

A Meta-Analytic Review of Neuropsychological Functioning in Treatment Resistant Schizophrenia

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Background

A diagnosis of schizophrenia has been associated with impairments in an individual's cognitive, social, and occupational functioning, and more severe cognition deficits have been linked to lowered quality of life and impaired daily functioning.¹ While schizophrenia can be treated with pharmacological and psychological interventions, approximately 30% of patients continue to have symptoms and can be considered treatment resistant (TRS).² TRS may be linked with less grey matter and an abnormal glutamate system, suggesting potential differences in the cognitive status of patients with TRS compared to patients with treatment responsive schizophrenia. There is emerging evidence to suggest that patients with TRS may be categorically distinct from their treatment responsive counterparts.

Research Objective

Quantify the differences in cognitive functioning between patients with TRS and patients with treatment responsive schizophrenia (non-TRS).

Methods

- EMBASE, PsycInfo, and PubMed databases systematically searched
- Study data (e.g., patient demographics, TRS definition, cognitive test scores) were extracted
- Cognitive domains were defined; each domain had to have 3 studies
- Cohen's *d* and their 95% confidence intervals were calculated using random effects models

Results

- Of 1,204 records, 25 articles were assessed for eligibility
- 7 studies had meta-analysable data with appropriately defined groups
- TRS patients showed significant deficits for verbal memory
- There were no differences between patients with TRS and treatment responsive patients for processing speed, working memory, verbal fluency, or problem-solving/reasoning

Conclusions

- Preliminary research suggests patients with TRS may face greater cognitive impairment (specifically for verbal memory) than treatment responsive counterparts
- Potential evidence further supporting that TRS is categorically distinct from treatment responsive schizophrenia
- Given the small number of studies, conclusions were limited, and more research is needed

Tables. Meta-Analytic Data

Table 1. Processing Speed Results

Study	nTRS N	TRS N	Tests	Std. Mean Difference (<i>d</i>)
Thomas et al. (2021)	35	17	Semantic Verbal Fluency	0.22 (-0.36, 0.80)
Iasevoli et al. (2016)	29	28	BACS Symbol Coding	0.19 (-0.33, 0.71)
Spangaro et al. (2021)	32	61	Category Instances	0.23 (-0.20, 0.66)
Total	96	106		0.22 (-0.07, 0.50)

Table 2. Working Memory Results

Study	nTRS N	TRS N	Tests	Std. Mean Difference (<i>d</i>)
Thomas et al. (2021)	35	17	Letter-Number Sequencing	0.11 (-0.47, 0.69)
Iasevoli et al. (2016)	29	28	Digit Sequencing	0.18 (-0.34, 0.70)
Spangaro et al. (2021)	32	61	Digit Sequencing	0.58 (0.14, 1.01)
Anderson et al. (2015)	16	35	Digit Span	0.13 (-0.46, 0.73)
Total	112	141		0.30 (0.04, 0.56)

Table 3. Verbal Fluency Results

Study	nTRS N	TRS N	Tests	Std. Mean Difference (<i>d</i>)
Thomas et al. (2021)	35	17	Phonological and Semantic	0.06 (-0.52, 0.64)
Iasevoli et al. (2016)	29	28	Semantic	0.19 (-0.33, 0.71)
Spangaro et al. (2021)	32	61	BACS Verbal Fluency	-0.02 (-0.45, 0.41)
Anderson et al. (2015)	16	35	Phonological and Semantic	-0.42 (-10.2, 0.18)
Total	112	141		-0.03 (-0.29, 0.23)

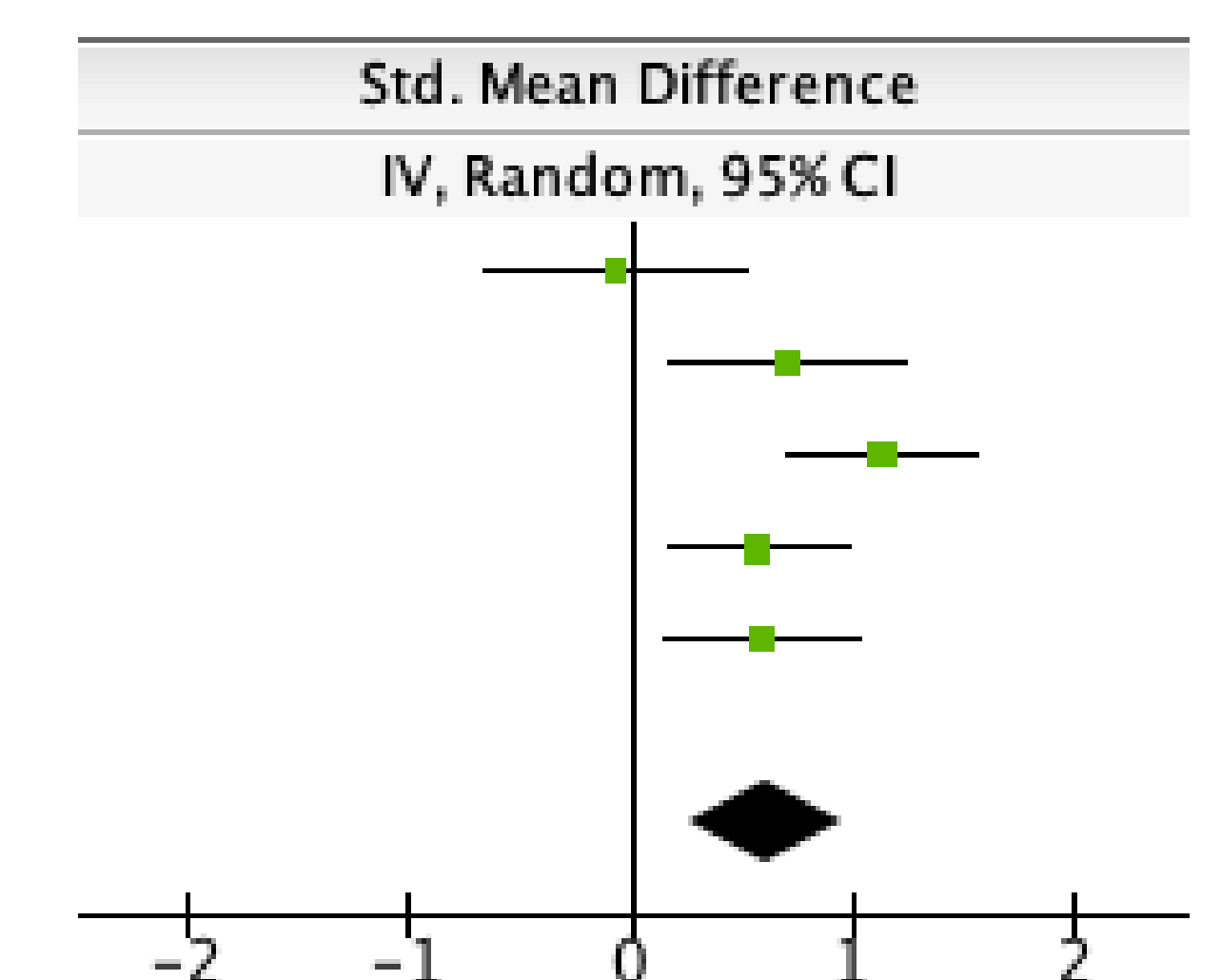
Table 4. Problem-Solving/Reasoning

Study	nTRS N	TRS N	Tests	Std. Mean Difference (<i>d</i>)
Wanes et al. (2018)	21	22	Stroop Effect Reaction	0.13 (-0.47, 0.73)
Iasevoli et al. (2016)	29	28	Tower Task	0.30 (-0.22, 0.82)
Spangaro et al. (2021)	32	61	Tower Task	0.54 (0.11, 0.98)
Anderson et al. (2015)	16	35	Stroop and Maze	-0.31 (-0.90, 0.29)
Thomas et al. (2021)	35	17	Stroop Effect Reaction	0.82 (0.22, 1.42)
Total	133	163		0.31 (-0.04, 0.66)

Table 5. Verbal Memory Results

Study	nTRS N	TRS N	Tests	Std. Mean Difference (<i>d</i>)
Iasevoli et al. (2021)	50	49	List Learning	1.14 (0.71, 1.56)
Iasevoli et al. (2016)	29	28	List Learning	0.70 (0.16, 1.24)
Spangaro et al. (2021)	32	61	BACS Word Recall	0.60 (0.16, 1.03)
Anderson et al. (2015)	16	35	Word Recall	-0.07 (-0.66, 0.52)
Kravariti et al. (2019)	113	32	List Learning	0.60 (0.16, 1.03)
Total	240	205		0.62 (0.27, 0.96)

Figure 1. Verbal Memory Forest Plot



References

1. Leifker, F. R., Bowie, C. R., & Harvey, P. D. (2009). Determinants of everyday outcomes in schizophrenia: the influences of cognitive impairment, functional capacity, and symptoms. *Schizophrenia research*, 115(1), 82-87. <https://doi.org/10.1016/j.schres.2009.09.004>
2. Gillespie, A. L., Samanaitte, R., Mill, J., Egerton, A., & MacCabe, J. H. (2017). Is treatment-resistant schizophrenia categorically distinct from treatment-responsive schizophrenia? A systematic review. *BMC psychiatry*, 17(1), 1-14. doi: 10.1186/s12888-016-1177-y



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Thank you to the BCPP team!

