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Processing Speed Impairment in Schizophrenia
An Updated Systematic Review and Meta-Analysis

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IMPORTANCE Cognition is impaired in people with schizophrenia, affecting quality of life and functioning. Therefore, it is important to understand and characterize this impairment.

OBJECTIVE To update and revisit the evidence for a central processing speed impairment in people with schizophrenia and examine the factors that moderate this impairment.

DATA SOURCES Articles were identified through the PubMed and PsycINFO databases from February 1, 2009, through November 2, 2023.

STUDY SELECTION Studies were included if they reported on a symbol coding test and at least 2 additional cognitive tests from 2 other cognitive domains, contrasted people with schizophrenia to controls, used contemporary diagnostic criteria, included sufficient detail to calculate Hedges *g* effect sizes, and were reported in English. Of 4530 identified articles, 115 studies met inclusion criteria.

DATA EXTRACTION AND SYNTHESIS This study followed the Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA) and Meta-Analysis of Observational Studies in Epidemiology (MOOSE) reporting guidelines. Means, SDs, and sample sizes were extracted for all cognitive tests that appeared in at least 3 of the 115 studies. Data were entered and visually checked by independent extractors. Data were generally pooled using random-effects models, except when specified. Measures of homogeneity (Q and I^2) and publication bias (fail-safe N and funnel plots) were also examined.

MAIN OUTCOMES AND MEASURES The primary outcome was the degree of cognitive impairment (Hedges *g*) observed for people with schizophrenia in 50 cognitive tests, focusing on symbol coding tests of processing speed. Further, this study aimed to identify clinical and study characteristics that moderate the degree of symbol coding impairment.

RESULTS Data were available for 10 114 people with schizophrenia and 13 235 controls from 115 studies. Symbol coding tasks were among the most impaired (g = −1.52; 95% CI, −1.65 to −1.40) but did not reliably differ from 15 other tests. Intelligence quotient and age difference from controls, composition of sex assigned at birth, inpatient status, and whether the sample included schizoaffective and schizophreniform diagnoses all moderated the degree of symbol coding impairment.

CONCLUSIONS AND RELEVANCE This meta-analysis provides insight into the consistency of the processing speed impairment for people with schizophrenia. Findings support that this impairment may be central to global cognitive impairments, which might be a consequence of altered brain connectivity.

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Supplemental content

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People with schizophrenia often experience cognitive impairments that are about 1 SD below their peers without a psychiatric diagnosis.[1-3] These cognitive impairments significantly affect quality of life[4-6] and impact both social[7,8] and role[9,10] functional capacity. Processing speed has repeatedly emerged as particularly impaired in this population, especially when measured by using digit symbol coding tests.[1,2,11] However, there have been significant changes to the underlying literature since this topic was last examined, such as greater representation of research from around the world, larger datasets, and novel or updated cognitive tests. Additionally, there is conflicting literature on whether first-generation antipsychotics, which have been prescribed less over time,[12] cause motor impairment and thus might explain the degree of processing speed impairment previously observed. Therefore, it is vital to assess the robustness of this finding in recent literature and further examine the potential factors contributing to this large impairment.

Processing speed is the speed at which cognitive operations can be executed.[2,13,14] Assessments of processing speed are typically speed tests, or tests that require individuals to complete as much as they can in a short amount of time of a task designed so that nearly anyone can complete any given item, compared to power tests that are intended to increase in difficulty and measure the extent of one's abilities in a given domain.[15,16] For example, digit symbol coding (henceforth, symbol coding) tests require participants to use a key—featuring the numbers 1 through 9 each paired with a unique symbol—to match a long and random series of either the symbols to the numbers[17] or the numbers to the symbols[18] as fast as they can without skipping any. Relative to the global cognitive impairment, people with schizophrenia demonstrate greater impairment on symbol coding tests, with meta-analytic estimates of performance being approximately 1.5 SDs below controls.[2,11] Since this finding, symbol coding tests have played an important role in psychosis research, including contributing to estimates of the risk an individual has of developing a psychotic disorder.[19]

According to Dickinson and colleagues,[2] the global cognitive impairment observed in people with schizophrenia may be the consequence of a central processing speed impairment. As processing speed is a lower-order cognitive operation, it may be necessary for performing many higher-order operations (eg, encoding and retrieval, information transformation, and decision-making), which are often measured with speed-dependent assessments.[2,20] Alternatively, processing speed may be particularly sensitive to altered brain connectivity, which may in turn be the mechanism driving broad cognitive impairment in people with schizophrenia.[2,21] However, connectivity and processing speed are only moderately associated,[22] and altered connectivity likely only partially explains the specific processing speed deficit, leaving much to be understood about cognitive impairment in this population.

Since the formative meta-analysis by Dickinson et al[2] identifying symbol coding tasks as the most impaired cognitive test for people with schizophrenia, there have been numerous changes to the clinical and research landscape. Therefore, the primary aim of this study is to replicate and update this meta-analysis by examining the impairment observed for symbol coding tests compared with other cognitive tests in people with schizophrenia. We hypothesize that symbol coding tasks will continue to emerge as particularly impaired. Following previous work by Knowles et al,[11] this study further aims to explore potential variables that may moderate symbol coding impairment, including clinical indicators (eg, antipsychotic medication dose and age at illness onset) and study characteristics (eg, publication date and participant age).

Key Points

Question Is there continued evidence of a central processing speed deficit for people with schizophrenia?

Findings In this systematic review and meta-analysis of 115 studies, symbol coding tests of processing speed remained among the most impaired cognitive tests for people with schizophrenia. Of the 49 other cognitive tests examined, symbol coding was reliably more impaired than 34 of them.

Meaning This study suggests that processing speed continues to emerge as a particularly impaired cognitive domain, and findings indicate there may be an underlying mechanism driving global cognitive impairment, such as altered brain connectivity, that processing speed is especially sensitive to.

Methods

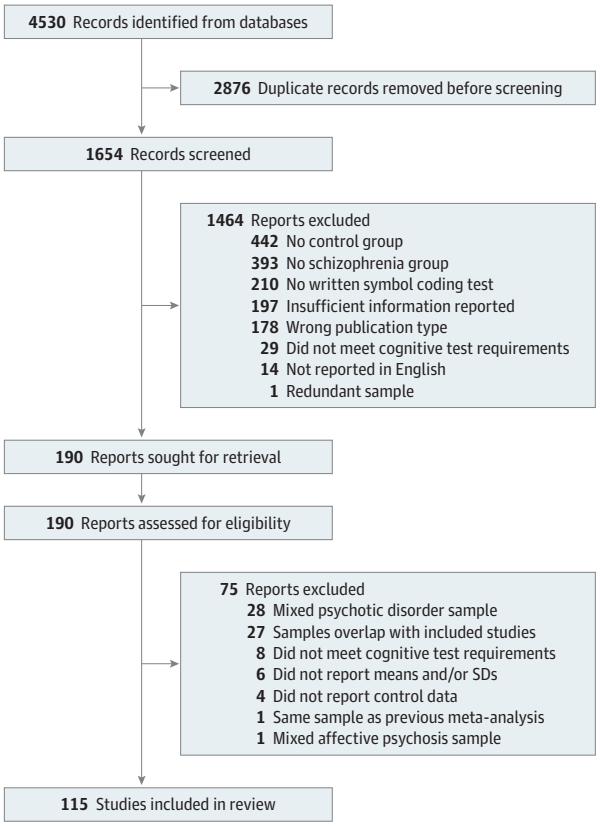
This meta-analysis was preregistered with the Open Science Framework. We followed the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) and Meta-Analysis of Observational Studies in Epidemiology (MOOSE) reporting guidelines.

Study Selection and Inclusion

Articles were identified through the PubMed and PsycINFO databases with combinations of the key words *schizophreni**, *cogniti**, *neuropsychologi**, *digit symbol*, *symbol coding*, *processing speed*, *perceptual speed*, and *psychomotor speed* from February 1, 2009, through November 2, 2023. Studies were included if they (1) reported on a written symbol coding task, (2) featured at least 2 additional cognitive assessments from at least 2 different cognitive domains, (3) contrasted a group of people with schizophrenia (schizoaffective and schizophreniform disorders permitted) with healthy controls, (4) used contemporary diagnostic criteria (eg, *DSM-IV*, *DSM-5*, or *International Classification of Diseases, Ninth Revision* or later version), (5) reported sufficient detail to calculate effect sizes, and (6) were reported in English (**Figure 1**; eTable 1 in Supplement 1).[23-137]

Means, SDs, and sample sizes for a written symbol coding test were recorded for all studies by 9 trained extractors and visually checked by an independent extractor. The same metrics were tracked for all cognitive tests that appeared in at least 3 of the included studies. Ultimately, 50 different cognitive tests from 10 cognitive domains were meta-analyzed. Individual tests were generally assessed separately; however, similar tests

Figure 1. PRISMA Diagram of Study Identification, Screening, and Inclusion



After removing 2876 duplicate records, 1654 articles were screened for inclusion. A total of 190 articles were sought for retrieval and 115 studies were included in this meta-analysis.

(eg, various word list-learning tests[138-140]) were combined for simplicity (eTable 2 in Supplement 1). Information on potential moderator variables was also recorded when available, including clinical variables on the severity and chronicity of illness, presence and dosage of antipsychotic medication, and study characteristics (eg, age, education, sex assigned at birth, race, and publication date). When reported data were unclear or appeared incorrect, efforts were made to contact the study's authors.

Data Analysis

A detailed description of the analytical plan is in the eMethods in Supplement 1. Analyses were performed using R, version 4.2.2 (R Project for Statistical Computing)[141] using the metafor[142] package. Most cognitive tests were reported so that higher scores reflect better performance. When higher scores reflected worse performance (eg, time to complete a task), the signs of the raw scores were reversed to aid in interpretation. All *P* values reported are 2-sided, with the statistical significance threshold set to $P < .05$.

To estimate the degree of impairment observed for each of the 50 cognitive tests, separate random-effects meta-analyses were run to calculate Hedges *g* effect sizes.[143] Measures of homogeneity (*Q* and I^2)[144,145] and publication bias (fail-safe N[146] and funnel plots) were also examined. Global cognitive and cognitive domain effect sizes were calculated via multivariate meta-analyses specifying cognitive tests nested within studies as a random effect to account for studies with multiple tests in the same domain. To directly compare whether symbol coding impairment differed from the other cognitive tests, subgroups of studies that included both symbol coding and the comparator cognitive tests were re-examined.[2,147] Specifically, multivariate meta-analyses with cognitive test (symbol coding vs comparator variable) as a moderator variable were conducted. Additionally, the results of this study were compared to the results reported in Dickinson et al[2] using fixed-effects meta-analyses specifying study (Pratt vs Dickinson) as a moderator variable. Further, a 2-way, average measures intraclass correlation (ICC) with absolute agreement was calculated for cognitive tests with at least 8 individual studies in each meta-analysis. Lastly, the effect of clinical and study moderator variables on symbol coding performance was examined using random-effects meta-regressions.

Results

A total of 115 studies met the inclusion criteria[23-137]; cognitive data were analyzed for 10 114 people with schizophrenia and 13 235 controls across these studies (eTable 1 in Supplement 1). For studies that report age, the sample-weighted mean (SD) age of the participants with schizophrenia was 36.98 (9.03) years (range, 15.79-63.50 years; number of studies [k] = 112) and 38.26 (9.88) years (range, 15.42-63.46 years; k = 110) for controls. Consistent with prior findings, people with schizophrenia exhibited a large global cognitive impairment relative to controls ($g = -1.12$; 95% CI, −1.21 to −1.03).

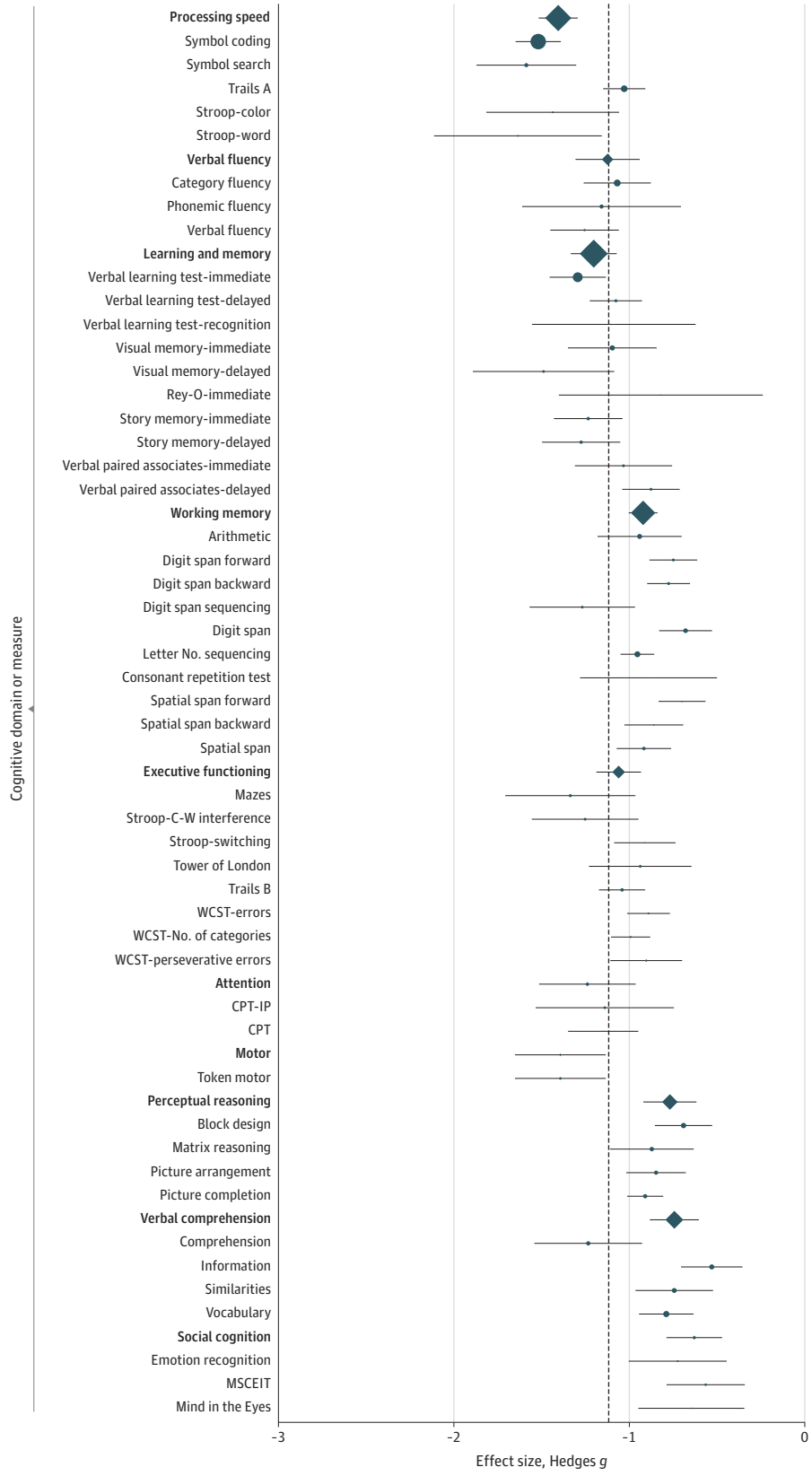
Symbol Coding Meta-Analysis

The random-effects meta-analysis on symbol coding impairment yielded a large effect size ($g = -1.52$; 95% CI, −1.65 to −1.40; k = 115), similar to prior meta-analyses ($g = -1.57$[2] and $g = -1.50$[11]). This finding indicates more than a 70% nonoverlap between people with schizophrenia and controls.[148] The fail-safe N indicated that 734 studies with null effects would have to be published to reduce the effect size to −0.2, and 14 431 null studies to reduce it to a nonsignificant finding. There was a large amount of heterogeneity among studies ($I^2 = 93.94\%$; $Q_{114} = 1441.72$; $P < .001$). Most studies are grouped around the overall effect, but many do not fall within the 95% CI (eFigure 1A in Supplement 1). Only 3 studies[37,63,125] did not find significant impairment relative to controls, and much of the variability comes from studies with quite large effect sizes (*g* range, −4.86 to −0.03) (eFigure 1B in Supplement 1).

Meta-Analyses of Other Cognitive Tests

Each individual cognitive test, as well as domain, was significantly impaired relative to controls (**Figure 2**; eTable 3 in Supplement 1). Effect sizes ranged from $g = -0.53$ (information) to $g = -1.64$ (Stroop-word reading). In contrast to previous meta-analyses, 2 other processing speed tests (Stroop-

Figure 2. Meta-Analytic Effect Size by Cognitive Tests and Domains



Circle points are individual tests, and diamond points with bolded labels are domains. The line at 0 represents the control group's relative performance. The dotted vertical line represents global cognitive impairment. The thickness of the 95% CIs is a function of the number of studies in the individual test's meta-analysis. The thickness of the points is a function of the total sample size for the individual test's meta-analysis. CPT indicates Continuous Performance Test; CPT-IP, Continuous Performance Test-Identical Pairs; C-W, color-word; MSCEIT, Mayer-Salovey-Caruso Emotional Intelligence Test; WCST, Wisconsin Card Sorting Test.

word reading and symbol search) had similar, but greater, impairments than symbol coding tests. Funnel and forest plots for each meta-analysis can be found in eFigures 1-50 in Supplement 1.

Matched Comparisons

Symbol coding impairment was reexamined in subsets of studies that include each comparator cognitive test, so tests could be compared with approximately equal sample sizes. All matched comparisons revealed that symbol coding exhibited greater impairment. However, the difference was not significant for 15 of the 49 comparator cognitive tests, and therefore, it cannot be concluded that symbol coding is reliably more impaired for people with schizophrenia on these tests (**Table 1**). These 15 tests were spread across all domains except for perceptual reasoning. Nearly half of these were tests of processing speed (3 of 4) and learning and memory (4 of 10).

Comparison With Previous Meta-Analysis Findings

To compare our findings with those in Dickinson et al,[2] effect sizes were compared for the 27 cognitive tests included in both meta-analyses (**Table 2**). Of these tests, only 5 of them differed significantly across studies: Stroop-word reading, category fluency, visual memory-delayed, information, and vocabulary. An ICC between cognitive tests that appeared in at least 8 studies in both meta-analyses revealed good agreement in the level of cognitive impairment observed (ICC = 0.814; 95% CI, 0.50-0.93).

Examination of Moderator Variables

As in Knowles et al,[11] the larger the difference in intelligence quotient (IQ) between people with schizophrenia and controls within a study, the larger the symbol coding impairment was (g = −0.02; 95% CI, −0.03 to −0.00; P = .009) (**Figure 3**A). However, unlike previous findings, there was no association of chlorpromazine equivalent (g = 0.00; 95% CI, −0.001 to 0.001; P = .53) or publication date (g = −0.03; 95% CI, −0.06 to 0.02; P = .06) with symbol coding performance.

Two additional study characteristics moderated the degree of symbol coding impairment for people with schizophrenia. First, we found that the difference in mean age between the schizophrenia and control groups within a study moderated the observed impairment; the older the people with schizophrenia were relative to the controls in a study, the larger the observed symbol coding impairment and vice versa (g = 0.06; 95% CI, 0.02-0.09; P = .001) (Figure 3B). Without considering the age of the control group, age of the schizophrenia group was not a significant moderator. Second, we found that as the percentage of females assigned at birth within a group of people with schizophrenia increases, the observed symbol coding impairment gets larger (g = 0.01; 95% CI, −0.02 to −0.00; P = .02) (Figure 3C). Neither the level of education among people with schizophrenia nor the difference in education between the control and schizophrenia groups moderated the symbol coding effect. There may be greater impairment observed in studies conducted in Asia (eFigure 51 in Supplement 1), but race was not a significant moderator. Notably, symbol coding impairment did not differ by test version used, except that the symbol coding test from the Brief Assessment of Cognition in Schizophrenia measured greater impairment than the Wechsler Adult Intelligence Scale coding version (g = −0.29; 95% CI, −0.57 to −0.01; P = .04).

Two clinical variables moderated the degree of symbol coding impairment in people with schizophrenia. Inpatients with schizophrenia showed more impairment on symbol coding tests compared with outpatients and mixed groups (g = −0.42; 95% CI, −0.77 to −0.08; P = .02) (Figure 3D). Further, groups that included people with schizoaffective disorder and/or schizophreniform disorder were less impaired than those with schizophrenia only (g = 0.46; 95% CI, 0.17-0.75; P = .002) (Figure 3E). Surprisingly, whether the participants were currently receiving medication, were drug-naive, were in a first episode, had an early onset of illness, or were in an acute or remitted phase of illness did not moderate the level of symbol coding impairment. Similarly, neither the duration of untreated psychosis nor age at psychosis onset moderated performance.

Discussion

In this meta-analysis, we examined the degree of cognitive impairment experienced by people with schizophrenia across 50 frequently used cognitive measures. Previous meta-analyses have found that symbol coding tests of processing speed are the most impaired cognitive measure for people with schizophrenia. Thus, 115 studies with a symbol coding test and at least 2 additional tests from 2 different cognitive domains were included in this study. We found that the level of impairment seen on symbol coding tests has remained consistent across meta-analyses, but that this impairment may not be uniquely greater than for all other cognitive tests. Additionally, several study and clinical characteristics were found to moderate the degree of symbol coding impairment.

In this study, symbol coding tests remained among the most impaired cognitive tests for people with schizophrenia, but the findings were nuanced. Across all included studies, Stroop-word reading and symbol search had larger overall effect sizes than symbol coding. However, these tests were featured in considerably fewer studies and when compared in matched samples, symbol coding was more impaired, although not significantly. Notably, these are all tests of processing speed, supporting that this domain is a particularly impaired for people with schizophrenia. However, they are also very different tasks with distinct cognitive demands, indicating that the underlying cause of impairment is not specific to symbol coding. In fact, in matched comparisons, symbol coding impairment did not significantly differ from the impairment observed in 15 of the 49 cognitive tests spanning all cognitive domains except perceptual reasoning. Of these 15 tests, only 6 are particularly speed dependent, and there is no clear cognitive operation that is common and unique to these tests. However, some caution is warranted while interpreting these nonsignificant findings; 6 of these 15 tests were not well represented in the literature (≤6 studies), and there were still notable differences in effect size magnitude for all tests aside from symbol search and mazes (9 tests

Table 1. Matched Comparisons with Symbol Coding Tests

Cognitive domain or measure	k	No. of participants		Effect size (SE)		z value	*P* value
		Schizophrenia	Control	Test	SC		
Processing speed							
Symbol search	9	1228	4001	−1.59 (0.14)	−1.65 (0.19)	0.260	.80
Trails A[a]	48	4422	4911	−1.03 (0.06)	−1.52 (0.11)	12.76	<.001
Stroop-color naming	8	495	1096	−1.44 (0.19)	−1.75 (0.34)	1.73	.08
Stroop-word reading	8	493	1104	−1.64 (0.24)	−2.02 (0.37)	1.41	.16
Verbal fluency							
Category fluency[a]	46	4166	5463	−1.07 (0.10)	−1.62 (0.13)	3.33	.001
Phonemic fluency	28	1928	3315	−1.16 (0.23)	−1.57 (0.12)	1.58	.11
Verbal fluency combined[a]	13	1206	1137	−1.26 (0.10)	−1.69 (0.12)	2.76	.006
Learning and memory							
Verbal learning-immediate[a]	64	6654	7737	−1.29 (0.08)	−1.60 (0.10)	2.42	.02
Verbal learning-delayed[a]	18	1787	1853	−1.08 (0.08)	−1.57 (0.11)	3.60	<.001
Verbal learning-recognition	4	98	158	−1.09 (0.24)	−2.14 (0.50)	1.91	.06
Visual memory-immediate[a]	21	2675	4270	−1.10 (0.13)	−1.61 (0.22)	2.03	.04
Visual memory-delayed	4	706	2366	−1.49 (0.21)	−1.92 (0.22)	1.41	.16
Rey-O-immediate	4	177	303	−0.82 (0.30)	−1.68 (0.37)	1.80	.07
Story memory-immediate	12	1174	3021	−1.23 (0.10)	−1.52 (0.12)	1.80	.07
Story memory-delayed[a]	10	1085	2950	−1.27 (0.11)	−1.62 (0.10)	2.24	.03
Verbal paired associates-immediate[a]	3	715	2528	−1.03 (0.14)	−1.75 (0.06)	4.65	<.001
Verbal paired associates-delayed[a]	3	712	2527	−0.88 (0.08)	−1.75 (0.06)	8.53	<.001
Working memory							
Arithmetic[a]	17	2029	4565	−0.94 (0.12)	−1.30 (0.13)	1.98	.05
Digit span forward[a]	15	1385	1975	−0.75 (0.07)	−1.69 (0.20)	4.36	<.001
Digit span backward[a]	15	1359	2085	−0.78 (0.06)	−1.58 (0.17)	4.37	<.001
Digit span sequencing[a]	19	1620	1507	−1.27 (0.15)	−1.83 (0.17)	2.42	.02
Digit span combined[a]	19	1642	4434	−0.68 (0.08)	−1.46 (0.14)	4.89	<.001
Letter number sequencing[a]	34	2751	5360	−0.95 (0.05)	−1.47 (0.08)	5.64	<.001
Consonant repetition test	4	219	203	−0.89 (0.20)	−1.26 (0.21)	1.27	.20
Spatial span forward[a]	5	572	409	−0.70 (0.07)	−1.80 (0.30)	3.63	<.001
Spatial span backward[a]	4	359	286	−0.86 (0.09)	−1.80 (0.40)	2.31	.02
Spatial span combined[a]	21	1851	2382	−0.92 (0.08)	−1.62 (0.22)	3.07	.002
Executive functioning							
Mazes	16	1901	1732	−1.34 (0.19)	−1.50 (0.26)	0.52	.60
Stroop-C-W interference[a]	14	1005	2112	−1.25 (0.16)	−1.78 (0.20)	3.14	.002
Stroop-switching[a]	3	226	404	−0.91 (0.09)	−1.41 (0.09)	17.87	<.001
Tower of London[a]	20	1651	1509	−0.94 (0.15)	−1.88 (0.17)	4.10	<.001
Trails B[a]	25	1504	2692	−1.04 (0.07)	−1.52 (0.08)	13.43	<.001
WCST-errors[a]	4	379	1251	−0.89 (0.06)	−1.59 (0.14)	16.32	<.001
WCST-No. of categories	6	545	1341	−0.99 (0.06)	−1.34 (0.28)	1.25	.21
WCST-perseverative errors[a]	9	668	1464	−0.90 (0.10)	−1.43 (0.19)	6.09	<.001
Attention							
CPT-IP	14	1507	1513	−1.14 (0.20)	−1.73 (0.33)	1.54	.12
CPT[a]	3	395	427	−1.15 (0.10)	−1.52 (0.09)	2.70	.007
Motor							
Token motor	16	1424	1362	−1.39 (0.13)	−1.69 (0.09)	1.87	.06
Perceptual reasoning							
Block design[a]	17	2173	4986	−0.69 (0.08)	−1.27 (0.12)	3.93	<.001
Matrix reasoning[a]	10	1371	4342	−0.87 (0.12)	−1.48 (0.12)	3.54	<.001
Picture arrangement[a]	8	1444	3847	−0.85 (0.09)	−1.61 (0.11)	5.30	<.001
Picture completion[a]	12	1330	4141	−0.91 (0.05)	−1.64 (0.14)	4.79	<.001

(continued)

Table 1. Matched Comparisons with Symbol Coding Tests (continued)

Cognitive domain or measure	k	No. of participants		Effect size (SE)		z value	*P* value
		Schizophrenia	Control	Test	SC		
Verbal comprehension							
Comprehension	11	1314	4188	−1.23 (0.16)	−1.49 (0.11)	1.35	.18
Information[a]	18	2083	4601	−0.53 (0.09)	−1.30 (0.12)	5.07	<.001
Similarities[a]	16	1877	4685	−0.74 (0.11)	−1.50 (0.09)	5.32	<.001
Vocabulary[a]	22	2818	5690	−0.79 (0.08)	−1.45 (0.08)	6.01	<.001
Social cognition							
Emotion recognition[a]	6	614	891	−0.72 (0.14)	−1.43 (0.30)	2.13	.03
MSCEIT[a]	10	1446	1272	−0.56 (0.11)	−1.46 (0.22)	3.70	<.001
Reading the Mind in the Eyes	4	392	561	−0.65 (0.15)	−1.15 (0.25)	1.71	.09

Abbreviations: CPT, Continuous Performance Test; CPT-IP, Continuous Performance Test-Identical Pairs; C-W, color-word; k, number of studies; MSCEIT, Mayer-Salovey-Caruso Emotional Intelligence Test; SC, subsetted symbol coding; Test, comparator test; WCST, Wisconsin Card Sorting Test.

[a] $P < .05$.

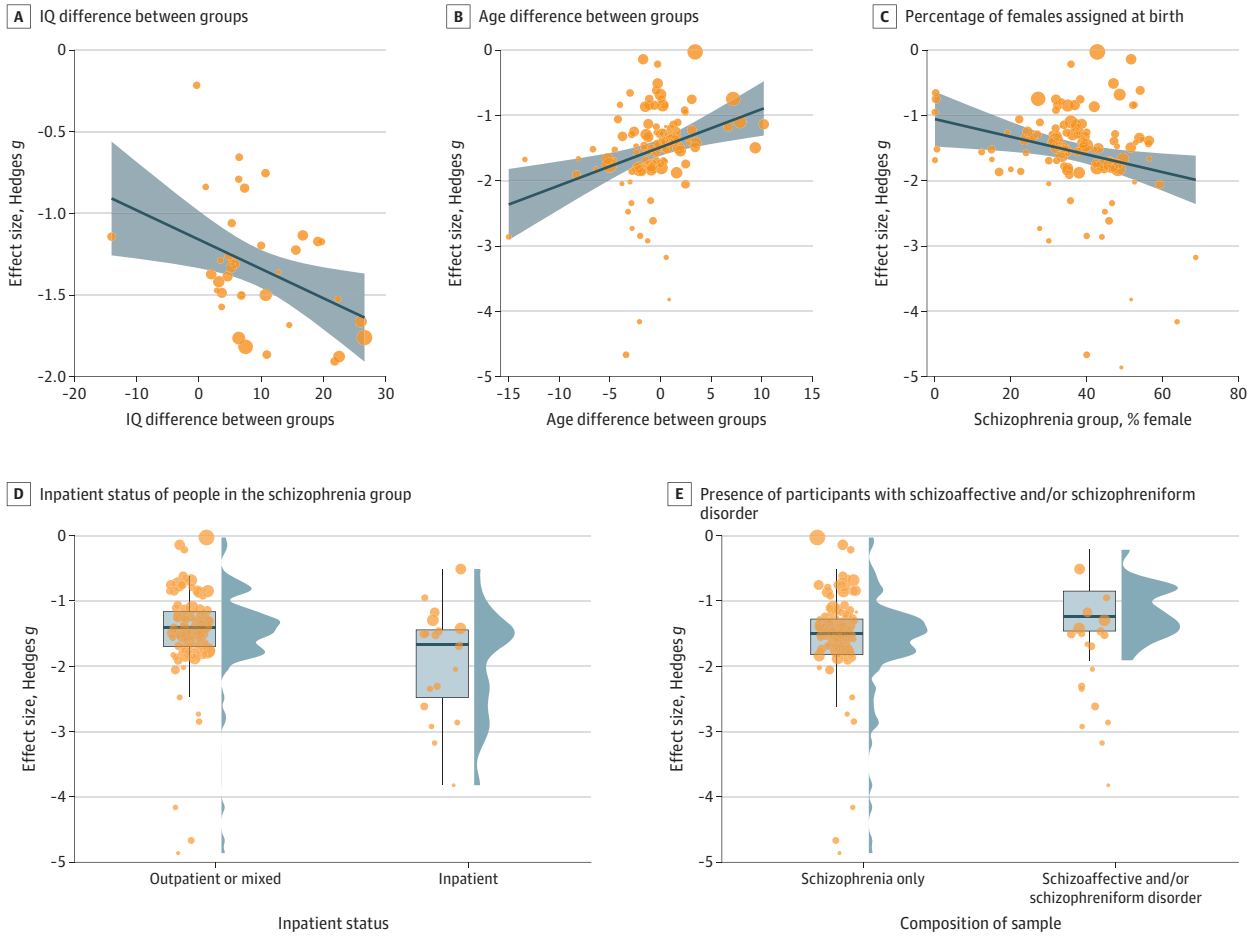
Table 2. Comparing Effect Sizes of Cognitive Tests Across Studies

Cognitive domain or measure	Effect size (SE)		z value	*P* value
	Dickinson	Pratt		
Processing speed				
Symbol coding	−1.57 (0.05)	−1.52 (0.07)	0.58	.56
Trails A	−0.88 (0.07)	−1.03 (0.07)	−1.52	.13
Stroop-word reading[a]	−0.97 (0.15)	−1.64 (0.24)	−2.37	.02
Verbal fluency				
Category fluency[a]	−1.41 (0.11)	−1.07 (0.10)	2.29	.02
Phonemic fluency	−0.83 (0.06)	−1.16 (0.23)	−1.39	.16
Learning and memory				
Verbal learning-immediate	−1.25 (0.10)	−1.29 (0.08)	−0.31	.76
Verbal learning-delayed	−1.09 (0.08)	−1.08 (0.08)	0.09	.93
Visual memory-immediate	−0.82 (0.10)	−1.10 (0.13)	−1.71	.09
Visual memory-delayed[a]	−0.78 (0.09)	−1.49 (0.21)	−3.11	.002
Rey-O-immediate	−1.03 (0.13)	−0.82 (0.30)	0.64	.52
Story memory-immediate	−1.19 (0.11)	−1.23 (0.10)	−0.27	.79
Story memory-delayed	−1.29 (0.11)	−1.27 (0.11)	0.13	.90
Verbal paired associates-immediate	−1.12 (0.26)	−1.03 (0.14)	0.31	.76
Working memory				
Arithmetic	−1.18 (0.10)	−0.94 (0.12)	1.54	.12
Digit span forward	−0.87 (0.15)	−0.75 (0.07)	0.73	.47
Digit span backward	−0.86 (0.14)	−0.78 (0.06)	0.53	.60
Digit span combined	−0.71 (0.06)	−0.68 (0.08)	0.30	.76
Letter number sequencing	−0.85 (0.11)	−0.95 (0.05)	−0.83	.41
Executive functioning				
Stroop-C-W interference	−0.99 (0.14)	−1.25 (0.16)	−1.22	.22
Trails B	−0.99 (0.06)	−1.04 (0.07)	−0.54	.59
WCST-No. of categories	−1.00 (0.10)	−0.99 (0.07)	−0.08	.93
WCST-perseverative errors	−0.81 (0.07)	−0.90 (0.10)	−0.74	.46
Attention				
CPT-IP	−0.86 (0.14)	−1.14 (0.20)	−1.15	.25
Perceptual reasoning				
Block design	−0.84 (0.12)	−0.69 (0.08)	1.04	.30
Verbal comprehension				
Information[a]	−0.82 (0.10)	−0.53 (0.09)	2.16	.03
Similarities	−0.90 (0.11)	−0.74 (0.11)	1.03	.30
Vocabulary[a]	−1.08 (0.10)	−0.79 (0.08)	2.27	.02

Abbreviations: CPT-IP, Continuous Performance Test-Identical Pairs; C-W, color-word; WCST, Wisconsin Card Sorting Test.

[a] $P < .05$.

Figure 3. Meta-Regressions of Significant Study Variables



The point size corresponds to the square root of the inverse of the SE. A, The IQ difference between groups; the lower the IQ among people in the schizophrenia group compared with those in the control group, the larger the effect size. B, The age difference between groups; the younger the age among people in the schizophrenia group is compared with those in the control group, the smaller the effect size. C, Percentage of females assigned at birth; the more females assigned at birth in the group, the larger the impairment. D, Inpatient status of people in the schizophrenia group; inpatient groups were more impaired than outpatient or mixed groups. E, Presence of participants with schizoaffective and/or schizophreniform disorder; groups that were mixed were less impaired than schizophrenia-only groups. IQ indicates intelligence quotient.

had small effect size differences of Δg = 0.2-0.49, 2 had medium differences of Δg = 0.5-0.8, and 2 had large differences of Δg >0.8). Therefore, it may not be that symbol coding tests measure a specific cognitive ability that is more impaired than other abilities, but rather that it is a good measure of an underlying impairment that variably influences other cognitive operations. This finding may be consistent with the altered brain connectivity hypothesis of processing speed,[104] and general cognitive,[149] impairment.

The cognitive impairment profile for people with schizophrenia has remained largely consistent across examinations, despite evolving research methods and novel clinical treatments. Previous meta-analyses found a global cognitive impairment of approximately 1 SD,[1,2] which is replicated presently. Although samples were nonoverlapping and from different periods (1990-2006 vs 2010-2023), there was good agreement in the pattern of cognitive impairment observed with Dickinson et al.[2] Of the 27 cognitive tests featured in both studies, the effect sizes of 22 of them did not significantly differ. Five cognitive tests revealed significantly different effect sizes over time, but it was not a uniform shift; 3 tests were observed to be less impaired in the present study, while 2 were observed to be more impaired. The differing tests were spread across different domains and do not have any clear qualities in common, making these differences difficult to interpret and likely the result of measurement error and expected sampling variation.

Several factors affect the degree of symbol coding impairment observed within a study. Three study characteristics significantly moderated the symbol coding effect. First, we found that the difference in IQ between the schizophrenia and control groups within a study affected the degree of symbol coding impairment observed. This finding is consistent with Knowles et al[11] and logical given that IQ is a measure of general cognitive ability and may even include a symbol coding task as part of the calculation. Second, we found that the dif-

ference in age between the groups within a study moderated the symbol coding impairment, which is consistent with the literature that processing speed slows as individuals age[150]; the younger the schizophrenia group is relative to the control group, the less impairment is observed. Interestingly, the mean age of the schizophrenia groups alone did not moderate the degree of impairment observed, indicating that the relative impairment is stable across the postdiagnosis lifespan, and processing speed might slow at a similar rate to controls. Third, we found that as the percentage of females assigned at birth among the schizophrenia groups increased, symbol coding performance was more impaired. This finding is rather confounding because females assigned at birth are typically observed to outperform males assigned at birth on symbol coding tests.[151-153] Therefore, future examination of this effect is warranted. Two clinical characteristics also moderated the degree of symbol coding impairment, including whether it was an inpatient group and whether the group included people with schizoaffective or schizophreniform disorders. These findings are also in line with the greater literature, where inpatient groups often show greater impairment than outpatient groups,[154] and people with other psychotic disorders show attenuated cognitive impairment relative to those with schizophrenia.[155]

Limitations

This study had several limitations. First, for parsimony and feasibility, similar tests were assessed together, as has been done previously.[1,2] It is unlikely that small methodological differences in test versions would fundamentally change the observed impairment, but it is possible. Second, while 115 studies were examined, this is only a fraction of studies on cognition in people with schizophrenia. Although our results are consistent with the literature and the matched comparison findings are encouraging, it is likely that effect sizes would differ marginally had the search criteria not been centered on symbol coding. Third, there was limited representation of cognitive domains such as reward and motivation in the included studies, and future research is needed to compare impairment in these domains with processing speed. Fourth, the results indicate considerable heterogeneity in the measurement of cognitive functions. We expected this heterogeneity because schizophrenia is a heterogeneous disorder, cognitive testing is psychometrically limited,[156] study methodology varies, and the effect of moderator variables on processing speed performance. However, some of this heterogeneity may be due to publication bias, highlighting the need to publish null findings, focus efforts on collecting sufficient sample sizes, and use careful methodology. Given that cognitive operations work in parallel, future research should examine how processing speed interacts with other cognitive abilities to either produce or avoid cognitive deficits. Additionally, although processing speed abilities can be ascertained quickly and easily, it is not clear that performance is firmly linked to any 1 brain system; therefore, its utility as a biomarker must be further examined.

Conclusion

In this meta-analysis, we found that despite evolving research methods and clinical interventions and better inclusion of research from understudied parts of the world, processing speed continues to emerge as particularly impaired for people with schizophrenia. Specifically, symbol coding tests reliably measured the full extent of cognitive impairment in people with schizophrenia. This work added to the substantial evidence that slowed information processing is a central feature of the cognitive impairment seen in schizophrenia, which is potentially a reflection of the altered brain connectivity in this population.

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