*Psychological Medicine*

**cambridge.org/psm**

# Cognitive heterogeneity in first-episode psychosis and its relationship with premorbid developmental adjustment

Eric J. Tan[1,2], Susan L. Rossell[1,2], Kenneth L. Subotnik[3], Joseph Ventura[3] and Keith H. Nuechterlein[3,4]

[1]Centre for Mental Health, Swinburne University of Technology, Melbourne, Australia; [2]Department of Psychiatry, St Vincent's Hospital, Melbourne, Australia; [3]Department of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA and [4]UCLA Department of Psychology, Los Angeles, CA, USA

## Original Article

**Cite this article:** Tan EJ, Rossell SL, Subotnik KL, Ventura J, Nuechterlein KH (2022). Cognitive heterogeneity in first-episode psychosis and its relationship with premorbid developmental adjustment. *Psychological Medicine* **52**, 3885–3894. https://doi.org/10.1017/S0033291721000738

Received: 21 October 2020
Revised: 10 February 2021
Accepted: 18 February 2021
First published online: 12 March 2021

**Key words:**
Cognition; cognitive cluster; education; first-episode psychosis; schizophrenia; symptoms

**Author for correspondence:**
Eric J. Tan, PhD, E-mail: erictan@swin.edu.au

## Abstract

**Background.** Patients with schizophrenia spectrum disorders have been increasingly recognised to form cognitive subgroups with differential levels of impairment. Using cluster analytical techniques, this study sought to identify cognitive clusters in a sample of first-episode psychosis (FEP) patients and examine clinical and developmental differences across the resultant groups.

**Methods.** In total, 105 FEP patients in the University of California Los Angeles Aftercare Research Program were assessed for cognition, symptoms and premorbid developmental adjustment. Hierarchical cluster analysis with Ward's method and squared Euclidean distance was conducted, confirmed by discriminant function analysis and optimised with *k*-means clustering. The stability of the solution was evaluated through split-sample (random, 80 and 70% samples) and alternate method (average linkage method) replication via Cohen's $\kappa$ analysis. Controlling for multiple comparisons, one-way analysis of variances examined group differences in symptom severity and premorbid adjustment.

**Results.** Three groups were identified: severely impaired ($n = 27$), moderately impaired ($n = 41$) and relatively intact ($n = 37$). There were no significant differences in symptom severity across the groups. Significant differences were observed for scholastic performance at three different developmental stages: childhood, early adolescence and late adolescence, with the relatively intact group demonstrating significantly better scholastic performance at all three stages than both the moderately impaired and severely impaired groups (who did not significantly differ from each other).

**Conclusions.** The findings add to growing evidence that cognitive clusters in FEP mirror that of later-stage schizophrenia. They also suggest that premorbid scholastic performance may not just be a risk factor for developing schizophrenia, but is also related to cognitive impairment severity and potentially to prognosis.

## Introduction

### *Cognitive heterogeneity in schizophrenia*

Cognitive impairments are a central aspect of schizophrenia spectrum disorders and have been repeatedly linked to poorer functioning and quality of life among patients (Green, 2016; Tan, Rossell, & Lee, 2020b; Tan, Thomas, & Rossell, 2014; Tolman & Kurtz, 2012). More recently, there is growing recognition that cognitive impairment severity varies among patients, ranging from broad deficits to performance at levels similar to healthy samples. Cluster analyses have been consistently employed in the endeavour to classify patients by cognitive impairment severity and depending on the cognitive domains being investigated and the statistical methodology employed, between two and five clusters or groups emerge (see Carruthers, Van Rheenen, Gurvich, Sumner, and Rossell, 2019b for a review). The identification of cognitive subgroups within schizophrenia spectrum disorders is empirically and theoretically driven and facilitates an appreciation of the heterogeneity of cognitive deficits in a way that continuous variables do not. Furthermore, cognitive clusters may guide the delivery of effective treatment strategies as we gain a better understanding of cognition-enhancing interventions. Overall, there is consensus for the existence of three broad groups: relatively intact, intermediately impaired and severely impaired (Carruthers et al., 2019b).

Previous characterisation of cognitive heterogeneity in schizophrenia has revealed differences in symptoms across the identified groups. The most common finding is for increased negative symptoms among the most cognitively compromised group (Carruthers et al., 2019a; Lewandowski, Baker, McCarthy, Norris, & Öngür, 2018; Sauvé, Malla, Joober, Brodeur, & Lepage, 2018; Wells et al., 2015), with some evidence for increased positive



CAMBRIDGE UNIVERSITY PRESS

symptoms (Lewandowski et al., 2018; Sauvé et al., 2018) as well as overall symptomatology compared to the cognitively intact group (Van Rheenen et al., 2017). It should be noted that differences in symptom profiles have not been observed across all cognitive subclusters in schizophrenia (Gilbert et al., 2014; Van Rheenen et al., 2017), with significant symptom differences being absent between the cognitively impaired subclusters (e.g. selective *v.* general cognitive impairment). Further, cognitively compromised schizophrenia patients have been shown to have a lower premorbid intelligence quotient (IQ) (Lewandowski et al., 2018; Van Rheenen et al., 2017), poorer socio-occupational functioning and premorbid functioning (Wells et al., 2015), and may be more susceptible to poorer long-term outcomes (Gilbert et al., 2014). Relating clinical and developmental characteristics to cognitive clusters is a relatively recent field of research, and further investigation is required.

The vast majority of current cognitive clustering work has occurred in chronic populations, with relatively few cognitive heterogeneity studies in first-episode psychosis (FEP). Published FEP studies to date have reported both three (Sauvé et al., 2018; Uren, Cotton, Killackey, Saling, & Allott, 2017) and four (Reser, Allott, Killackey, Farhall, & Cotton, 2015) cluster cognitive structures. In all cases, relatively intact and severely impaired groups were identified. Sauvé et al. (2018) and Uren et al. (2017) also identified a single intermediate impairment cluster, while Reser et al. (2015) reported two intermediately impaired groups that differed on measures of attention, working memory and visual recognition memory. Different FEP cognitive clusters were characterised by differing levels of premorbid intelligence and negative symptoms (Reser et al., 2015; Uren et al., 2017), with decreasing cognitive function related to poorer levels of daily functioning (Holthausen et al., 2002; Uren et al., 2017), even six months post-assessment (Uren et al., 2017).

### Factors affecting cognitive function

The limited number of cognitive heterogeneity studies in FEP requires extension and replication, notably to aid in improving the characterisation of cognitive impairment in FEP. A key factor that has yet to be clarified is the role of premorbid functioning in the prediction of future cognitive impairment in schizophrenia. Poor premorbid social and work adjustment has been observed in the most cognitively compromised schizophrenia patients (Wells et al., 2015); however, such studies have often been limited to periods close or just prior to symptom onset. The relationship between adjustment in the developmental years and future cognitive impairment is still unclear. For example, reduced educational duration and attainment and premorbid intelligence are common among individuals with schizophrenia and have been related to the age of illness onset (Chen, Selvendra, Stewart, & Castle, 2018; Neill et al., 2020) as well as some cognitive impairments (Bucci et al., 2018; Lee et al., 2017), but are yet to be investigated in relation to a broad range of cognitive domains.

### The current study

In light of these issues, the present study sought to identify cognitive clusters in a group of FEP patients using cluster analysis and to further investigate their relationships with both symptoms and premorbid developmental adjustment factors. Based on previous work, we hypothesised that two to four clusters would emerge, with at least one cognitively intact and one generally impaired cluster. We predicted significant differences in demographic and clinical features, notably years of education, premorbid IQ and negative symptoms, between the clusters. We also expected significant differences between the clusters on premorbid developmental adjustment domains. We used a premorbid adjustment assessment that allowed separation of early scholastic *v.* social development to determine whether they differed in their association with cognitive impairment after psychosis onset.

## Method

### Participants

Data was obtained from 105 participants (56 schizophrenia, 13 schizoaffective disorder, depressed type and 36 schizophreniform disorder) in the University of California Los Angeles (UCLA) Aftercare Research Program, an outpatient clinic for recent-onset schizophrenia spectrum disorders. All participants had a DSM-IV (American Psychiatric Association, 1994) diagnosis of schizophreniform, schizophrenia, or schizoaffective disorder, depressed subtype based on SCID interview (First, Spitzer, Gibbon, & Williams, 2001). They were aged between 18 and 45 years, had stable outpatient status, with no medication changes in the month prior to assessment. Participants with a history of neurological disorder, significant head injury, or substance or alcohol abuse or dependence in the last six months were excluded. All patients were taking oral risperidone at the time of assessment (Subotnik et al., 2015) and were being assessed at the baseline point of a randomised clinical trial of cognitive remediation and long-acting *v.* oral risperidone (Nuechterlein et al., 2020). Informed consent was obtained from all patients. All assessments were completed ~3 months after entry into the outpatient UCLA Aftercare Research Program.

### Measures

#### Cognition and premorbid intelligence

A modified beta version of the MATRICS consensus cognitive battery (MCCB; Nuechterlein et al., 2008) was used. This consisted of 16 tests assessing seven cognitive domains administered by certified testers. These are briefly described in Table 1. Each cognitive domain was represented by at least two tests. While the original MCCB beta version consisted of 20 tests, 4 were excluded due to concerns regarding practicality, psychometrics and redundancy (crossover with other included measures). Periodic checks on test administration and scoring practices were conducted for ongoing quality assurance. Premorbid intelligence was assessed using the Wechsler test of adult reading (WTAR; Wechsler, 2001).

#### Premorbid adjustment

The premorbid adjustment scale (PAS; Cannon-Spoor, Potkin, & Wyatt, 1982) is a widely used retrospective scale, conducted via semi-structured interview, to assess social and academic functioning in the years prior to psychotic symptom onset. In total, four time periods are covered: childhood (age: 5–11 years), early adolescence (age: 12–15 years), late adolescence (age: 16–18 years) and adulthood (age: ≥19 years). Five functioning domains were covered including sociability and withdrawal, peer relationships, scholastic performance, adaptation to school and social–sexual aspects of life. Academic items are excluded in adulthood, as are social–sexual aspects of childhood. Items are rated on a scale from 0 to 6, with higher scores reflecting poorer adjustment.

https://doi.org/10.1017/S0033291721000738 Published online by Cambridge University Press

**Table 1.** Descriptions of the 16 MCCB beta version tests and means and standard deviations of raw scores of participants ($N = 105$)

| Domain | Tests | Scoring variable | *M* (S.D.) |
|---|---|---|---|
| Speed of processing | Trail making, part A (TMT-A)[a] (Army, 1944) | Completion time | 32.56 (14.26) |
| | BACS, symbol coding (BACS SC)[a] (Keefe, 1999) | Total number correct | 47.19 (11.38) |
| | Category fluency test, animal naming (Fluency)[a] (Spreen & Strauss, 1998) | Total number of animals named in 1 min | 18.33 (4.26) |
| Attention/vigilance | CPT, identical pairs (CPT-IP)[a] (Cornblatt, Risch, Faris, Friedman, & Erlenmeyer-Kimling, 1988) | Mean d′ across 2-, 3-, and 4-digit conditions | 2.22 (0.77) |
| | 3–7 CPT (Nuechterlein, Edell, Norris, & Dawson, 1986) | Overall d′ | 4.03 (1.06) |
| Working memory | WMS, 3rd edn. Spatial Span (WMS-III SS)[a] (Wechsler, 1997b) | Sum of raw forward and backward scores | 16.65 (3.86) |
| | Letter-number span test (LNS)[a] (Gold, Carpenter, Randolph, Goldberg, & Weinberger, 1997) | Number of correct trials | 13.62 (4.36) |
| | BACS, digit sequencing test (BACS DS) (Keefe, 1999) | Total number correct | 19.19 (5.25) |
| Verbal learning | Hopkins verbal learning test – Revised (HVLT-R)[a] (Brandt & Benedict, 2001) | Total recall over three learning trials | 22.65 (5.47) |
| | NAB, daily living memory (NAB DLM) (White & Stern, 2003) | Total recall across three trials | 54.69 (9.36) |
| Visual learning | Brief visual memory test – Revised (BVMT-R)[a] (Benedict, 1997) | Total recall score over three learning trials | 21.91 (6.54) |
| | NAB shape learning (NAB SL) (White & Stern, 2003) | Total learning score over three trials | 15.45 (4.28) |
| Reasoning and problem solving | NAB Mazes (NAB Mazes)[a] (White & Stern, 2003) | Total raw score | 18.23 (5.43) |
| | WAIS – 3rd edn. block design (WAIS-III BD) (Wechsler, 1997a) | Total raw score | 38.08 (13.31) |
| Social cognition | MSCEIT, managing emotions branch (MSCEIT ME)[a] (Mayer, Salovey, & Caruso, 2002) | Branch score using general consensus scoring | 85.85 (11.41) |
| | MSCEIT, perceiving emotions branch (MSCEIT PE) (Mayer et al., 2002) | Branch score using general consensus scoring | 102.00 (17.43) |

BACS, Brief assessment of cognition in schizophrenia; CPT, Continuous performance test; WMS, Wechsler memory scale; NAB, neuropsychological assessment battery; WAIS, Wechsler adult intelligence scale; MSCEIT, Mayer–Salovey–Caruso emotional intelligence test.
[a]Included in the final 10-test MCCB.

A total score for each domain by time period was calculated. To account for the potential influence of active psychosis, the adulthood PAS data were excluded here due to possible validity issues (Van Mastrigt & Addington, 2002).

### *Symptoms and demographics*

The 24-item expanded brief psychiatric rating scale (BPRS; Ventura et al., 1993) was used to assess current symptoms. The BPRS for the two-week period covering the period of MCCB administration was used. Five symptom domain scores were calculated including affect, negative, positive, activation and disorganisation (Shafer, Dazzi, & Ventura, 2017), as well as a total score summing these together. Basic demographic and clinical information such as age, years of education, age of psychosis onset and medication dose were also collected.

## *Data preparation and statistical analysis*

Prior to analysis, data was screened for missing variables and univariate and multivariate normality. Missing data was minimal (2.68% of data points) and were imputed using the expectation-maximisation algorithm. Normality was assessed using the Shapiro–Wilks test and examination of skewness/kurtosis values. All non-normal variables were log transformed. To standardise the scale of measurement, *z*-scores were calculated for all 16 individual tests (based on the 105 patient participants here, not relative to healthy control norms) that were used for the cluster analyses. All statistical analysis was conducted using IBM SPSS Statistics version 26.

Hierarchical cluster analysis with Ward's method and squared Euclidean distance was employed, with collaborative inspection of the agglomeration schedule/scree plot and dendrogram used to determine the initial number of clusters. This was confirmed by discriminant function analysis. A *k*-means iterative partitioning technique was subsequently used to optimise the retained clusters, with initial partitions in the *k*-means solution defined using the cluster means obtained from the initial clustering procedure. The stability of the cluster solution was evaluated through split-sample (random 80 and 70% samples), abridged (social cognition excluded) and alternate method (average linkage) replication via Cohen's $\kappa$ analysis. To clarify any observed impairment severity within identified clusters, an overall composite *T*-score for the ten tasks contained within the final MCCB was calculated for each cluster using the MCCB Computer Scoring Program, which compares performance to community norms (Nuechterlein & Green, 2006). Identified clusters were also compared on demographic, clinical and PAS variables using analysis of variance and chi-square tests ($\chi^2$) as applicable. Cohen's *d* and Cramer's *V* were chosen as measures of effect size for the *post hoc* pairwise comparisons and $\chi^2$ analyses, respectively. Bonferroni correction was employed to account for multiple comparisons ($\alpha = 0.002$).

https://doi.org/10.1017/S0033291721000738 Published online by Cambridge University Press

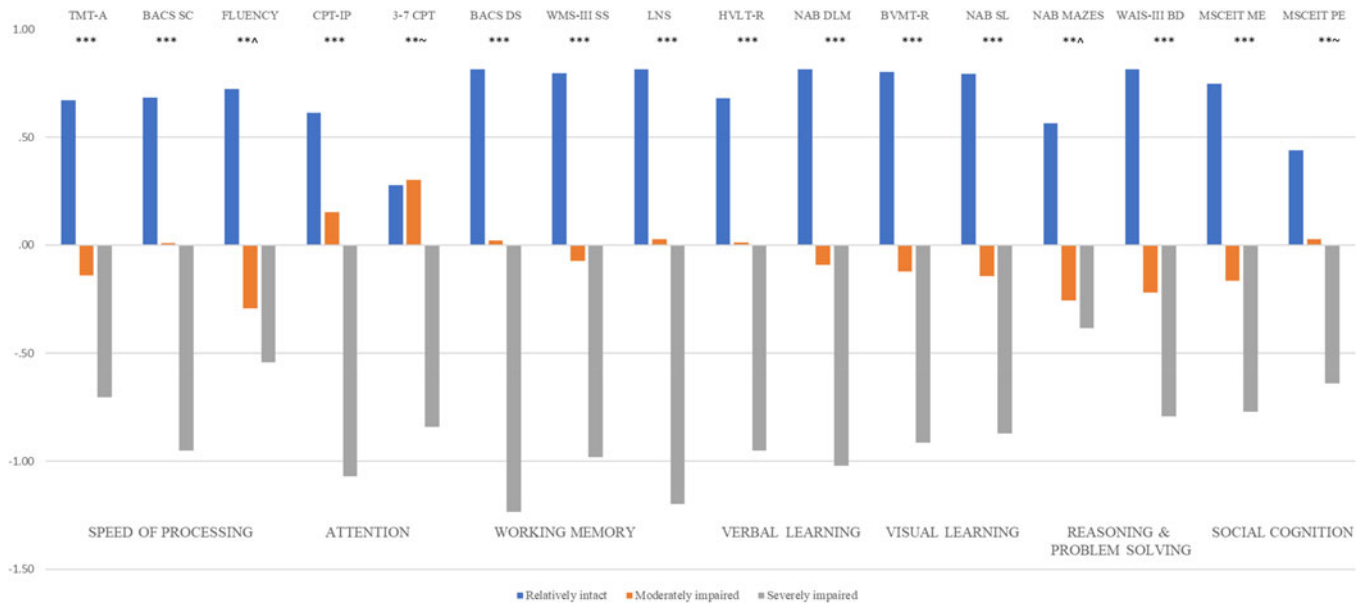


**Fig. 1.** Comparison of cognitive performance for the three emergent clusters, based on *z*-scores derived from the FEP patient sample.
*Note*: This figure reflects the mean *z*-scores for each cluster on cognitive tasks and domains calculated using only scores from the 105 patients in this study. Comparison of overall cognitive impairment severity of the clusters to normative levels is presented in 'Cluster analysis' section. TMT-A, trail-making test A; BACS SC, brief assessment of cognition in schizophrenia symbol coding; CPT-IP, continuous performance test-identical pairs; 3–7 CPT, 3–7 continuous performance test; BACS DS, brief assessment of cognition in schizophrenia digit sequencing; WMS-III SS, Wechsler memory scale spatial span; LNS, letter-number span; HVLT-R, Hopkins verbal learning test revised; NAB DLM, neuropsychological assessment battery daily living memory; BVMT-R, brief visual memory test revised; NAB SL, neuropsychological assessment battery shape learning; NAB MAZES, neuropsychological assessment battery Mazes; WAIS-III BD, Wechsler adult intelligence scale block design; MSCEIT ME, Mayer–Salovey–Caruso emotional intelligence test managing emotions; MSCEIT PE, Mayer–Salovey–Caruso emotional intelligence test perceiving emotions.

## Results

Exploration of the data revealed no extreme outliers in any of the measures, and only TMT-A time to completion scores were found to be non-normal. These were consequently log transformed and reverse scored to align with the directionality of the other measures (i.e. increasing score = better performance).

### *Cluster analysis*

Examination of the agglomeration schedule, scree plot and dendrogram revealed a three-cluster solution (Fig. 1; online Supplementary Material S1), with substantial to almost perfect agreement over multiple design iterations required to validate the final clustering solution obtained (see Table 2). The discriminant plot of the final *k*-means solution indicated relatively cohesive clusters with three distinct centroids (Fig. 2). Examination of the MCCB overall composite *T* scores based on community norms revealed the mean score of one cluster was within 1 S.D. of the mean of the healthy community sample ($M = 50.00$, S.D. = 10.00), one cluster was >2 S.D.s below the mean and the final cluster was >3 S.D.s below the mean (online Supplementary Material S2).

Cluster 1 emerged as the moderately impaired cluster with significant performance differences in both directions compared to both other clusters on 12 tasks (see online Supplementary Material S2 for detailed comparisons). Cluster 2 emerged as the relatively intact cluster, outperforming the other clusters on all measures except the 3–7 Continuous Performance Test and the Mayer–Salovey–Caruso emotional intelligence test perceiving emotions task, where their scores was not significantly different from the moderately impaired cluster but were significantly better than the remaining cluster. Cluster 3 emerged as the severely impaired cluster, with significantly poorer performance on all tasks compared to the relatively intact cluster and on 14 tasks compared to the moderately impaired cluster (no significant differences were observed in Fluency and Mazes performance).

### *Demographic, clinical and premorbid adjustment comparisons*

As seen in Table 3, among demographic variables, significant differences were observed between the clusters for years of education. The relatively intact cluster had significantly more years of education than the moderately impaired ($d = 0.71$) and severely impaired ($d = 1.20$) clusters, which did not significantly differ from each other. Similarly, as might be expected for clusters based on current cognitive performance, estimated premorbid IQ based on the WTAR was significantly higher for the relatively intact cluster compared to the other two ($d = 1.34$–$1.40$). No significant differences were observed for age, gender, age of illness onset, medication dose or on any of the BPRS symptom domain or BPRS total scores.

Significant differences between the clusters were observed for premorbid scholastic performance across all three developmental periods: childhood, early adolescence and late adolescence. In all these, the relatively intact cluster had significantly better performance than both the moderately impaired ($d = 0.66$–$0.85$) and severely impaired ($d = 1.02$–$1.44$) clusters, which did not significantly differ from each other. No significant differences were observed for the other premorbid adjustment domains: sociability and withdrawal, peer relationships, adaptation to school and socio-sexual life aspects.

## Discussion

The present study sought to explore cognitive heterogeneity in FEP patients and potential associated differences in symptoms

https://doi.org/10.1017/S0033291721000738 Published online by Cambridge University Press

**Table 2.** Percentage agreement and $\kappa$ coefficient scores between final cluster solution and cluster replications

| | Cluster 1 Good | Cluster 2 Moderate | Cluster 3 Poor | $\kappa$ coefficient (95% confidence interval) |
|---|---|---|---|---|
| *Random 80% subset* | | | | |
| Cluster 1 | 29 (96.7%) | 1 (3.3%) | 0 | $\kappa = 0.83$ (0.74–0.93), $p < 0.001$ |
| Cluster 2 | 8 (20.0%) | 32 (80.0%) | 0 | |
| Cluster 3 | 0 | 1 (4.5%) | 21(95.5%) | |
| *Random 70% subset* | | | | |
| Cluster 1 | 24 (100.0%) | 0 | 0 | $\kappa = 0.89$ (0.80–0.97), $p < 0.001$ |
| Cluster 2 | 9 (30.0%) | 20 (66.7%) | 1 (3.3%) | |
| Cluster 3 | 0 | 3 (15.8%) | 16 (84.2%) | |
| *14 variable solution*[a] | | | | |
| Cluster 1 | 35 (94.6%) | 2 (5.4%) | 0 | $\kappa = 0.74$ (0.63–0.85), $p < 0.001$ |
| Cluster 2 | 8 (19.5%) | 27 (65.9%) | 6 (14.6%) | |
| Cluster 3 | 0 | 2 (7.4%) | 25 (92.6%) | |
| *Average linkage solution* | | | | |
| Cluster 1 | 32 (86.5%) | 5 (13.5%) | 0 | $\kappa = 0.90$ (0.83–0.97), $p < 0.001$ |
| Cluster 2 | 1 (2.4%) | 40 (97.6%) | 0 | |
| Cluster 3 | 0 | 1 (3.7%) | 26 (96.3%) | |

[a]Excluding social cognition tasks.

and premorbid developmental adjustment domains. Aligned with our first hypothesis, three distinct cognitive performance clusters were identified: relatively intact, moderately impaired and severely impaired. The second hypothesis was partially supported, with significant group differences observed for years of education and premorbid IQ, but not for any symptom severity measures. Our third hypothesis was supported, with significant differences in childhood, early adolescent and late adolescent scholastic performance observed between the clusters.

### Cognitive heterogeneity and related factors in FEP

Our findings are aligned with previous work demonstrating three distinct cognitive clusters in FEP (Sauvé et al., 2018; Uren et al., 2017). The resultant clusters were characterised by relatively intact (Cluster 2), moderately impaired (Cluster 1) and severely impaired (Cluster 3) cognitive performance, supporting the presence of cognitive heterogeneity in FEP and the notion of a continuum of cognitive functioning (Béchard-Evans, Iyer, Lepage, Joober, & Malla, 2010). The resultant three cluster structure also mirrors that observed in chronic/multi-episode schizophrenia (Ammari, Heinrichs, & Miles, 2010; Sauvé et al., 2018; Van Rheenen et al., 2017), which is broadly aligned with evidence that cognitive impairment severity in schizophrenia is generally consistent post-onset (Hoff, Svetina, Shields, Stewart, & DeLisi, 2005; Tan, Neill, Tomlinson, & Rossell, 2020a). Notably, cluster sizes as a proportion of the overall sample in the current study – severely impaired (26%), moderately impaired (39%) and relatively intact (35%) – are roughly comparable to the only three-cluster solution FEP study (Uren et al., 2017) which reported an 18% severely impaired, 53% moderately impaired and 29% relative intact split. Both studies had the highest percentage of participants in the moderately impaired cluster, and the least in the severely impaired cluster. Circumscribed impairments in specific domains were not apparent between the cognitive performance clusters emerging here, with largely quantitative but not qualitative differences between them.

FEP patients in the relatively intact cluster had significantly more years of education and higher premorbid IQ than those in either the moderately impaired or severely impaired clusters. Our findings are largely consistent with previous work in both FEP (Reser et al., 2015; Uren et al., 2017) and chronic samples (Lewandowski et al., 2018; Van Rheenen et al., 2017). This suggests a general continuity of cognitive functioning over time, such that better premorbid cognitive ability (estimated premorbid IQ) is associated with higher levels of education and better overall cognitive function (MCCB performance) after psychosis onset. This also aligns with evidence that reduced educational success is related to poorer cognitive function (Lee et al., 2017) and longitudinal work reporting that lower school scores at age 16 and lower education at age 34 predicted greater cognitive decline in schizophrenia (Rannikko et al., 2015). Different cognitive clusters do not appear to be associated with current age, gender, age of illness onset or current medication dosage.

Unexpectedly, no significant differences were observed between the clusters on measures of current symptom severity. This contradicts both previous FEP-specific work (Reser et al., 2015; Uren et al., 2017), and also chronic and combined group studies (Carruthers et al., 2019a; Sauvé et al., 2018; Van Rheenen et al., 2017; Wells et al., 2015), although aligning with notions that cognitive function and schizophrenia symptoms are distinct (Thomas et al., 2019). One possible explanation may involve the lower overall levels of symptom severity within the current FEP sample, who were all stable outpatients. Indeed, our symptom severity scores were lower than those reported in the other FEP cognitive clustering studies (Reser et al., 2015;

https://doi.org/10.1017/S0033291721000738 Published online by Cambridge University Press

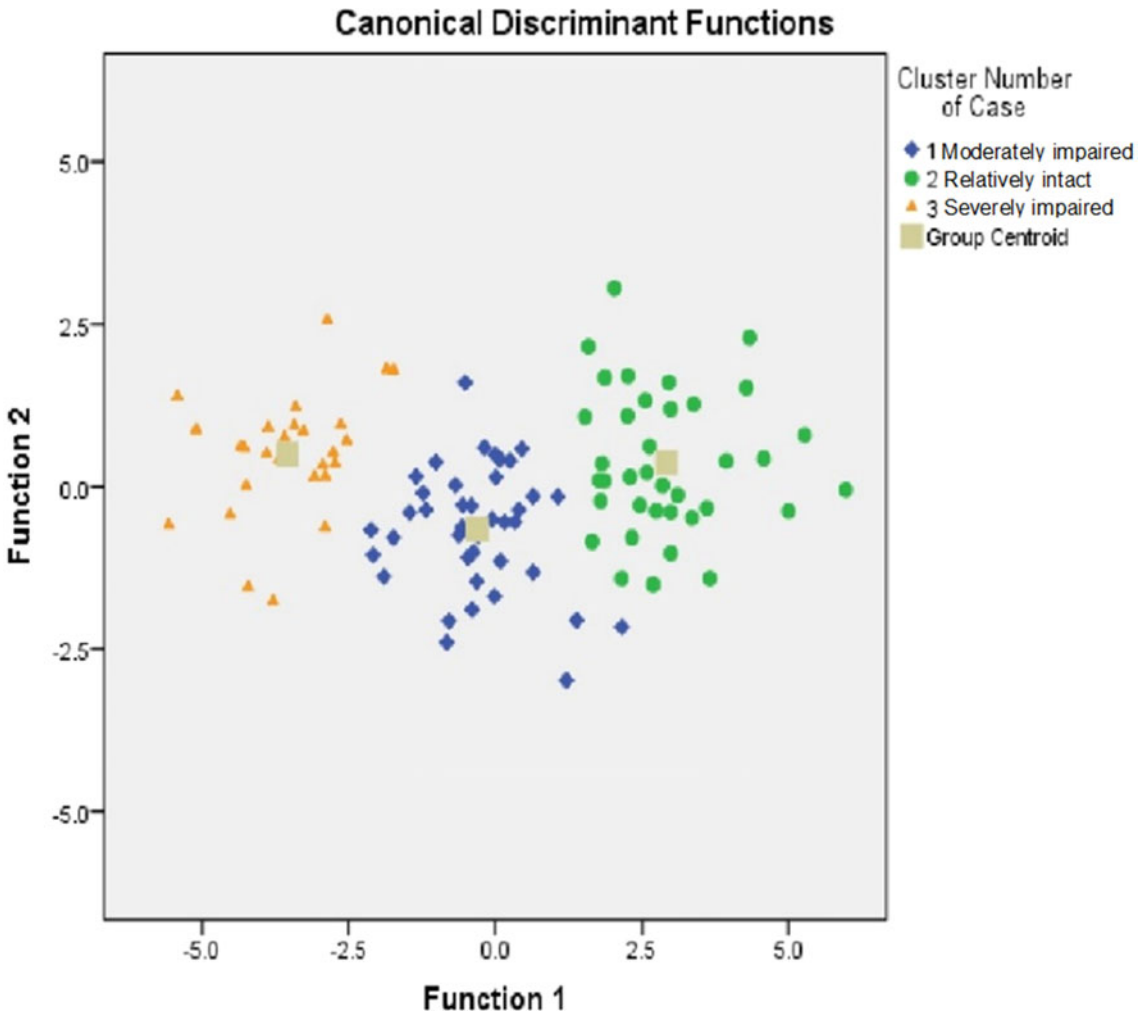


**Fig. 2.** *k*-means cluster solution discriminant plot.

Uren et al., 2017). Additionally, negative symptoms are more prominent in later illness stages (Stahl, 2004), suggesting they would be more easily detected among cognitive cluster members in chronic schizophrenia samples. FEP has also been associated with less severe negative symptoms and broad symptom volatility (Malla & Payne, 2005).

The current age and age of illness onset of our sample were comparable to other FEP studies (Reser et al., 2015; Uren et al., 2017), so discrepancies with previous literature are less likely to be due to age or situational factors around onset. Additionally, while we used the BPRS to assess negative symptoms compared to the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1984) in the other FEP studies, these two measures have been shown to be highly correlated (Czobor, Bitter, & Volavka, 1991) so the choice of measure is unlikely to have been consequential here. Relatedly, both previous studies assessed positive symptoms using the BPRS as we did, finding no significant differences either with similar levels of symptom severity to our current sample. It is notable that our patients were assessed around 3 months after outpatient clinic entry while the other FEP studies conducted assessments between 1 and 18 months post-service entry (Killackey et al., 2013). This temporal variation in assessment periods may be responsible for some discrepancies between the studies, particularly given the aforementioned symptom volatility during FEP (Malla & Payne, 2005).

This study considered five domains of premorbid developmental adjustment: sociability and withdrawal, peer relationships, scholastic performance, adaptation to school and social–sexual life aspects. Only scholastic performance across all three developmental periods (childhood, early adolescence and late adolescence) was significantly better in the relatively intact cluster when compared to the moderate and severely impaired clusters, which did not differ from each other. This mirrors and extends our current findings with years of education by demonstrating that it is not only duration but also relative educational achievement/success during the developmental period, even as early as childhood, that relates to future cognitive function. It also extends the findings of Rannikko et al. (2015) by demonstrating the added relevance of scholastic performance in childhood and early adolescence, in addition to late adolescence, to future cognitive functioning in schizophrenia. Educational opportunities are curtailed by the earlier onset of psychotic symptoms in schizophrenia (Hakulinen et al., 2019), which may have contributed to the relationship to the late adolescent scholastic performance observed here; however, our conclusions are strengthened by the fact that age of onset does not differ between the resultant clusters in the current study. Thus, the observed differences in scholastic

https://doi.org/10.1017/S0033291721000738 Published online by Cambridge University Press

**Table 3.** Comparison of demographic, clinical and premorbid adjustment variables between cognitive performance clusters

| Variable | Relatively Intact ($N = 37$) | Moderately impaired ($N = 41$) | Severely impaired ($N = 27$) | Test statistic ($F$ or $\chi^2$) | $p$ | Contrasts |
|---|---|---|---|---|---|---|
| | *M* (s.d.) | | | | | |
| Age | 22.05 (*3.66*) | 22.12 (*3.62*) | 21.96 (*4.32*) | 0.01 | 0.99 | – |
| Gender (% male) | 65.9 | 83.8 | 74.1 | 3.27[a] | 0.20 | – |
| Education (years) | 13.57 (*1.89*) | 12.37 (*1.48*) | 11.67 (*1.18*) | 12.19 | **0.001** | Intact > moderate = severe |
| Premorbid IQ (WTAR) | 108.68 (*9.51*) | 94.98 (*10.89*) | 93.26 (*12.34*) | 21.27 | **0.001** | Intact > moderate = severe |
| Age of onset | 20.44 (*3.26*) | 21.28 (*3.84*) | 19.88 (*4.48*) | 1.10 | 0.34 | – |
| Medication (CPZE) | 295.95 (*123.82*) | 385.98 (*172.12*) | 350.93 (*125.67*) | 3.77 | 0.03 | – |
| *BPRS* | | | | | | |
| Total | 37.73 (*8.01*) | 37.61 (*9.70*) | 40.44 (*9.98*) | 0.91 | 0.40 | – |
| Affect | 5.59 (*2.61*) | 4.29 (*1.75*) | 4.41 (*1.85*) | 4.25 | 0.02 | – |
| Negative | 5.81 (*2.41*) | 5.59 (*2.63*) | 6.48 (*3.11*) | 0.93 | 0.40 | – |
| Positive | 5.59 (*3.05*) | 7.15 (*4.37*) | 6.89 (*3.79*) | 1.78 | 0.17 | – |
| Activation | 3.14 (*0.48*) | 3.17 (*0.67*) | 3.89 (*2.04*) | 4.11 | 0.02 | – |
| Disorganisation | 3.89 (*1.05*) | 4.24 (*1.36*) | 4.52 (*1.28*) | 2.07 | 0.13 | – |
| *Cannon-Spoor PAS* | | | | | | |
| Childhood sociability and withdrawal | 1.06 (*1.39*) | 1.24 (*1.40*) | 1.58 (*1.33*) | 1.03 | 0.36 | – |
| Childhood peer relationships | 1.09 (*1.23*) | 1.16 (*1.28*) | 1.85 (*1.19*) | 3.21 | 0.04 | – |
| Childhood scholastic performance | 1.21 (*1.36*) | 2.18 (*1.59*) | 2.65 (*1.16*) | 8.25 | **0.001** | Intact > moderate = severe |
| Childhood adaptation to school | 1.00 (*1.30*) | 0.95 (*1.25*) | 1.38 (*1.13*) | 1.07 | 0.35 | – |
| Early adolescence sociability and withdrawal | 1.39 (*1.20*) | 1.21 (*1.30*) | 1.46 (*1.27*) | 0.35 | 0.70 | – |
| Early adolescence peer relationships | 1.27 (*1.28*) | 1.37 (*1.22*) | 1.62 (*1.02*) | 0.63 | 0.54 | – |
| Early adolescence scholastic performance | 1.48 (*1.30*) | 2.71 (*1.59*) | 3.27 (*1.19*) | 13.03 | **0.001** | Intact > moderate = severe |
| Early adolescence adaptation to school | 0.94 (*1.25*) | 1.37 (*1.44*) | 1.73 (*1.40*) | 2.47 | 0.09 | – |
| Early adolescence social–sexual aspects of life | 1.45 (*1.33*) | 1.29 (*1.14*) | 1.77 (*1.50*) | 1.05 | 0.36 | – |
| Late adolescence sociability and withdrawal | 1.55 (*1.46*) | 1.53 (*1.45*) | 1.77 (*1.48*) | 0.25 | 0.78 | – |
| Late adolescence peer relationships | 1.48 (*1.37*) | 1.42 (*1.37*) | 1.58 (*1.10*) | 0.11 | 0.90 | – |
| Late adolescence scholastic performance | 2.03 (*1.78*) | 3.18 (*1.49*) | 3.65 (*1.38*) | 8.72 | **0.001** | Intact > moderate = severe |
| Late adolescence adaptation to school | 1.21 (*1.56*) | 1.84 (*1.69*) | 2.42 (*1.60*) | 4.10 | 0.02 | – |
| Late adolescence social–sexual aspects of life | 1.52 (*1.37*) | 1.55 (*1.48*) | 1.88 (*1.70*) | 0.52 | 0.60 | – |

WTAR, Wechsler test of adult reading; MCCB, MATRICS consensus cognitive battery; CPZE, chlorpromazine equivalent; BPRS, brief psychiatric rating scale; PAS, premorbid adjustment scale.
A $\chi^2$ for gender, all other test statistics are $F$ values. $p$ values in bold are significant post-Bonferroni correction.
*Note: Post hoc* contrasts reported only for significant main effects. The significance of these is just to highlight the significant results (bold) and the variable sub-categories (italics).

https://doi.org/10.1017/S0033291721000738 Published online by Cambridge University Press

performance and educational duration here are not attributable to the onset of psychosis.

Although there is some indication that other premorbid adjustment domains (e.g. adolescent adaptation to school) might also differ between cognitive clusters, these were not significant after Bonferroni correction. Consequently, our findings suggest that premorbid educational performance factors relate to future cognitive performance more clearly than premorbid social factors. This relative specificity of associations to the domain of premorbid educational performance suggests that early social development may be more related to other features of later schizophrenia, rather than to cognitive impairment.

### *Limitations and future directions*

These findings should be considered with some caveats. First, we were unable to independently verify participant responses to the PAS. Second, while our use of the MCCB overall composite *T* scores provided a reasonable estimation of the degree of cognitive impairment or intactness in the emergent clusters, the inclusion of a demographically matched healthy control group in future analyses would be beneficial. Third, resultant clusters are largely dependent on the cognitive measures chosen. While our final cluster structure aligns with the general consensus for three cognitive clusters (Carruthers et al., 2019b), replication is still required. A notable point relates to the effects of antipsychotic medication dose on cognitive performance (Faber, Smid, Van Gool, Wiersma, & Van Den Bosch, 2012; Takeuchi et al., 2013). While the groups here did not significantly differ on medication dose, future studies should consider investigating this issue to elucidate whether resultant clusters are influenced by antipsychotic medication dose or whether cognitive impairment severity influences the choice of antipsychotic dosage.

In summary, this is the first study to explore the relationship between premorbid adjustment over several developmental periods and statistically derived cognitive clusters in FEP. The findings confirm cognitive heterogeneity in FEP, with the resultant three clusters showing differences in years of education, premorbid IQ and developmental scholastic performance. FEP patients with relatively intact cognitive performance were more likely to have spent more time, and performed better, in school and have higher premorbid IQ compared to FEP patients with moderate or severe cognitive impairment. Furthermore, the better educational functioning of the group with relatively intact cognition after psychosis onset was evident even in childhood. Future studies should continue advancing the study of cognitive heterogeneity in FEP and premorbid factors that may contribute to it.

**Supplementary material.** The supplementary material for this article can be found at https://doi.org/10.1017/S0033291721000738

**Acknowledgements.** The authors would like to thank Denise D Abcede, MA, for helping to collate the data. We also thank the patients who have generously agreed to participate in this study. We gratefully acknowledge the assistance of the UCLA Aftercare Research Program research assistants and clinical staff.

**Financial support.** This work was supported by NIMH research grant R01 MH037705 (KHN, PI) and Center grant P50 MH066286 (KHN, PI). EJT and SLR are in receipt of Early Career (GNT1142424) and Senior Research (GNT1154651) fellowships, respectively, from the National Health & Medical Research Council of Australia.

**Conflict of interest.** KHN is an officer of MATRICS Assessment Inc., the non-profit publisher of the MCCB, but does not receive any financial remuneration for his roles. KLS has received research funding from Janssen Scientific Affairs, LLC, and Genentech Inc., through grants to KHN and JV.KLS has received funding from Alkermes Inc., and from Janssen Scientific Affairs, LLC through grants to KHN and JV. Dr KLS has received research funding from Alkermes and served as a consultant to Alkermes Inc., Medincell Inc., and Teva Pharmaceutical USA Inc., and has been on the speaker's bureaus for Janssen Canada and Otsuka America Pharmaceutical Inc. J.V has received funding from Genentech Inc. (C4-150335). He has served as a consultant to Brain Plasticity Inc. and Boehringer-Ingelheim GmbH. KHN has received research grants from Janssen Scientific Affairs (R092670SCH4005; RIS-NAP-4009), Genentech (ML28264), and Posit Science (BPI-1000-11) and has been a consultant to Astellas, Genentech, Janssen, Medincell, Otsuka, Takeda and Teva. All other authors declare they have no conflicts of interest.

**Ethical standards.** The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

## References

American Psychiatric Association (1994). *DSM-IV: Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: The Association.

Ammari, N., Heinrichs, R. W., & Miles, A. A. (2010). An investigation of 3 neurocognitive subtypes in schizophrenia. *Schizophrenia Research*, *121*(1), 32–38.

Andreasen, N. C. (1984). *Scale for the assessment of negative symptoms* (*SANS*). Iowa City, IA: University of Iowa.

Army, U. (1944). *Army individual test battery: Manual of directions and scoring*. Washington, DC: Adjutant General's Office, War Department.

Béchard-Evans, L., Iyer, S., Lepage, M., Joober, R., & Malla, A. (2010). Investigating cognitive deficits and symptomatology across pre-morbid adjustment patterns in first-episode psychosis. *Psychological Medicine*, *40*(5), 749–759. doi: 10.1017/S0033291709991097

Benedict, R. H. B. (1997). *Brief visuospatial memory test – revised: Professional manual*. Odessa: Psychological Assessment Resources, Inc.

Brandt, J., & Benedict, R. H. B. (2001). *The hopkins verbal learning test – revised: Professional manual*. Odessa, FL: Psychological Assessment Resources, Inc.

Bucci, P., Galderisi, S., Mucci, A., Rossi, A., Rocca, P., Bertolino, A., … Maj, M. (2018). Premorbid academic and social functioning in patients with schizophrenia and its associations with negative symptoms and cognition. *Acta Psychiatrica Scandinavica*, *138*(3), 253–266. doi: 10.1111/acps.12938

Cannon-Spoor, H. E., Potkin, S. G., & Wyatt, R. J. (1982). Measurement of premorbid adjustment in chronic schizophrenia. *Schizophrenia Bulletin*, *8*(3), 470–484. doi: 10.1093/schbul/8.3.470

Carruthers, S. P., Gurvich, C., Meyer, D., Bousman, C., Everall, I. P., Neill, E., … Rossell, S. L. (2019a). Exploring heterogeneity on the wisconsin card sorting test in schizophrenia spectrum disorders: A cluster analytical investigation. *Journal of the International Neuropsychological Society*, *25*(7), 750–760. doi: 10.1017/s1355617719000420

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. *Neuroscience and Biobehavioral Reviews*, *107*, 252–278. doi: https://doi.org/10.1016/j.neubiorev.2019.09.006

Chen, L., Selvendra, A., Stewart, A., & Castle, D. (2018). Risk factors in early and late onset schizophrenia. *Comprehensive Psychiatry*, *80*, 155–162. doi: 10.1016/j.comppsych.2017.09.009

Cornblatt, B. A., Risch, N. J., Faris, G., Friedman, D., & Erlenmeyer-Kimling, L. (1988). The Continuous Performance Test, identical pairs version (CPT-IP): I. New findings about sustained attention in normal families. *Psychiatry Research*, *26*(2), 223–238. doi: 10.1016/0165-1781(88)90076-5

Czobor, P., Bitter, I., & Volavka, J. (1991). Relationship between the brief psychiatric rating scale and the scale for the assessment of negative symptoms: A study of their correlation and redundancy. *Psychiatry Research*, *36*(2), 129–139. doi: 10.1016/0165-1781(91)90125-9

Faber, G., Smid, H. G., Van Gool, A. R., Wiersma, D., & Van Den Bosch, R. J. (2012). The effects of guided discontinuation of antipsychotics on neurocognition in first onset psychosis. *European Psychiatry*, *27*(4), 275–280. doi: 10.1016/j.eurpsy.2011.02.003

First, M. B., Spitzer, R., Gibbon, M., & Williams, J. (2001). Structured Clinical Interview for DSM-IV Axis I Disorders – Patient Edition (SCID-I/P). Retrieved from New York.

Gilbert, E., Merette, C., Jomphe, V., Emond, C., Rouleau, N., Bouchard, R. H., … Maziade, M. (2014). Cluster analysis of cognitive deficits may mark heterogeneity in schizophrenia in terms of outcome and response to treatment. *European Archives of Psychiatry and Clinical Neuroscience*, *264*(4), 333–343. doi: 10.1007/s00406-013-0463-7

Gold, J. M., Carpenter, C., Randolph, C., Goldberg, T. E., & Weinberger, D. R. (1997). Auditory working memory and Wisconsin Card Sorting Test performance in schizophrenia. *Archives of General Psychiatry*, *54*, 159–165.

Green, M. F. (2016). Impact of cognitive and social cognitive impairment on functional outcomes in patients with schizophrenia. *The Journal of Clinical Psychiatry*, *77*(Suppl 2), 8–11. doi:10.4088/JCP.14074su1c.02.

Hakulinen, C., McGrath, J. J., Timmerman, A., Skipper, N., Mortensen, P. B., Pedersen, C. B., & Agerbo, E. (2019). The association between early-onset schizophrenia with employment, income, education, and cohabitation status: Nationwide study with 35 years of follow-up. *Social Psychiatry and Psychiatric Epidemiology*, *54*(11), 1343–1351. doi: 10.1007/s00127-019-01756-0

Hoff, A. L., Svetina, C., Shields, G., Stewart, J., & DeLisi, L. E. (2005). Ten year longitudinal study of neuropsychological functioning subsequent to a first episode of schizophrenia. *Schizophrenia Research*, *78*(1), 27–34. doi: http://dx.doi.org/10.1016/j.schres.2005.05.010

Holthausen, E. A. E., Wiersma, D., Sitskoorn, M. M., Hijman, R., Dingemans, P. M., Schene, A. H., & van den Bosch, R. J. (2002). Schizophrenic patients without neuropsychological deficits: Subgroup, disease severity or cognitive compensation? *Psychiatry Research*, *112*(1), 1–11. doi: https://doi.org/10.1016/S0165-1781(02)00184-1

Keefe, R. S. (1999). Brief Assessment of Cognition in Schizophrenia (BACS) Manual – A: Version 2.1. Duke University Medical Center. Durham, NC.

Killackey, E., Allott, K., Cotton, S. M., Jackson, H., Scutella, R., Tseng, Y.-P., … McGorry, P. D. (2013). A randomized controlled trial of vocational intervention for young people with first-episode psychosis: Method. *Early intervention in psychiatry*, *7*(3), 329–337. doi: 10.1111/eip.12066

Lee, J., Rizzo, S., Altshuler, L., Glahn, D. C., Miklowitz, D. J., Sugar, C. A., … Green, M. F. (2017). Deconstructing Bipolar Disorder and Schizophrenia: A cross-diagnostic cluster analysis of cognitive phenotypes. *Journal of Affective Disorders*, *209*, 71–79. doi: 10.1016/j.jad.2016.11.030

Lewandowski, K. E., Baker, J. T., McCarthy, J. M., Norris, L. A., & Öngür, D. (2018). Reproducibility of cognitive profiles in psychosis using cluster analysis. *Journal of the International Neuropsychological Society*, *24*(4), 382–390. doi: 10.1017/S1355617717001047

Malla, A., & Payne, J. (2005). First-episode psychosis: Psychopathology, quality of life, and functional outcome. *Schizophrenia Bulletin*, *31*(3), 650–671. doi: 10.1093/schbul/sbi031

Mayer, J. D., Salovey, P., & Caruso, D. R. (2002). *Mayer-Salovey-Caruso emotional intelligence test* (*MSCEIT*) *user's manual*. Toronto: Multi-Health System Publishers.

Neill, E., Tan, E. J., Toh, W. L., Selvendra, A., Morgan, V. A., Rossell, S. L., & Castle, D. J. (2020). Examining which factors influence age of onset in males and females with schizophrenia. *Schizophrenia Research*, *223*, 265–270. doi: https://doi.org/10.1016/j.schres.2020.08.011

Nuechterlein, K. H., Edell, W. S., Norris, M., & Dawson, M. E. (1986). Attentional vulnerability indicators, thought disorder, and negative symptoms. *Schizophrenia Bulletin*, *12*(3), 408–426. doi: 10.1093/schbul/12.3.408

Nuechterlein, K. H., & Green, M. F. (2006). *MATRICS consensus cognitive battery manual*. USA: MATRICS Assessment Inc.

Nuechterlein, K. H., Green, M. F., Kern, R. S., Baade, L. E., Barch, D. M., Cohen, J. D., … Marder, S. R. (2008). The MATRICS consensus cognitive battery, part 1: Test selection, reliability, and validity. *The American Journal of Psychiatry*, *165*(2), 203–213. doi: http://dx.doi.org/10.1176/appi.ajp.2007.07010042

Nuechterlein, K. H., Ventura, J., Subotnik, K. L., Gretchen-Doorly, D., Turner, L. R., Casaus, L. R., … Medalia, A. (2020). A randomized controlled trial of cognitive remediation and long-acting injectable risperidone after a first episode of schizophrenia: Improving cognition and work/school functioning. *Psychological Medicine*, 1–10. doi: 10.1017/s0033291720003335

Rannikko, I., Murray, G. K., Juola, P., Salo, H., Haapea, M., Miettunen, J., … Jääskeläinen, E. (2015). Poor premorbid school performance, but not severity of illness, predicts cognitive decline in schizophrenia in midlife. *Schizophrenia Research: Cognition*, *2*(3), 120–126. doi: https://doi.org/10.1016/j.scog.2015.08.001

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 Research*, *229*(3), 819–827. doi: https://doi.org/10.1016/j.psychres.2015.07.084

Sauvé, G., Malla, A., Joober, R., Brodeur, M. B., & Lepage, M. (2018). Comparing cognitive clusters across first- and multiple-episode of psychosis. *Psychiatry Research*, *269*, 707–718. doi: https://doi.org/10.1016/j.psychres.2018.08.119

Shafer, A., Dazzi, F., & Ventura, J. (2017). Factor structure of the Brief Psychiatric Rating Scale—Expanded (BPRS-E) in a large hospitalized sample. *Journal of Psychiatric Research*, *93*, 79–86. doi: 10.1016/j.jpsychires.2017.05.011

Spreen, O., & Strauss, E. (1998). *A compendium of neuropsychological tests: Administration, norms, and commentary*. New York: Oxford University Press.

Stahl, S. M. (2004). Symptoms and circuits, part 3: Schizophrenia. *The Journal of Clinical Psychiatry*, *65*(1), 8–9. doi: 10.4088/jcp.v65n0102

Subotnik, K. L., Casaus, L. R., Ventura, J., Luo, J. S., Hellemann, G. S., Gretchen-Doorly, D., … Nuechterlein, K. H. (2015). Long-acting injectable risperidone for relapse prevention and control of breakthrough symptoms after a recent first episode of schizophrenia. A randomized clinical trial. *JAMA Psychiatry*, *72*(8), 822–829. doi: 10.1001/jamapsychiatry.2015.0270

Takeuchi, H., Suzuki, T., Remington, G., Bies, R. R., Abe, T., Graff-Guerrero, A., … Uchida, H. (2013). Effects of risperidone and olanzapine dose reduction on cognitive function in stable patients with schizophrenia: An open-label, randomized, controlled, pilot study. *Schizophrenia Bulletin*, *39*(5), 993–998. doi: 10.1093/schbul/sbt090

Tan, E. J., Neill, E., Tomlinson, K., & Rossell, S. L. (2020a). Semantic memory impairment across the schizophrenia continuum: A meta-analysis of category fluency performance. *Schizophrenia Bulletin Open*, *1*(1). doi: 10.1093/schizbullopen/sgaa054

Tan, E. J., Rossell, S. L., & Lee, S. J. (2020b). Impaired meaning-based cognitive skills are specifically associated with poorer subjective quality of life in schizophrenia. *Personalized Medicine in Psychiatry*, *23–24*, 100062. doi: https://doi.org/10.1016/j.pmip.2020.100062

Tan, E. J., Thomas, N., & Rossell, S. L. (2014). Speech disturbances and quality of life in schizophrenia: Differential impacts on functioning and life satisfaction. *Comprehensive Psychiatry*, *55*, 693–698. doi: http://dx.doi.org/10.1016/j.comppsych.2013.10.016

Thomas, E. H., Rossell, S. L., Tan, E. J., Neill, E., Van Rheenen, T. E., Carruthers, S. P., … Gurvich, C. (2019). Do schizotypy dimensions reflect the symptoms of schizophrenia? *Australian and New Zealand Journal of Psychiatry*, *53*(3), 236–247.

Tolman, A., & Kurtz, M. M. (2012). Neurocognitive predictors of objective and subjective quality of life in individuals with schizophrenia: A meta-analytic investigation. *Schizophrenia Bulletin*, *38*(2), 304–315.

Uren, J., Cotton, S. M., Killackey, E., Saling, M. M., & Allott, K. (2017). Cognitive clusters in first-episode psychosis: Overlap with healthy controls and relationship to concurrent and prospective symptoms and functioning. *Neuropsychology*, *31*(7), 787–797. doi: 10.1037/neu0000367

Van Mastrigt, S., & Addington, J. (2002). Assessment of premorbid function in first-episode schizophrenia: Modifications to the Premorbid Adjustment Scale. *Journal of Psychiatry and Neuroscience*, *27*(2), 92–101.

Van Rheenen, T. E., Lewandowski, K. E., Tan, E. J., Ospina, L. H., Ongur, D., Neill, E., … Burdick, K. E. (2017). Characterizing cognitive heterogeneity on the schizophrenia–bipolar disorder spectrum. *Psychological Medicine*, *47*(10), 1848–1864. doi: 10.1017/s0033291717000307

Ventura, J., Lukoff, D., Nuechterlein, K., Liberman, R. P., Green, M. F., & Shaner, A. (1993). Brief Psychiatric Rating Scale Expanded version 4.0: Scales anchor points and administration manual. *Int J Meth Psychiatr Res*, *13*, 221–244.

Wechsler, D. (1997a). *Wechsler adult intelligence scale*. San Antonio, TX: Psychological Corporation.

Wechsler, D. (2001). *Wechsler test of adult reading*. San Antonio, TX: Psychological Corporation.

Wells, R., Swaminathan, V., Sundram, S., Weinberg, D., Bruggemann, J., Jacomb, I., … Weickert, T. W. (2015). The impact of premorbid and current intellect in schizophrenia: Cognitive, symptom, and functional outcomes. *npj Schizophrenia*, *1*(1), 15043. doi: 10.1038/npjschz.2015.43

White, T., & Stern, R. A. (2003). *Neuropsychological assessment battery: Psychometric and technical manual*. Lutz, FL: Psychological Assessment Resources, Inc.

https://doi.org/10.1017/S0033291721000738 Published online by Cambridge University Press