



Transdiagnostic comparisons of intellectual abilities and work outcome in patients with mental disorders: multicentre study

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Background

Cognitive impairment is common in people with mental disorders, leading to transdiagnostic classification based on cognitive characteristics. However, few studies have used this approach for intellectual abilities and functional outcomes.

Aims

The present study aimed to classify people with mental disorders based on intellectual abilities and functional outcomes in a data-driven manner.

Method

Seven hundred and forty-nine patients diagnosed with schizophrenia, bipolar disorder, major depression disorder or autism spectrum disorder and 1030 healthy control subjects were recruited from facilities in various regions of Japan. Two independent *k*-means cluster analyses were performed. First, intelligence variables (current estimated IQ, premorbid IQ, and IQ discrepancy) were included. Second, number of work hours per week was included instead of premorbid IQ.

Results

Four clusters were identified in the two analyses. These clusters were specifically characterised in terms of IQ discrepancy in the first cluster analysis, whereas the work variable was the most

salient feature in the second cluster analysis. Distributions of clinical diagnoses in the two cluster analyses showed that all diagnoses were unevenly represented across the clusters.

Conclusions

Intellectual abilities and work outcomes are effective classifiers in transdiagnostic approaches. The results of our study also suggest the importance of diagnosis-specific strategies to support functional recovery in people with mental disorders.

Keywords

Schizophrenia; bipolar disorder; major depression disorder; autism spectrum disorder; work outcome; intelligence.

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The cognitive and intellectual decline associated with schizophrenia (SCZ) has been studied extensively. It has been reported that this decline is partially independent of clinical symptoms 1,2 and that it prevents favourable functional outcomes. 3,4 Cognitive impairments are thought to be related to genes and have therefore been suggested to represent a cognitive endophenotype 5 . Recently, real-world outcomes closely linked to cognition (e.g. vocational functioning) were also reported to be a candidate endophenotype of mental disorders, 6,7 because they meet the criteria (e.g. heritability). For example, a family study reported that vocational deficits were much more likely to co-occur between index cases with SCZ and their first-degree relatives than between the cases and healthy controls. 8 The odds ratio (OR = 3.4) was much higher than those for other clinical traits such as schizotypal signs (OR = 1.9) or social avoidance (OR = 1.6).

Cognitive impairments are also noticeable in other disorders, including bipolar disorder ⁹⁻¹³ and autism spectrum disorder (ASD). ¹⁴ The commonality of cognitive impairments in mental disorders has led to transdiagnostic studies aiming to identify subgroups based on cognitive functioning. A previous study with a data-driven approach found distinct subgroups, including a neuropsychologically normal cluster, a globally impaired cluster, and one or two additional clusters with mixed cognitive profiles. ¹⁵ This finding was replicated using an established assessment tool, MATRICS Consensus Cognitive Battery, ¹⁶ in a different sample. ¹⁷

Although evidence has been accumulated to validate transdiagnostic classification based on cognitive impairments, ^{15,17,18} few studies have addressed classification from the perspective of intellectual abilities in people with mental disorders. Intelligence is a multifaceted construct. Therefore, the development of Wechsler Adult Intelligence Scale (WAIS) batteries has eliminated dual IQ (i.e., verbal IQ and performance IQ) and produced four indices – verbal comprehension, working memory, processing speed and perceptual reasoning – in the WAIS-4. Verbal comprehension is considered to reflect knowledge-based intelligence (crystallised intelligence), whereas the other indices reflect performance-based intelligence (fluid intelligence).

As is the case for cognition, it was assumed that people with mental disorders could also be classified based on their intellectual functioning. In addition, the endophenotypic nature of real-world outcomes suggests that they would also be effective as transdiagnostic classifiers.

The current study aimed first to investigate subgroups of people with mental disorders from the perspective of their intellectual abilities and, second, to classify patients by adding work outcome. For these purposes, two independent k-means cluster analyses were conducted, including variables related to intellectual abilities and work outcome. In both analyses, we also examined distributions of diagnoses and profiles for crystallised and fluid intelligence.

Method

Participants

Seven hundred and forty-nine patients and 1030 healthy controls were enrolled in the study. Inclusion criteria for patients included (a) meeting the DSM-IV criteria for SCZ (n = 528), bipolar disorder (n = 54), major depression disorder (MDD, n = 86), or ASD (n =81); and (b) being 70 years old or younger. The details of participants' demographic and clinical characteristics are summarised in Supplementary Table 1 available at https://doi.org/10.1192/bjo. 2022.50. Patients were recruited at the following facilities: Osaka University Hospital, Hokkaido University Hospital, University of Tokyo Hospital, Kyushu University Hospital, Okayama University Hospital, Nagoya University Hospital, Hospital of the University of Occupational and Environmental Health, University of Tsukuba Hospital, Kanazawa Medical University Hospital, Tokushima University Hospital, Toyama University Hospital, Nippon Medical School Hospital and Nara Medical University Hospital. Healthy controls were recruited at Osaka University, Tokyo University, Nagoya University, Kanazawa Medical University, Tokushima University, Nara Medical University, Toyama University, Nippon Medical School, and the University of Occupational and Environmental Health. Data were obtained between 2016 and 2018. All participants provided written informed consent. The study was approved by the ethical committee of each facility. 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.

Assessments

Demographic and clinical variables

Demographic information (age and education) was obtained from all participants. For the patients, clinical variables (age at onset, duration of illness, and antipsychotic medication) were also measured.

Variables for intelligence

Current estimated intellectual ability (current EIQ) was assessed by the abbreviated version of the WAIS-3, which includes similarities and symbol search. The third edition was used because the WAIS-4 had not been released in Japan during the data collection period. The short form showed validity, with high predictive accuracy ($R^2 = 0.8$) for full IQ. Premorbid IQ was estimated using the Japanese version of the Adult Reading Test. It is composed of 50 Japanese kanjis (ideographic scripts), and the reading task is considered to be equivalent to the irregular word reading employed in the National Adult Reading Test. IQ discrepancy was estimated by subtracting premorbid IQ from current EIQ.

A variable for work outcome

Total work hours per week were obtained from the Social Activity Assessment (SAA)²³ and used as a measure of work outcome. The SAA is a simplified version of the Modified Social Adjustment Scale-Work Outcome (details available from the author on request).^{24,25} It is composed of work for pay, work at home, and student sections. The former two sections evaluate work activities including work hours per week in the past 3 months. If a participant experienced both work for pay and work at home, the work hours of the sections were summed. For the purposes of the current study, the student section was excluded. The instrument was administered in a self-report manner or through interviews with psychologists or doctors.

Statistical analyses

Cluster analyses

k-means cluster analyses were conducted to identify subgroups, one using variables related to intelligence (current EIQ, premorbid IQ and IQ discrepancy) and the other using work instead of premorbid IQ. Premorbid IQ was excluded from the latter analysis because it did not seem to be related to the cluster characteristics in the former analysis. The scores were standardised using the means and standard deviations of healthy controls. The number of clusters was set to 4 following previous studies. ^{15,17} The fit of the cluster solutions was examined using linear discriminant analyses.

Characteristics by cluster

Cluster profiles were compared regarding demographic (age and education), clinical (age at onset, duration of illness and antipsychotic use), intelligence (current EIQ, premorbid IQ and IQ discrepancy) and work outcome variables using multivariate analysis of variance. In addition, the similarities and symbol search scores used to estimate current EIQ were independently compared across the clusters to examine profile differences between crystallised (performance on similarities) and fluid (performance on symbol search) intelligence.

Diagnostic distributions by cluster

Distributions by clinical diagnoses across clusters were examined with χ^2 statistics.

Results

Cluster analysis by intellectual abilities

Linear discriminant analysis indicated a good fit for the four-cluster solution, with a 98.0% classification accuracy on average (cluster 1, 99.1%; cluster 2, 95.6%; cluster 3, 97.9%; cluster 4, 98.6%).

Characteristics by cluster in the first cluster analysis

The characteristics of the clusters are summarised in Table 1, and the cluster profiles for the classification variables are shown in Fig. 1(a–c). Current EIQ gradually decreased from cluster 1 to cluster 4, with an approximately 10–15 point decrease (Fig. 1(a), Table 1). For premorbid IQ, all clusters fell into the near-normal range (>85, within 100 ± 1 s.d.[15]), although cluster differences tended to be significant owing to a relatively large cluster size (>100, at least). Relatively uniform premorbid IQs were considered not to be a critical variable when classifying individuals with mental disorders based on their intellectual functioning. Thus, this variable was not included in the second cluster analysis described below.

Unlike the IQ variables, a sharp contrast was observed for IQ discrepancies. Roughly, clusters were divided into two groups, one showing a less than 10 point decline (clusters 1 and 2) and the other showing an almost 20 point decline (clusters 3 and 4) (Fig. 1(c), Table 1). Based on previous studies, ^{26–29} cluster 1 and cluster 2 were defined as 'preserved', as the patients had a normal range of IQ (above 90) and a less than 10 point IQ decline. On the other hand, cluster 3 and cluster 4 were defined as 'discrepant' ('deteriorated' in the terms of previous studies), as the patients showed a greater than 10 point decline. The discrepant group received larger amounts of antipsychotics than the preserved group (Table 1). Regarding other variables, age did not significantly differ among clusters, and education was almost the same in cluster 2 (preserved group) and cluster 3 (discrepant group) (Table 1).

The profiles based on the subtests exhibited a disassociation between similarity and symbol search; they were 2–3 points lower in the latter case than in the former, except in cluster 4 (Fig. 1(d), Table 1).

| Table 1 Characteristics of clusters | tics of clusters | | | | | | | | | | | | |
|---|-----------------------|-----------|-------|-----------|-----------|-------|-----------|-------|-----------|-------|--------------------------------------|---------|---------------------------|
| | OH HC | | clus | Cluster 1 | Cluster 2 | er 2 | Cluster 3 | er 3 | Cluster 4 | er 4 | | | |
| Variable | Σ | s.d. | Σ | s.d. | Σ | s.d. | Σ | s.d. | Σ | s.d. | $F(d.f. = 4, 1774) / X^2 (d.f. = 4)$ | P-value | Bonferroni |
| N | 1030 | 230 | 182 | 193 | 144 | | | | | | | | |
| Male/female | 567/463 | 143/88 | 90/95 | 104/85 | 62/79 | 12.53 | 900.0 | | | | | | |
| Age, years | 33.2 | 14.4 | 38.5 | 13.1 | 41.3 | 14.4 | 37.6 | 11.4 | 38.4 | 13.2 | 20.85 | 0.000 | HC < C3 = C4 = C1 = C2 |
| Education, years | 15.2 | 2.1 | 14.7 | 2.3 | 13.4 | 2.2 | 13.8 | 2.2 | 12.2 | 2.0 | 87.48 | 0.000 | HC = C1 > C3 = C2 > C4 |
| Antipsychotics, CPZ | I | | 389.1 | 449.1 | 363.0 | 410.2 | 481.3 | 486.3 | 564.6 | 551.7 | 5.42 | 0.001 | C4 = C3; $C4 > C1$, $C2$ |
| Current EIQ | 109.0 | 11.4 | 104.5 | 8.3 | 94.9 | 8.3 | 79.3 | 8.2 | 68.2 | 10.1 | 747.26 | 0.000 | HC > C1 > C2 > C3 > C4 |
| Similarities | 11.9 | 2.4 | 12.3 | 1.8 | 10.1 | 1.8 | 7.3 | 2.1 | 2.0 | 2.2 | 445.12 | 0.000 | HC = C1 > C2 > C3 > C4 |
| Symbol search | 11.9 | 2.8 | 8.8 | 2.8 | 8.1 | 3.1 | 5.6 | 2.6 | 4.4 | 2.5 | 423.49 | 0.000 | HC > C1 = C2 > C3 > C4 |
| Premorbid IQ | 109.4 | 9.9 | 112.5 | 4.4 | 95.8 | 5.9 | 105.4 | 5.6 | 87.7 | 6.4 | 584.38 | 0.000 | C1 > HC > C3 > C2 > C4 |
| IQ discrepancy | -0.3 | 10.8 | -7.9 | 8.1 | -0.8 | 8.0 | -26.1 | 8.9 | -19.5 | 9.2 | 359.66 | 0.000 | HC = C2 > C1 > C4 > C3 |
| CPZ, chlorpromazine equivalent; HC, healthy controls. | ralent; HC, healthy c | controls. | | | | | | | | | | | |
| | | | | | | | | | | | | | |

Diagnostic distribution by cluster in the first cluster analysis

Table 2 presents the χ^2 statistics for the clusters. All diagnoses were represented in each cluster but not evenly. Figure 1(e) illustrates a contrasting trend between SCZ and other diagnoses; the peak occurred in cluster 3 for SCZ and in cluster 1 for other diagnoses. Overall, SCZ was overrepresented in discrepant clusters, yielding larger χ^2 statistics in cluster 3 (χ^2 = 4.2) and cluster 4 (χ^2 = 6.4), in contrast to bipolar disorder, MDD and ASD, which had the largest representations in the preserved cluster (cluster 1, bipolar disorder: χ^2 = 5.2, MDD: χ^2 = 4.1, ASD: χ^2 = 13.0).

Cluster analysis with work outcome

The classification accuracy determined by linear discriminant analysis was 97.6% on average (cluster 1, 98.3%; cluster 2, 97.3%; cluster 3, 97.4%; cluster 4, 96.9%), indicating a good fit for the four-cluster solution.

Characteristics by cluster in the second cluster analysis

The characteristics of the clusters are summarised in Table 3. As shown in the table, the cluster profiles largely differed between work outcome and intellectual abilities. Work outcome was dichotomised into just one 'functional' cluster (cluster 1) and three 'lessfunctional' clusters (clusters 2–4). The patients in the former cluster worked longer (43.28 h/week) than healthy controls (40.70 h/week), whereas those in the latter clusters worked less than 10 h/week (8.09 h/week, on average) (Table 3).

However, the profiles based on the intelligence variables did not follow this trend. To illustrate this clearly, cluster profiles for the classification variables are presented in Fig. 2(a–c). Cluster 2 belonged to the less-functional group, despite its members having almost equivalent intellectual abilities to those of the healthy controls (Fig. 2(b), 2(c)). The performance on symbol search was approximately 2–3 points worse than that on similarities, except in cluster 3 (Fig. 2(d), Table 3).

Diagnostic distribution by cluster in the second cluster analysis

Table 4 presents the χ^2 statistics for the clusters, and Fig. 2(e) shows the distributions by diagnosis. The distribution was roughly unimodal for SCZ and ASD. The peak for SCZ occurred in a lower intellectual abilities and less-functional cluster (cluster 4), whereas the peak for ASD occurred in a higher intellectual abilities and less-functional cluster (cluster 2). The distributions for bipolar disorder and MDD were bimodal, with peaks in cluster 2 and cluster 4. SCZ was largely overrepresented in cluster 3 ($\chi^2 = 7.9$), whereas for other diagnoses, overrepresentation was noticeable in cluster 2 (bipolar disorder: $\chi^2 = 4.2$, MDD: $\chi^2 = 11.1$, ASD: $\chi^2 = 6.3$).

Discussion

This study was conducted to classify patients with SCZ, bipolar disorder, MDD and ASD based on intellectual abilities and work outcome. *k*-means cluster analyses using these variables identified four independent clusters. The effect of diagnoses on the classifications was evident, as revealed by uneven diagnosis distributions across clusters. Performance on symbol search was worse than that on similarities in most clusters.

Cluster analysis by intellectual abilities

The characteristics of the clusters identified by intellectual abilities were mostly in accordance with the findings of a previous study reporting gradual decrements in cognitive functions across four clusters. ¹⁷ The current study also found that these clusters could be categorised into

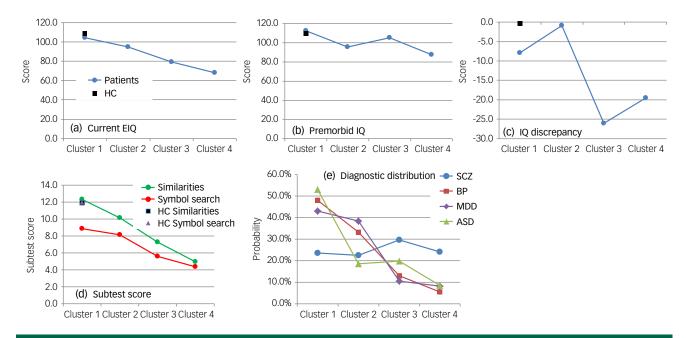


Fig. 1 Cluster profiles and diagnostic distributions across clusters for intelligence variables: (a) current EIQ, (b) premorbid IQ, (c) IQ discrepancy, (d) subtest score and (e) diagnostic distribution from the first cluster analysis. HC, healthy controls.

preserved (clusters 1 and 2) and discrepant (clusters 3 and 4) groups according to IQ discrepancy. A similar distinction was also found in the distribution of clinical diagnoses: SCZ was largely represented in the discrepant clusters, whereas bipolar disorder, MDD and ASD were so in the preserved clusters (Fig. 1(e), Table 2). These observations are similar to those of previous transdiagnostic studies^{30,31} that reported that IQ decline was more specific to SCZ than to other mental disorders. This may be related to the structural and functional brain abnormalities found in SCZ that varied with the degree of IQ discrepancy.³²

Cluster analysis with work outcome

The profiles for work outcome were not parallel to those for intellectual variables (Fig. 2(a-c)). Specifically, cluster 2 showed the

highest intellectual abilities, although it belonged to the less-functional group. This suggests that a considerable number of patients (n = 220, 29.4%) did not work despite their preserved intellectual function. There are several possible reasons for shorter work hours, including a paucity of support (e.g. work placement) and stigma. Psychological reasons such as inadequate metacognition (e.g. self-stigma), decreased self-efficacy or attenuated motivation may also explain worse work outcomes.

Selective impairment in processing speed

Symbol search performance was worse, by almost two points, than similarities performance in all clusters except cluster 4 in the first cluster analysis and cluster 3 in the second cluster analysis (Figs. 1

| | SCZ | BP | MDD | ASD | Total | <i>P</i> -value |
|-------------------------|-------|-------|-------|-------|-------|-----------------|
| Cluster 1 | | | | | | |
| Observed frequency | 125 | 26 | 37 | 43 | 231 | |
| Expected frequency | 162.8 | 16.7 | 26.5 | 25.0 | 231.0 | |
| Percentage ^a | 23.7% | 48.1% | 43.0% | 53.1% | | |
| χ^2 contribution | 8.8 | 5.2 | 4.1 | 13.0 | 31.2 | 0.000 |
| Cluster 2 | | | | | | |
| Observed frequency | 119 | 18 | 33 | 15 | 185 | |
| Expected frequency | 130.4 | 13.3 | 21.2 | 20.0 | 185.0 | |
| Percentage ^a | 22.5% | 33.3% | 38.4% | 18.5% | | |
| χ^2 contribution | 1.00 | 1.63 | 6.51 | 1.25 | 10.4 | 0.016 |
| Cluster 3 | | | | | | |
| Observed frequency | 157 | 7 | 9 | 16 | 189 | |
| Expected frequency | 133.2 | 13.6 | 21.7 | 20.4 | 189.0 | |
| Percentage ^a | 29.7% | 13.0% | 10.5% | 19.8% | | |
| χ^2 contribution | 4.2 | 3.2 | 7.4 | 1.0 | 15.9 | 0.001 |
| Cluster 4 | | | | | | |
| Observed frequency | 127 | 3 | 7 | 7 | 144 | |
| Expected frequency | 101.5 | 10.4 | 16.5 | 15.6 | 144.0 | |
| Percentage ^a | 24.1% | 5.6% | 8.1% | 8.6% | | |
| χ^2 contribution | 6.4 | 5.2 | 5.5 | 4.7 | 21.9 | 0.000 |
| Total | 528 | 54 | 86 | 81 | 749 | |

ASD, autism spectrum disorder; BP, bipolar disorder; CPZ, chlorpromazine equivalent; HC, healthy controls; MDD, major depression disorder; SCZ, schizophrenia. a. Observed frequency in cluster/observed frequency in total. Pearson $\chi^2_9 = 79.3$ (P < 0.001).

| Table 3 Characteristics of clusters | stics of clusters | | | | | | | | | | | | |
|--|---------------------|----------|-----------|--------|-----------|--------|-----------|--------|--------|-----------|---------------------------------------|---------|--------------------------------|
| | OH HC | | Cluster 1 | er 1 | Cluster 2 | r 2 | Cluster 3 | r 3 | Clust | Cluster 4 | | | |
| Variable | M | s.d. | N | s.d. | M | s.d. | M | s.d. | | | $F (d.f. = 4, 1774) / X^2 (d.f. = 4)$ | P-value | Bonferroni |
| 2 | 1030 | 121 | 220 | 153 | 255 | | | | | | | | |
| M/F | 567/463 | 92/29 | 131/89 | 81/72 | 125/130 | 5.31 | 0.15078 | | | | | | |
| Age, yr | 33.15 | 14.41 | 36.48 | 12.22 | 39.45 | 14.56 | 38.31 | 11.99 | 40.04 | 12.75 | 20.37 | 0.0000 | HC < C3,C2,C4 |
| Education, yr | 15.20 | 2.09 | 14.40 | 2.25 | 14.20 | 2.23 | 12.84 | 2.25 | 13.33 | 2.37 | 68.48 | 0.0000 | HC > C1 = C2 > C4 = C3 |
| Antipsychotics, CPZ | | | 312.43 | 395.44 | 359.36 | 432.69 | 551.29 | 537.33 | 493.62 | 482.84 | 7.46 | 0.0001 | C3 = C4; $C4 > C1$; $C2 = C1$ |
| Currrent EIQ | 109.03 | 11.39 | 94.06 | 67.6 | 105.70 | 7.80 | 66.35 | 9.35 | 85.19 | 7.15 | 778.37 | 0.0000 | HC > C2 > C1 > C4 > C3 |
| Simiralirties | 11.88 | 2.44 | 10.08 | 2.44 | 12.20 | 1.88 | 4.73 | 2.24 | 8.56 | 2.01 | 405.36 | 0.0000 | HC = C2 > C1 > C4 > C3 |
| Symbole search | 11.94 | 2.79 | 77.7 | 2.58 | 6.65 | 2.78 | 3.88 | 2.27 | 6.16 | 2.44 | 485.63 | 0.0000 | HC > C2 > C1 > C4 > C3 |
| Premorbid IQ | 109.36 | 6.61 | 103.45 | 10.37 | 106.29 | 9.37 | 96.28 | 11.35 | 100.48 | 9.92 | 126.11 | 0.0000 | HC > C2 = 2 > C4 > C3 |
| IQ discrepancy | -0.33 | 10.82 | -9.39 | 8.98 | -0.59 | 7.72 | -29.93 | 8.20 | -15.20 | 92.9 | 402.74 | 0.0000 | HC = C2 > C1 > C4 > C3 |
| Work hours, wk | 40.70 | 18.68 | 43.28 | 15.46 | 10.82 | 12.47 | 8.33 | 13.90 | 5.13 | 7.69 | 426.89 | 0.0000 | HC = C1 > C2,C3,C4; C2 > |
| | | | | | | | | | | | | | C4 |
| CPZ, chlorpromazine equivalent; HC, healthy controls | valent; HC, healthy | controls | | | | | | | | | | | |
| | | | | | | | | | | | | | |

(d), 2(d); Tables 1, 3). The results suggest a relatively severe impairment in fluid intelligence in patients with mental disorders. Meta-analyses^{33–35} and empirical studies^{11,12,36,37} have reported that processing speed, as measured by digit symbol coding, is selectively impaired in SCZ and bipolar disorder. The current observations regarding symbol search performance provide further evidence of impairment in processing speed in people with mental disorders.

Intriguingly, worse processing speed performance was observed even in clusters with a current EIQ in the normal range (Figs. 1(d), 2 (d)). This result suggests that patients with spared intellectual abilities (i.e. no or minor decline in intelligence) may be less competent in some domains of fluid intelligence. It is possible that impairment in fluid intelligence, specifically processing speed, may be a more sensitive and effective phenotypical marker for some mental disorders in comparison with crystallised intelligence. In fact, less competent performance on tests of this cognitive domain was reported in recent-onset SCZ patients who otherwise had intact intellectual function. 38

Diagnostic distributions and the relation to transdiagnostic classification in mental disorders

The two cluster analyses conducted in this study showed that all diagnoses were unevenly represented across the four clusters (Tables 2, 4). To illustrate the relationship between clusters and diagnoses more clearly, the means and 95% confidence intervals for clusters and diagnoses were plotted for three key variables (i.e. current EIQ, IQ discrepancy in the first cluster analysis and work in the second cluster analysis), with healthy control data as a reference (Fig. 3(a-c)). In general, patients with SCZ exhibited lower means and narrower 95% confidence intervals in all variables compared with patients with bipolar disorder, MDD or ASD. The narrower confidence intervals were possibly due to the larger sample size for SCZ. The lower means may reflect the uniqueness of the disorder. Intellectual abilities, in particular, are reported to develop differently in individuals with SCZ compared with healthy controls or individuals with other mental disorders. Large-scale longitudinal studies have shown that the lag in fluid intelligence has already started by the early teens, long before the onset of SCZ; this phenomenon has not been observed in other disorders, including depression. 30,31 Although all the mental disorders considered in this study were associated with lower intellectual status compared with that of healthy controls (Fig. 3(a, b)), different pathophysiological mechanisms may underlie these observations. Thus, it is thought that although current diagnostic systems (e.g. DSM) may not directly correspond to classifications based on intellectual abilities or functional outcomes, the former (diagnostic systems) may still be loosely associated with the latter (transdiagnostic classifications). Figure 3(d) presents a hypothetical mapping for this relationship. Genetic variations (Fig. 3(d), bottom) have been thought to emerge as disease-specific symptoms³⁹ that are behaviourally observable. Although the disease specificity may become less clear in phenotypical psychosocial representations (Fig. 3(d), upper three levels), the diagnostic distinctions may remain to some extent. This mapping could validate transdiagnostic studies as a research paradigm in psychiatry. Moreover, the loose association between diagnoses and psychosocial outcomes noted above also suggests the importance of developing diagnosis-specific strategies to support functional recovery. Specifically, work status is one of the most important functional outcomes in terms of the financial independence of patients, reduction of medical and welfare costs, 40,41 and therapeutic benefits. For example, work experiences alleviate psychiatric symptoms,⁴ enhance self-esteem and efficacy, 43 and provides better insight

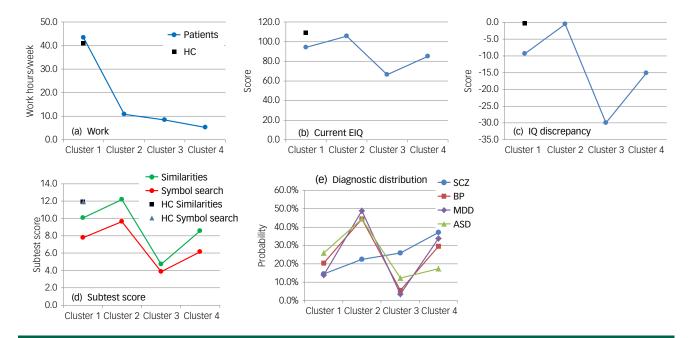


Fig. 2 Cluster profiles and diagnostic distributions across clusters for intelligence variables and work outcome: (a) current EIQ, (b) premorbid IQ, (c) IQ discrepancy, (d) subtest score and (e) diagnostic distribution from the first cluster analysis. HC, healthy controls.

into work competency.⁴⁴ In particular, it may be important for patients who maintain intellectual abilities but are distributed in the less-functional cluster (e.g. cluster 2 in Fig. 2(e)) to be fully supported so that they can achieve more favourable work outcomes.

Strengths and limitations

Our study is likely the first to use intellectual abilities and work outcomes to classify a large number of patients with a range of psychiatric condition using a data-driven approach. In particular, a quantified outcome measure of work hours and several aspects of

intelligence were employed. Several limitations should be mentioned. First, the severity of symptoms was not controlled for, owing to a lack of common measures across the disorders. Second, some SAA data were obtained in a self-report manner, which could be less objective than collection through interviews. At the time of analyses, the number of patients assigned to self-reporting was not known. Third, the number of SCZ patients was the largest in our sample. As noted above, this diagnosis tended to be distributed in lower bands for intellectual abilities and work outcome. Thus, characteristics of clusters with respect to these variables should be interpreted with caution. Finally, we focused only on

| | SCZ | BP | MDD | ASD | Total | <i>P</i> -value |
|-----------------------------|-------|-------|-------|-------|-------|-----------------|
| Cluster 1 | | | | | | |
| Observed frequency | 77 | 11 | 12 | 21 | 121 | |
| Expected frequency | 85.3 | 8.7 | 13.9 | 13.1 | 121 | |
| Percentage ^a | 14.6% | 20.4% | 14.0% | 25.9% | | |
| χ^2 contribution | 0.8 | 0.6 | 0.3 | 4.8 | 6.4 | 0.092 |
| Cluster 2 | | | | | | |
| Observed frequency | 118 | 24 | 42 | 36 | 220 | |
| Expected frequency | 155.1 | 15.9 | 25.3 | 23.8 | 220 | |
| Percentage ^a | 22.3% | 44.4% | 48.8% | 44.4% | | |
| χ ² contribution | 8.9 | 4.2 | 11.1 | 6.3 | 30.4 | 0.000 |
| Cluster 3 | | | | | | |
| Observed frequency | 137 | 3 | 3 | 10 | 153 | |
| Expected frequency | 107.9 | 11.0 | 17.6 | 16.5 | 153 | |
| Percentage ^a | 25.9% | 5.6% | 3.5% | 12.3% | | |
| χ ² contribution | 7.9 | 5.8 | 12.1 | 2.6 | 28.4 | 0.000 |
| Cluster 4 | | | | | | |
| Observed frequency | 196 | 16 | 29 | 14 | 255 | |
| Expected frequency | 179.8 | 18.4 | 29.3 | 27.6 | 255 | |
| Percentage ^a | 37.1% | 29.6% | 33.7% | 17.3% | | |
| χ^2 contribution | 1.5 | 0.3 | 0.0 | 6.7 | 8.5 | 0.037 |
| Total | 528 | 54 | 86 | 81 | 749 | |

ASD, autism spectrum disorder; BP, bipolar disorder; HC, healthy controls; MDD, major depression disorder; SCZ, schizophrenia. a. Observed frequency in cluster/observed frequency in total. Pearson $\chi_2^2 = 315.0 \ (P < 0.001)$.

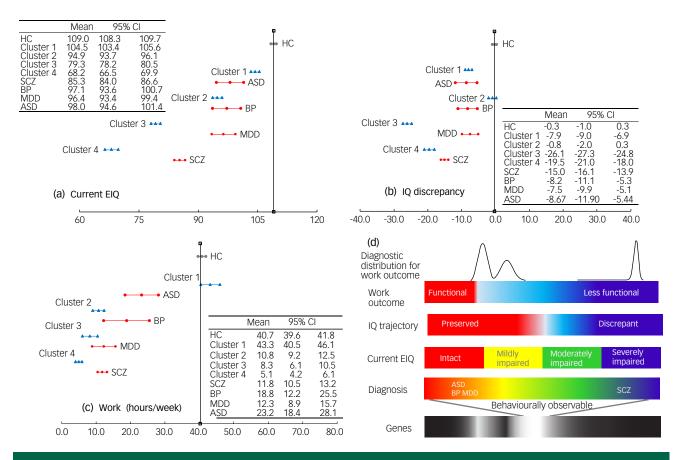


Fig. 3 Means and 95% confidence intervals for clusters and diagnoses regarding three key variables: (a) current EIQ, (b) IQ discrepancy from the first cluster analysis and (c) work (hours/week) from the second cluster analysis. (d) Schematic representation of the correspondence between phenotypical distinctions, clinical diagnoses, transdiagnostic classifications and diagnostic distribution for work outcome.

quantity of work (e.g. work hours/week) and did not examine qualitative aspects of work such as task complexity, demands and responsibilities. It is possible that transdiagnostic classifications would have appeared differently in our sample if those aspects were taken into account. Future studies should aim to address this issue.

Implications

The current study revealed distinct clusters in patients with SCZ, mood disorders or autism on the basis of intellectual abilities and work outcome. Our data confirmed the importance of diagnostic-specific strategies as well as a transdiagnostic approach to support functional recovery in people with mental disorders.

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Supplementary material

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Data availability

The data that support the findings of this study are available upon reasonable request to the senior author (R.H., ryotahashimoto55@ncnp.go.jp).

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Author contributions

R.H. and C.S. designed the study, and TS supervised it. C.S. conducted analyses and H.F. reviewed them. K.O., F.H., H.M, M.F., Y.Y., Y.U. J.T., K.M., A.K., M.Y., Y.O, A.S., E.K., M.K., Y.H., M.N., J.M., K.M., N.H., M.M., T.T, K.N., T.K., and M.S. prepared data and performed interpretation of the results.

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