes in first episode psychosis: 10-year follow-up study of the PAFIP cohort. Psychol. Med. 53, 66–77.
Barulli, D., Stern, Y., 2013. Efficiency, capacity, compensation, maintenance, plasticity: emerging concepts in cognitive reserve. Trends Cogn. Sci. (Regul. Ed.) 17, 502–509.
Bauer, I.E., Pascoe, M.C., Wollenhaupt-Aguiar, B., Kapczinski, F., Soares, J.C., 2014. Inflammatory mediators of cognitive impairment in bipolar disorder. J. Psychiatr. Res. 56, 18–27.
Beck, A.T., Steer, R.A., Brown, G.K., 1996. Beck Depression Inventory-Second Edition (BDI-II). Psychological Corporation San Antonio, Tx.
Bernstein, D.P., Fink, L., 1998. Childhood Trauma Questionnaire: A Retrospective Self-Report. Manual. Psychological Corporation.
Betz, L.T., Penzel, N., Kambeitz-Ilankovic, L., Rosen, M., Chisholm, K., Stainton, A., Haidl, T.K., Wenzel, J., Bertolino, A., Borgwardt, S., 2020. General psychopathology links burden of recent life events and psychotic symptoms in a network approach. NPJ. Schizophr. 6, 40.
Bowie, C.R., Depp, C., McGrath, J.A., Wolyniec, P., Mausbach, B.T., Thornquist, M.H., Luke, J., Patterson, T.L., Harvey, P.D., Pulver, A.E., 2010. Prediction of real-world functional disability in chronic mental disorders: A comparison of schizophrenia and bipolar disorder. Am. J. Psychiatry 167, 1116–1124.
Boyle, R., Knight, S.P., De Looze, C., Carey, D., Scarlett, S., Stern, Y., Robertson, I.H., Kenny, R.A., Whelan, R., 2021. Verbal intelligence is a more robust cross-sectional measure of cognitive reserve than level of education in healthy older adults. Alzheimers. Res. Ther. 13, 1–18.
Brown, E., Bedi, G., McGorry, P., O'Donoghue, B., 2020. Rates and predictors of relapse in first-episode psychosis: an Australian cohort study. Schizophrenia Bulletin Open 1, sgaa017.
Burdick, K.E., Russo, M., Frangou, S., Mahon, K., Braga, R.J., Shanahan, M., Malhotra, A. K., 2014. Empirical evidence for discrete neurocognitive subgroups in bipolar disorder: clinical implications. Psychol. Med. 44, 3083–3096.
Camprodon-Boadas, P., De Prisco, M., Rabelo-da-Ponte, F.D., Sugranyes, G., Clougher, D., Baeza, I., Torrent, C., Castro-Fornieles, J., Tosetti, Y., Vieta, E., 2024. Cognitive reserve and cognition in mood disorders: A systematic review and meta-analysis. Psychiatry Res. 339, 116083.
Cannon-Spoor, H.E., Potkin, S.G., Wyatt, R.J., 1982. Measurement of premorbid adjustment in chronic schizophrenia. Schizophr. Bull. 8, 470–484.
Carruthers, S.P., Gurvich, C.T., Meyer, D., Bousman, C., Everall, I.P., Neill, E., Pantelis, C., Sumner, P.J., Tan, E.J., Thomas, E.H., Van Rheenen, T., Rossell, S., 2019a. Exploring heterogeneity on the Wisconsin card sorting test in Schizophrenia spectrum disorders: A cluster analytical investigation. J. Int. Neuropsychol. Soc. 1–11.
Carruthers, S.P., Van Rheenen, T.E., Gurvich, C., Sumner, P.J., Rossell, S.L., 2019b. Characterising the structure of cognitive heterogeneity in schizophrenia spectrum disorders—A systematic review and narrative synthesis. Neurosci. Biobehav. Rev. 107, 252–278.

Carruthers, S.P., Van Rheenen, T.E., Karantonis, J.A., Rossell, S.L., 2021. Characterising demographic, clinical and functional features of cognitive subgroups in Schizophrenia spectrum disorders: A systematic review. Neuropsychol. Rev. 1–21.
Caruana, G.F., Carruthers, S.P., Berk, M., Rossell, S.L., Van Rheenen, T.E., 2024. To what extent does white matter map to cognition in bipolar disorder? A systematic review of the evidence. Prog. Neuropsychopharmacol. Bol. Psychiatry 128, 110868.
Correa-Ghisays, P., Sánchez-Ortí, J.V., Balanzá-Martínez, V., Selva-Vera, G., Vila-Francés, J., Magdalena-Benedito, R., Victor, V.M., Escribano-López, I., Hernández-Mijares, A., Vivas-Lalinde, J., 2022. Transdiagnostic neurocognitive deficits in patients with type 2 diabetes mellitus, major depressive disorder, bipolar disorder, and schizophrenia: A 1-year follow-up study. J. Affect. Disord. 300, 99–108.
Crouse, J.J., Chitty, K.M., Iorfino, F., Carpenter, J.S., White, D., Nichles, A., Zmicerevska, N., Tickell, A.M., Lee, R.S.C., Naismith, S.L., Scott, E.M., Scott, J., Hermens, D.F., Hickie, I.B., 2020. Transdiagnostic neurocognitive subgroups and functional course in young people with emerging mental disorders: a cohort study. BJPsych. Open. 6, e31.
Crouse, J.J., Moustafa, A.A., Bogaty, S.E., Hickie, I.B., Hermens, D.F., 2018. Parcellating cognitive heterogeneity in early psychosis-spectrum illnesses: a cluster analysis. Schizophr. Res. 202, 91–98.
Czepielewski, L.S., Wang, L., Gama, C.S., Barch, D.M., 2016. The relationship of intellectual functioning and cognitive performance to brain structure in schizophrenia. Schizophr. Bull. 43, 355–364.
DeCarli, C., Maillard, P., Pase, M.P., Beiser, A.S., Kojis, D., Satizabal, C.L., Himali, J.J., Aparicio, H.J., Fletcher, E., Seshadri, S., 2024. Trends in intracranial and cerebral volumes of Framingham heart study participants born 1930 to 1970. JAMa Neurol. 81, 471–480.
Dutta, R., Murray, R.M., Hotopf, M., Allardyce, J., Jones, P.B., Boydell, J., 2010. Reassessing the long-term risk of suicide after a first episode of psychosis. Arch. Gen. Psychiatry 67, 1230–1237.
Fares-Otero, N.E., Borràs, R., Solé, B., Torrent, C., Garriga, M., Serra-Navarro, M., Forte, M.F., Montejo, L., Salgado-Pineda, P., Montoro, I., 2024. Cognitive reserve moderates the relationship between childhood maltreatment, objective and subjective cognition, and psychosocial functioning in individuals with first-episode psychosis. Psychol. Trauma: Theory, Research, Practice, Policy.
Farias, S.T., Mungas, D., Reed, B., Carmichael, O., Beckett, L., Harvey, D., Olichney, J., Simmons, A., DeCarli, C., 2012. Maximal brain size remains an important predictor of cognition in old age, independent of current brain pathology. Neurobiol. Aging 33, 1758–1768.
Gale, C.R., Walton, S., Martyn, C.N., 2003. Foetal and postnatal head growth and risk of cognitive decline in old age. Brain 126, 2273–2278.
Green, M.J., Girshkin, L., Kremerskothen, K., Watkeys, O., Quidé, Y., 2020. A systematic review of studies reporting data-driven cognitive subtypes across the psychosis spectrum. Neuropsychol. Rev. 30, 446–460.
Guo, W., Liu, B., Wei, X., Ju, Y., Wang, M., Dong, Q., Lu, X., Sun, J., Zhang, L., Guo, H., Zhao, F., Li, W., Li, Z., Liao, M., Zhang, L., Liu, J., Zhang, Y., Li, L., 2023. The longitudinal change pattern of cognitive subtypes in medication-free patients with major depressive disorder: a cluster analysis. Psychiatry Res. 327, 115413.
Gurvich, C., Thomas, N., Hudaib, A.-R., Van Rheenen, T.E., Thomas, E.H.X., Tan, E.J., Neill, E., Carruthers, S.P., Sumner, P.J., Romano-Silva, M., Bozaoglu, K., Kulkarni, J., Rossell, S.L., 2023. The relationship between cognitive clusters and telomere length in bipolar-schizophrenia spectrum disorders. Psychol. Med. 53, 5119–5126.
Haidl, T.K., Schneider, N., Dickmann, K., Ruhrmann, S., Kaiser, N., Rosen, M., Seves, M., Lichtenstein, T., Upthegrove, R., Salokangas, R.K., 2020. Validation of the bullying scale for adults-results of the PRONIA-study. J. Psychiatr. Res. 129, 88–97.
Hall, R.C., 1995. Global assessment of functioning: a modified scale. Psychosomatics. 36, 267–275.
Harada, C.N., Love, M.C.N., Triebel, K., 2013. Normal cognitive aging. Clin. Geriatr. Med. 29, 737.
Hasselbalch, B.J., Knorr, U., Hasselbalch, S., Gade, A., Kessing, L.V., 2013. The cumulative load of depressive illness is associated with cognitive function in the remitted state of unipolar depressive disorder. Eur. Psychiatry 28, 349–355.
Herrero, P., Contador, I., Stern, Y., Fernandez-Calvo, B., Sánchez, A., Ramos, F., 2020. Influence of cognitive reserve in schizophrenia: A systematic review. Neurosci. Biobehav. Rev. 108, 149–159.
Johnson, S.K., 2021. Latent profile transition analyses and growth mixture models: A very non-technical guide for researchers in child and adolescent development. New Dir. Child Adolesc. Dev. 2021, 111–139.
Karantonis, J., Hughes, M., Rossell, S.L., Wannan, C., Pantelis, C., Cropley, V., Rheenen, T.E.V., 2021a. A systematic review of brain morphology-cognition relationships on the schizophrenia-bipolar disorder spectrum. Schizophr. Bull.
Karantonis, J.A., Carruthers, S.P., Burdick, K.E., Pantelis, C., Green, M., Rossell, S.L., Hughes, M.E., Cropley, V., Van Rheenen, T.E., 2022. Brain morphological characteristics of cognitive subgroups of Schizophrenia-Spectrum Disorders and Bipolar Disorder: A systematic review with narrative synthesis. Neuropsychol. Rev. 192–220.
Karantonis, J.A., Rossell, S.L., Carruthers, S.P., Sumner, P., Hughes, M., Green, M.J., Pantelis, C., Burdick, K.E., Cropley, V., Van Rheenen, T.E., 2020. Cognitive validation of cross-diagnostic cognitive subgroups on the schizophrenia-bipolar spectrum. J. Affect. Disord. 266, 710–721.
Karantonis, J.A., Rossell, S.L., Carruthers, S.P., Sumner, P., Hughes, M., Green, M.J., Pantelis, C., Burdick, K.E., Cropley, V., Van Rheenen, T.E., 2021b. Does brain morphology map to cognition on the bipolar-schizophrenia-spectrum? A cross-diagnostic study of cognitive subgroups. J. Affect. Disord.
Kay, S.R., Flszbein, A., Opfer, L.A., 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr. Bull. 13, 261–276.
Kim, H.-Y., 2013. Statistical notes for clinical researchers: assessing normal distribution (2) using skewness and kurtosis. Restor. Dent. Endod. 38, 52.
Lewandowski, K.E., Baker, J.T., McCarthy, J.M., Norris, L.A., Öngür, D., 2018a. Reproducibility of cognitive profiles in psychosis using cluster analysis. J. Int. Neuropsychol. Soc. 24, 382–390.
Lewandowski, K.E., McCarthy, J.M., Öngür, D., Norris, L.A., Liu, G.Z., Juelich, R.J., Baker, J.T., 2018b. Functional connectivity in distinct cognitive subtypes in psychosis. Schizophr. Res.
Lewandowski, K.E., McCarthy, J.M., Öngür, D., Norris, L.A., Liu, G.Z., Juelich, R.J., Baker, J.T., 2019. Functional connectivity in distinct cognitive subtypes in psychosis. Schizophr. Res. 204, 120–126.
Lewandowski, K.E., Pinkham, A.E., Van Rheenen, T.E., 2024. Social cognition across the schizophrenia–bipolar disorder spectrum. Nature Reviews Psychology.
Lewandowski, K.E., Sperry, S.H., Cohen, B.M., Öngür, D., 2014. Cognitive variability in psychotic disorders: a cross-diagnostic cluster analysis. Psychol. Med. 44, 3239–3248.
Lupien, S.J., Maheu, F., Tu, M., Fiocco, A., Schramek, T.E., 2007. The effects of stress and stress hormones on human cognition: implications for the field of brain and cognition. Brain Cogn. 65, 209–237.
Martin, D.M., Wollny-Huttarsch, D., Nikolin, S., McClintock, S.M., Alonzo, A., Lisanby, S. H., Loo, C.K., 2020. Neurocognitive subgroups in major depressive disorder. Neuropsychology. 34, 726.
Mortimer, J.A., Snowdon, D.A., Markesbery, W.R., 2003. Head circumference, education and risk of dementia: findings from the Nun Study. J. Clin. Exp. Neuropsychol. 25, 671–679.
Muthén, L.K., Muthén, B.O., 2010. Mplus user's guide: statistical analysis with latent variables: User'ss guide. Muthén Muthén.
Oliveira, M.O.d., Nitrini, R., Yassuda, M.S., Brucki, S.M.D., 2014. Vocabulary is an appropriate measure of premorbid intelligence in a sample with heterogeneous educational level in Brazil. Behav. Neurol., 875960, 2014.
Pu, S., Noda, T., Setoyama, S., Nakagome, K., 2018. Empirical evidence for discrete neurocognitive subgroups in patients with non-psychotic major depressive disorder: clinical implications. Psychol. Med. 48, 2717–2729.
Reser, M.P., Allott, K.A., Killackey, E., Farhall, J., Cotton, S.M., 2015. Exploring cognitive heterogeneity in first-episode psychosis: what cluster analysis can reveal. Psychiatry Res. 229, 819–827.
Richard-Devantoy, S., Berlim, M., Jollant, F., 2014. A meta-analysis of neuropsychological markers of vulnerability to suicidal behavior in mood disorders. Psychol. Med. 44, 1663–1673.
Ringin, E., Cropley, V., Zalesky, A., Bruggemann, J., Sundram, S., Weickert, C.S., Weickert, T.W., Bousman, C.A., Pantelis, C., Van Rheenen, T.E., 2021. The impact of smoking status on cognition and brain morphology in schizophrenia spectrum disorders. Psychol. Med. 1–19.
Ringin, E., Dunstan, D.W., McIntyre, R.S., Owen, N., Berk, M., Rossell, S.L., Hallgren, M., Van Rheenen, T.E., 2023. Differential associations of mentally-active and passive sedentary behaviours and physical activity with putative cognitive decline in healthy individuals and those with bipolar disorder: findings from the UK Biobank cohort. Ment. Health Phys. Act., 100514
Ringin, E., Dunstan, D.W., Meyer, D., McIntyre, R.S., Owen, N., Berk, M., Hallgren, M., Rossell, S.L., Van Rheenen, T.E., 2024. Relative associations of behavioral and physiological risks for cardiometabolic disease with cognition in bipolar disorder during mid and later-life: findings from the UK biobank. Psychol. Med. 1–11.
Russo, M., Van Rheenen, T.E, Shanahan, M., Mahon, K., Mercedes Perez-Rodriguez, M., Cuesta-Diaz, A., AK, M., Burdick, K., 2017. Neurocognitive subtypes in patients with bipolar disorder and their unaffected siblings. Psychol. Med. 47, 2892–2905.
Stern, Y., 2009. Cognitive reserve. Neuropsychologia 47, 2015–2028.
Stern, Y., Albert, M., Barnes, C.A., Cabeza, R., Pascual-Leone, A., Rapp, P.R., 2023. A framework for concepts of reserve and resilience in aging. Neurobiol. Aging 124, 100–103.
Tan, R., Gould, R.V., Combes, H., Lehmann, S., 2014. Distress, trauma, and recovery: adjustment to first episode psychosis. Psychology and Psychotherapy: Theory, Research and Practice 87, 80–95.
Van Loenhoud, A.C., Groot, C., Vogel, J.W., Van Der Flier, W.M., Ossenkoppele, R., 2018. Is intracranial volume a suitable proxy for brain reserve? Alzheimers. Res. Ther. 10, 1–12.
Van Rheenen, T., Cropley, V., Fagerlund, B., Wannan, C., Bruggemann, J., Lenroot, R.K., Sundram, S., Weickert, C.S., Weickert, T.W., Zalesky, A., Bousman, C.A., Pantelisa, C., 2020a. Cognitive reserve attenuates age-related cognitive decline in the context of putatively accelerated brain ageing in schizophrenia-spectrum disorders. Psychol. Med. 50, 1475–1489.
Van Rheenen, T., Rossell, S., 2016. Facial emotion recognition impairments in bipolar disorder. A cognitive problem? J. Int. Neuropsychol. Society: JINS 22, 1–3.
Van Rheenen, T.E., Bryce, S., Tan, E.J., Neill, E., Gurvich, C., Louise, S., Rossell, S.L., 2016. Does cognitive performance map to categorical diagnoses of schizophrenia, schizoaffective disorder and bipolar disorder? A discriminant functions analysis. J. Affect. Disord. 192, 109–115.
Van Rheenen, T.E., Cropley, V., Wells, R., Bruggemann, J., Swaminathan, V., Sundram, S., Weinberg, W., Jacomb, I., Lenroot, R., Pereira, A.M., Zalesky, A., Bousman, C., Shannon Weickert, C., Weickert, T.W., Pantelis, C., 2018. Widespread volumetric reductions in schizophrenia and schizoaffective patients displaying compromised cognitive abilities. Schizophr. Bull. 44, 560–574.
Van Rheenen, T.E., Lewandowski, K.E., Bauer, I.E., Kapczinski, F., Miskowiak, K., Burdick, K.E., Balanzá-Martínez, V., 2020b. Current understandings of the trajectory and emerging correlates of cognitive impairment in bipolar disorder: an overview of evidence. Bipolar. Disord. 22, 13–27.

Van Rheenen, T.E., Lewandowski, K.E., Ongur, D., Tan, E.J., Neill, E., Gurvich, C., Pantelis, C., Malhotra, A., Rossell, S.L., Burdick, K.E., 2017. Characterizing cognitive heterogeneity on the schizophrenia – bipolar disorder spectrum. Psychol. Med. 47, 1848–1864.

Vicent-Gil, M., Portella, M.J., Serra-Blasco, M., Navarra-Ventura, G., Crivillés, S., Aguilar, E., Palao, D., Cardoner, N., 2021. Dealing with heterogeneity of cognitive dysfunction in acute depression: a clustering approach. Psychol. Med. 51, 2886–2894.

Wechsler, D., 1997. Wechsler Adult Intelligence Scale-Revised: Adminstration and Scoring Manual. The Psychological Corporation, San Antonio, TX.

Wells, R., Jacomb, I., Swaminathan, V., Sundram, S., Weinberg, D., Bruggemann, J., Cropley, V., Lenroot, R.K., Pereira, A.M., Zalesky, A., 2020. The impact of childhood adversity on cognitive development in schizophrenia. Schizophr. Bull. 46, 140–153.

Wenzel, J., Badde, L., Haas, S.S., Bonivento, C., Van Rheenen, T.E., Antonucci, L.A., Ruef, A., Penzel, N., Rosen, M., Lichtenstein, T., Lalousis, P.A., Paolini, M., Stainton, A., Dannlowski, U., Romer, G., Brambilla, P., Wood, S.J., Upthegrove, R., Borgwardt, S., Meisenzahl, E., Salokangas, R.K.R., Pantelis, C., Lencer, R., Bertolino, A., Kambeitz, J., Koutsouleris, N., Dwyer, D.B., Kambeitz-Ilankovic, L., Dong, M.S., Erkens, A., Gussmann, E., Haas, S., Hasan, A., Hoff, C., Khanyaree, I., Melo, A., Muckenhuber-Sternbauer, S., Kohler, J., Ozturk, O.F., Popovic, D., Rangnick, A., von Saldern, S., Sanfelici, R., Spangemacher, M., Tupac, A., Urquijo, M.F., Weiske, J., Wosgien, A., Ruhrmann, S., Betz, L., Blume, K., Seves, M., Kaiser, N., Pilgram, T., Lichtenstein, T., Woopen, C., Schmidt, A., Riecher-Rössler, A., Andreou, C., Egloff, L., Harrisberger, F., Lenz, C., Leanza, L., Mackintosh, A., Smieskova, R., Studerus, E., Walter, A., Widmayer, S., Chisholm, K., Day, C., Griffiths, S.L., Iqbal, M., Pelton, M., Mallikarjun, P., Lin, A., Denissoff, A., Ellila, A., From, T., Heinimaa, M., Ilonen, T., Jalo, P., Laurikainen, H., Lehtinen, M., Luutonen, A., Makela, A., Paju, J., Pesonen, H., Armio, R.-L., Sormunen, E., Toivonen, A., Turtonen, O., Hietala, J., Kolkka, M., Luutonen, S., Walta, M., Tuominen, L., Solana, A.B., Abraham, M., Hehn, N., Schirmer, T., Altamura, C., Belleri, M., Bottinelli, F., Ferro, A., Re, M., Monzani, E., Percudani, M., Sberna, M., D'Agostino, A., Del Fabro, L., Perna, G., Nobile, M., Alciati, A., Balestrieri, M., Cabras, G., Fabbro, F., Garzitto, M., Piccin, S., Blasi, G., Pergola, G., Caforio, G., Facio, L., Quarto, T., Gelao, B., Romano, R., Andriola, I., Falsetti, A., Barone, M., Passatiore, R., Sangiuliano, M., Surman, M., Bienek, O., Schultze-Lutter, F., Schmidt-Kraepelin, C., Neufang, S., Korda, A., Rohner, H., 2024. Transdiagnostic subgroups of cognitive impairment in early affective and psychotic illness. Neuropsychopharmacology 49, 573–583.

Wenzel, J., Haas, S.S., Dwyer, D.B., Ruef, A., Oeztuerk, O.F., Antonucci, L.A., von Saldern, S., Bonivento, C., Garzitto, M., Ferro, A., 2021. Cognitive subtypes in recent onset psychosis: distinct neurobiological fingerprints? Neuropsychopharmacology 46, 1475–1483.

Zahodne, L.B., Stern, Y., Manly, J.J., 2015. Differing effects of education on cognitive decline in diverse elders with low versus high educational attainment. Neuropsychology. 29, 649.