Psychosocia : Journal of Applied Psychology and Social Psychology
E-ISSN : 3031-2442
Volume. 4 Issue 1 January 2026
Page No: 1-13

Effectiveness of a Multimodal Therapeutic Approach for Disorganization Symptoms in Hebephrenic Schizophrenia: A Case Report

Affan Tsaqif Taufiqurrahman[1], Winaryani[2], Hafid Algristian[3]
Universitas Nahdlatul Ulama Surabaya, Indonesia[13]
Rumah Sakit Radjiman Wediodiningrat Lawang, Indonesia[2]
Correspondent: dr.hafid@unusa.ac.id [3]

Received : October 6, 2025
Accepted : November 07, 2025
Published : January 30, 2026

Citation: Taufiqurrahman, A, T., Winaryani., & Algristian, H. (2026). Effectiveness of a Multimodal Therapeutic Approach for Disorganization Symptoms in Hebephrenic Schizophrenia: A Case Report. Psychosocia : Journal of Applied Psychology and Social Psychology, 4(1), 1-13. https://doi.org/10.61978/psychosocia.v4i1

ABSTRACT: Hebephrenic schizophrenia, or disorganized-type schizophrenia, represents one of the most disabling and treatment-resistant subtypes of psychotic disorders, marked by disorganized thinking, affect, and behavior. These symptoms often persist despite standard pharmacological treatment and are associated with poor cognitive and social functioning. This case report explores the effectiveness of an integrated multimodal therapeutic approach that combines pharmacological, cognitive-behavioral, and metabolic strategies in managing a young woman with chronic hebephrenic schizophrenia. The patient, a 23-year-old female with a six-year illness duration and history of medication nonadherence, was treated with aripiprazole 15 mg/day (dopamine D2 partial agonist), trifluoperazine 5 mg/day (full D2 antagonist), folic acid 1 mg/day, and vitamin B6 100 mg/day. Cognitive Behavioral Therapy (CBT) and family psychoeducation were conducted twice weekly for three weeks. After treatment, she demonstrated measurable improvement, including a 1-point reduction in conceptual disorganization and a 2-point improvement in blunted affect (PANSS-R), alongside qualitative gains in coping with auditory hallucinations and affective responsiveness. These results suggest that synergistic modulation of dopaminergic circuits, cognitive restructuring, and metabolic support may yield short-term benefits for patients with treatment-resistant disorganization symptoms. Further longitudinal studies are warranted to evaluate long-term outcomes and neurobiological mechanisms.

Keywords: Hebephrenic Schizophrenia, Disorganization Symptoms, Multimodal Therapy, Aripiprazole, Cognitive Behavioral Therapy, Case Report.

INTRODUCTION

Schizophrenia is a chronic and disabling neuropsychiatric disorder affecting nearly 24 million people worldwide and remains a major contributor to global disability-adjusted life years (DALYs) (World Health Organization, 2023). Despite advances in pharmacotherapy and community mental

health services, schizophrenia continues to be associated with premature mortality, unemployment, socioeconomic burden, and reduced quality of life for patients and caregivers (Charlson et al., 2018; Laursen et al., 2021). Among its clinical presentations, hebephrenic or disorganized schizophrenia represents one of the most severe and functionally impairing subtypes. Disorganization is marked by fragmented thinking, loosened associations, thought derailment, purposeless or bizarre behavior, and inappropriate affect—symptoms that interfere with communication, self-care, vocational functioning, and social integration (González-Pablos et al., 2023; Trifu et al., 2020).

Clinically, disorganization has a closer relationship to neurocognitive deficits than to positive or negative symptoms. Patients frequently display impairments in verbal working memory, semantic processing, decision-making, and emotional regulation. These deficits contribute to long-term disability, institutionalization, and treatment resistance (Harvey & Strassnig, 2019; Perkovic, 2023). Neuroimaging studies have consistently demonstrated dysconnectivity within frontotemporal and cingulate networks, including the dorsolateral prefrontal cortex (DLPFC), anterior cingulate cortex, and superior temporal gyrus—regions responsible for cognitive integration, speech organization, and affective coherence (Koutsouleris et al., 2023). Such findings support that disorganized schizophrenia is not a purely psychotic state but a network-level disorder involving structural and functional disintegration.

Pharmacological treatment remains challenging. First- and second-generation antipsychotics primarily rely on dopamine D2 receptor blockade, which is effective for hallucinations and delusions but often insufficient for disorganization and negative symptoms (Tandon et al., 2008). Excessive dopaminergic blockade in the prefrontal cortex may further suppress cognitive functioning, motivation, and affective responsiveness—paradoxically worsening functional impairment (Reynolds, 2021). These limitations have stimulated interest in dopaminergic "functional stabilization," a model in which partial agonists such as aripiprazole preserve cortical dopamine tone while antagonists reduce mesolimbic hyperactivity (Tuplin & Holahan, 2017).

Equally important are psychosocial and metabolic factors. Cognitive Behavioral Therapy for psychosis (CBTp) has demonstrated effectiveness in reducing distress toward hallucinations, improving coping, and increasing behavioral organization, even in cases with limited insight (Sitko et al., 2020). Family psychoeducation plays a critical role in relapse prevention, adherence, and improving home environments, particularly in settings with limited community psychiatric resources (Hasan, 2023). In addition, growing evidence links disorganization and cognitive decline to metabolic disruptions—especially elevated homocysteine and folate deficiency—affecting NMDA receptor signaling, prefrontal activation, and myelination (Roffman et al., 2013). Recent meta-analytic findings indicate that supplementation with folic acid and vitamin B6 can support cognitive performance and negative symptom reduction, particularly when baseline folate is low (Cheng et al., 2022).

Despite this emerging evidence, few published case reports describe an integrated approach that simultaneously combines dopaminergic stabilization, targeted metabolic supplementation, CBTp, and family psychoeducation for hebephrenic schizophrenia. Most available studies remain single-

intervention focused, overlooking potential synergistic effects across neural, cognitive, and metabolic pathways (Li & Wang, 2021). This case report addresses that gap by exploring the short-term effect of a multimodal treatment strategy in a young woman with chronic disorganized schizophrenia and documented medication nonadherence. The report highlights measurable improvement at functional and symptomatic levels, suggesting that synchronizing pharmacological, psychological, and metabolic domains may provide clinical benefits in cases where monotherapy shows limited impact.

Theoretical Framework

The pathophysiology of disorganized schizophrenia involves complex interactions across neurochemical, neurocognitive, and metabolic systems (Sousa et al., 2019). Recent multimodal neuroimaging research has identified widespread disturbances in frontotemporal and cingulate networks, especially the dorsolateral prefrontal cortex (DLPFC), anterior cingulate cortex (ACC), and superior temporal gyrus (Porter et al., 2023). These regions are responsible for cognitive integration, emotional regulation, and speech organization—domains profoundly impaired in hebephrenic schizophrenia. Structural MRI and diffusion tensor studies also demonstrate disrupted white matter integrity between these cortical hubs, reflecting functional disconnection that underlies conceptual disorganization and emotional blunting (Ochi et al., 2022).

From a neurochemical perspective, the dual-pathway hypothesis remains central: mesolimbic hyperdopaminergia contributes to positive symptoms, while mesocortical hypodopaminergia contributes to disorganization and cognitive deficits (Bliźniewska-Kowalska & Gałecki, 2024; Nielsen et al., 2022). First- and second-generation antipsychotics often suppress mesolimbic hyperactivity at the cost of worsening prefrontal dopamine deficits. Consequently, novel approaches target "functional stabilization" of dopamine signaling across circuits (Tuplin & Holahan, 2017). Aripiprazole, a dopamine D2 partial agonist, functions contextually—acting as an antagonist in hyperdopaminergic regions and as an agonist where dopamine is deficient. When paired with a full D2 antagonist like trifluoperazine, the combination allows fine-tuned dopaminergic modulation, potentially optimizing both antipsychotic efficacy and cognitive functioning.

Beyond neurochemistry, cognitive and psychosocial dimensions strongly influence the persistence of disorganization. Cognitive Behavioral Therapy (CBT) for psychosis provides a framework for addressing maladaptive cognitive appraisals and emotional dysregulation. Rather than disputing delusional content, CBT emphasizes coping and reattribution of psychotic experiences (Penn et al., 2010; Yildiz, 2021). Behavioral activation and thought structuring can restore cognitive order, even when insight is limited (Cezar et al., 2022). Family psychoeducation complements CBT by reinforcing adherence, reducing expressed emotion, and promoting stable interpersonal support (Meis et al., 2022).

At the metabolic level, growing evidence implicates one-carbon metabolism dysfunction in schizophrenia, particularly elevated homocysteine levels linked to cognitive deficits and negative

symptoms (Misiak et al., 2014). Folic acid and vitamin B6 serve as key cofactors in methylation processes essential for neurotransmitter synthesis, NMDA receptor regulation, and myelination (Ahmed et al., 2022; Roffman et al., 2013). Deficiencies in these pathways can impair glutamatergic and dopaminergic neurotransmission, further contributing to disorganization. Integrating targeted vitamin supplementation therefore represents a biologically rational adjunct within the multimodal framework.

In sum, hebephrenic schizophrenia can be conceptualized as a disorder of network disintegration—a failure of connectivity and regulation across neurochemical, cognitive, and metabolic systems. Multimodal interventions that restore these systems synchronously—through dopaminergic modulation, cognitive restructuring, and metabolic normalization—align with the current neurobiological understanding of the disorder and hold promise for improving outcomes in treatment-resistant presentations.

METHOD

This case report followed the CARE Guidelines. Written informed consent was obtained from the patient's legal guardian.

Patient Background and Clinical Assessment

The patient, referred to as Ms. D, is a 23-year-old Indonesian woman diagnosed with hebephrenic schizophrenia (F20.12) and medication nonadherence (Z91.1). She had a six-year illness course characterized by disorganized speech, inappropriate affect, and auditory hallucinations. Her symptoms emerged after severe bullying during adolescence, followed by social withdrawal and cognitive decline.

Baseline assessment using the PANSS-R, BAVQ-R, and CGI-S indicated severe psychopathology, including conceptual disorganization, affective flattening, and limited insight.

Therapeutic Intervention

Pharmacological Treatment:

- Aripiprazole 15 mg/day
- Trifluoperazine 5 mg/day
- Trihexyphenidyl 2 mg/day (for EPS prevention)
- Folic acid 1 mg/day
- Vitamin B6 100 mg/day

Folic acid and vitamin B6 were chosen for their specific role in homocysteine regulation and neurotransmitter synthesis, rather than broad multivitamin use (Roffman et al., 2013).

Psychosocial Interventions:

- CBT for psychosis: Conducted twice weekly for three weeks (60 minutes each). Sessions focused on cognitive restructuring, distress reduction, and coping skills related to auditory hallucinations.
- Family psychoeducation: Focused on understanding schizophrenia, adherence, and supportive home environment.
- Group therapy: Targeted social skills and emotional regulation.

Follow-Up and Evaluation

The patient was monitored weekly. Post-intervention assessments showed measurable improvement.

Table 1. Comparison of Pre- and Post-Intervention Psychometric Scores.

Scale	Item	Baseline	3-Week Follow-up	Change
PANSS-R	Conceptual disorganization	5	4	-1
PANSS-R	Blunted affect	5	3	-2
PANSS-R	Bizarre posturing	4	3	-1
CGI-S	Severity	5 (markedly ill)	5 (markedly ill)	0
CGI-I	Improvement	N/A	3 (minimally improved)	—

Note: BAVQ-R quantitative data unavailable; qualitative improvement observed in emotional regulation and coping.

RESULT AND DISCUSSION

The present case illustrates that a short-term multimodal therapeutic approach can produce meaningful symptomatic and functional improvement in a patient with chronic hebephrenic schizophrenia—one of the most treatment-resistant and functionally disabling clinical subtypes. Although changes in standardized scoring instruments such as PANSS-R and CGI-I were numerically modest, qualitative improvement in thought organization, socioemotional responsiveness, hygiene, adherence, and coping abilities indicates a clinically relevant step toward recovery. In contemporary psychiatric research, functional stabilization is increasingly recognized as a more realistic and meaningful outcome than full symptomatic remission, especially for chronic and disorganized presentations (Vita & Barlati, 2021).

1. Pharmacological Mechanisms and Dopaminergic Stabilization

The pharmacological strategy used in this case—combining aripiprazole, a dopamine D2 partial agonist, with trifluoperazine, a full antagonist—was based on a mechanistic rationale rather than polypharmacy by default. Aripiprazole moderates dopamine signaling contextually, functioning as an antagonist in hyperdopaminergic mesolimbic regions but partially agonizing where dopamine is deficient, such as the prefrontal cortex (Ebrahimi & Asmundson, 2024; Giordano et al., 2022). In contrast, trifluoperazine blocks excessive dopaminergic transmission implicated in hallucinations and erratic behavior. When administered together, these medications may achieve "functional dopamine stabilization," avoiding the cognitive dulling associated with high D2 blockade while reducing positive symptoms (Cookson et al., 2023).

This aligns with evidence showing that D2 blockade above 80% occupancy correlates with emotional blunting and reduced incentive salience (Correll, 2020). By maintaining prefrontal dopaminergic tone, aripiprazole may support attention, goal-directed planning, and speech organization—core neurocognitive domains affected in disorganized schizophrenia. Neuroimaging studies support this interpretation: restoration of connectivity between the dorsolateral prefrontal cortex and anterior cingulate cortex predicts improvement in conceptual organization and executive functioning (Najmi & Akhondzadeh, 2022; Nibbio et al., 2020). Thus, although pharmacological effects alone did not dramatically alter CGI-S scores, they may have created the neurobiological conditions necessary for psychosocial interventions to be effective.

2. Cognitive Behavioral Therapy and Thought Structuring

Cognitive Behavioral Therapy for psychosis (CBTp) served as a cognitive and behavioral scaffold to reduce disorganization. Patients with hebephrenic schizophrenia commonly show fragmented thinking, derailment, impaired abstraction, and poor insight, which often lead clinicians to assume that psychotherapy would be ineffective. However, accumulating evidence suggests the opposite: even when insight is limited, structured CBTp can improve coping, reduce distress toward hallucinations, and foster clearer thought sequencing (O'Connor et al., 2021).

In this case, the patient initially believed her auditory hallucinations carried supernatural meaning. Through guided reattribution and cognitive restructuring, she began perceiving the voices as internal experiences rather than external threats. This shift reduced emotional distress and improved self-regulation. Neuropsychological research indicates that appraising hallucinations as internally generated decreases limbic reactivity and increases frontal inhibitory control (Linden, 2023). This may explain the observed improvement in affect and conceptual coherence.

Additionally, behavioral techniques such as stimulus control, activity scheduling, and thought organization exercises allowed the patient to regain daily structure. As disorganized schizophrenia often leads to purposeless wandering, impaired hygiene, and chaotic routines, these gains represent meaningful indicators of recovery.

3. Family Psychoeducation and Relapse Prevention

Family involvement is one of the strongest predictors of treatment adherence and relapse risk in schizophrenia. High expressed emotion—characterized by criticism, hostility, and overinvolvement—can increase relapse probability by up to threefold, whereas structured psychoeducation reduces hospitalization and improves medication compliance. In this case, psychoeducation helped the family understand that disorganized behaviors were symptoms of illness rather than intentional actions. This reduced interpersonal conflict and created a calmer home environment. It also improved medication supervision—critical for a patient with a history of nonadherence.

This component is particularly important in low- and middle-income countries, where family members frequently serve as primary caregivers due to limited availability of psychiatric residential services.

4. Metabolic Enhancement: Folate and Vitamin B6

One-carbon metabolism plays a crucial role in neurotransmitter synthesis, DNA methylation, and neural plasticity. Elevated homocysteine and folate deficiency are repeatedly reported among individuals with schizophrenia and strongly correlate with cognitive impairment, negative symptoms, and structural brain abnormalities (Olaso-Gonzalez et al., 2021). Clinical trials show that folic acid and vitamin B6 can improve processing speed, emotional regulation, and negative symptoms, particularly when baseline folate levels are low or when MTHFR polymorphisms are present.

Although homocysteine levels were not measured in this case, supplementation was chosen intentionally rather than empirically. The observed improvement in affect and engagement may reflect enhanced NMDA signaling and glutamate regulation, supporting the integration of pharmacotherapy and CBTp. This reinforces growing evidence from nutritional psychiatry suggesting that metabolic correction can serve as a neurobiological catalyst for therapeutic efficacy.

5. Systems-Level Synergy

The improvements observed in this patient likely did not arise from a single intervention but from synergistic interaction across biological, psychological, and social domains. Pharmacological stabilization reduced psychotic intensity enough for CBTp to be effective. CBTp reduced distress and increased insight, making medication adherence more feasible. Family psychoeducation ensured environmental stability and daily structure. Metabolic support facilitated neurochemical balance and cognitive readiness for learning.

This systemic interaction aligns with modern models conceptualizing schizophrenia as a multisystem dysconnectivity disorder rather than a purely dopaminergic illness (Patel, 2024; Selvaraj & Fatemi, 2022). By addressing multiple pathways simultaneously, the treatment moves closer to personalized and recovery-oriented psychiatric care.

6. Functional Outcomes as Evidence of Recovery

Although PANSS scores changed by only 1–2 points, the patient demonstrated significant behavioral change: improved self-care, better hygiene, more coherent speech, reduced isolation, and more adaptive coping with hallucinations. Research has repeatedly shown that functional outcomes—rather than symptom scores—best predict long-term recovery, quality of life, and community reintegration (Organization, 2023; Porter et al., 2023). Therefore, the results of this case should be interpreted as clinically meaningful despite modest numerical change.

7. Relevance for Low-Resource Settings

This case has practical value for low-resource clinical settings, where availability of long-acting injectables, inpatient rehabilitation, or social support infrastructure may be limited. The therapeutic components used—aripiprazole, trifluoperazine, CBT-based sessions, family psychoeducation, and vitamin supplementation—are feasible, affordable, and scalable in district hospitals or outpatient programs. Implementing similar multimodal strategies could reduce institutional dependency, hospitalization, and caregiver burden.

8. Future Research

Future studies should evaluate:

- biomarker-guided metabolic supplementation (e.g., homocysteine, MTHFR genotyping),
- maintenance CBTp for preventing cognitive relapse,
- long-term follow-up to assess the durability of improvement,
- neuroimaging to map structural and functional brain changes after combined therapy,
- integration of digital CBTp platforms to expand access.

Final Interpretation

In summary, this case offers real-world evidence that synchronized pharmacological, psychological, and metabolic interventions can produce early functional improvement in treatment-resistant disorganized schizophrenia. The outcomes support a shift from monotherapy-focused models toward multidisciplinary, recovery-oriented care. (Kronenberg et al., 2009; Mervis et al., 2017)

CONCLUSION

This case report demonstrates that a multimodal therapeutic approach—integrating dopaminergic stabilization, metabolic supplementation, structured Cognitive Behavioral Therapy for psychosis, social-skills training, and family psychoeducation—can yield meaningful improvement in a patient

with chronic hebephrenic schizophrenia. Although numerical changes in psychometric scales such as the PANSS-R and CGI-I were modest, the patient exhibited clinically significant gains in conceptual organization, emotional responsiveness, coping with hallucinations, daily functioning, and adherence. These changes represent early markers of recovery and align with current recovery-oriented frameworks emphasizing functionality, adaptation, and quality of life rather than complete remission.

From a mechanistic perspective, the combination of a partial dopamine agonist (aripiprazole) and a full antagonist (trifluoperazine) likely produced functional stabilization of dopaminergic pathways, supporting cognitive control while preventing mesolimbic hyperactivation. Cognitive Behavioral Therapy facilitated thought structuring, reduced distress toward internal stimuli, and supported reattribution of hallucinations. Family psychoeducation reduced interpersonal conflict and improved medication supervision—critical in a patient with a nonadherence history. Meanwhile, folic acid and vitamin B6 addressed one-carbon metabolic disruptions linked to cognitive slowing and negative symptoms, potentially enhancing neuroplasticity and amplifying treatment gains.

This case provides practical evidence that short-term, cost-efficient, and scalable multimodal interventions can be implemented even in resource-limited settings. The outcome supports a shift from monotherapeutic, symptom-based treatment to integrated, personalized, biopsychosocial management—especially for treatment-resistant and disorganized presentations of schizophrenia.

However, the conclusions are limited by the short observation period and single-case design. Future research should integrate longitudinal follow-up, neuroimaging and metabolic biomarkers, genotyping (e.g., MTHFR), and comparative trials to verify generalizability. Nonetheless, this report highlights that combined pharmacological, psychological, and metabolic approaches may offer clinically meaningful benefits where standard treatment alone provides insufficient progress.

Clinical Implication:

Integrated, multidisciplinary strategies can stabilize complex symptom domains where monotherapy fails. Realistic clinical goals should emphasize stabilization and improved functionality rather than complete remission (Marone et al., 2022).

Limitations:

The short observation period and single-case design limit generalizability. Future studies should extend follow-up duration, include biomarkers such as homocysteine or neuroimaging data, and employ randomized designs for validation.

Future Direction:

Biomarker-guided multimodal trials could identify subgroups benefiting most from metabolic augmentation and dopaminergic modulation. Collaborative care integrating psychiatry, psychology, and nutritional neuroscience may enhance long-term outcomes.

REFERENCE

Ahmed, A., El-Gharieb, M., & Salama, R. (2022). Vitamin B6 supplementation and cognition in psychotic disorders: A randomized controlled trial. *Nutrients*, *14*(9), 1853. https://doi.org/10.3390/nu14091853

Bliźniewska-Kowalska, K., & Gałecki, P. (2024). Dopaminergic system dysfunction and novel pharmacological targets in schizophrenia treatment. *Pharmacological Reports*, *76*(1), 1–12. https://doi.org/10.1007/s43440-023-00497-w

Cezar, R., Lopes, R. T., Oliveira, I. R., & Rangé, B. P. (2022). Cognitive Behavioral Therapy for psychotic symptoms: A case study and literature review. *Revista Brasileira de Terapias Cognitivas*, *18*(1), 1–10. https://doi.org/10.5935/1678-5568.20220001

Charlson, F. J., Ferrari, A. J., & Santomauro, D. F. (2018). Global epidemiology and burden of schizophrenia: Findings from the Global Burden of Disease Study. *Psychological Medicine*, *48*(3), 1–12. https://doi.org/10.1017/S003329171700324X

Cheng, P., Liu, Y., & Ning, L. (2022). Homocysteine-lowering vitamins for cognitive deficits and negative symptoms in schizophrenia: Systematic review and meta-analysis. *Schizophrenia Research*, *243*, 84–92. https://doi.org/10.1016/j.schres.2022.04.014

Cookson, J., Pimm, J., & Brentnall, A. (2023). Partial agonists of dopamine receptors: Clinical effects and receptor interactions when combining aripiprazole with full antagonists. *BJPsych Advances*, *29*(2), 106–115. https://doi.org/10.1192/bja.2022.61

Correll, C. U. (2020). From receptor pharmacology to improved outcomes: Individualizing antipsychotic treatment. *Journal of Clinical Psychiatry*, *81*(3), 19 12980. https://doi.org/10.4088/JCP.19rp12980

Ebrahimi, A., & Asmundson, G. J. G. (2024). Multidisciplinary approaches in psychiatric treatment: Improving adherence and patient outcomes. *Journal of Psychiatric Research*, *170*, 113–121. https://doi.org/10.1016/j.jpsychires.2023.12.006

Giordano, F., Granata, G., & Manuli, A. (2022). Polypharmacy and schizophrenia: The challenge of antipsychotic treatment adherence. *Journal of Clinical Medicine*, *11*(18), 5285. https://doi.org/10.3390/jcm11185285

González-Pablos, E., Torre-Luque, A., Iruretagoyena, B., & González-Torres, M. A. (2023). Language disorganization in schizophrenia and its relation to social functioning. *International*

Journal of Environmental Research and Public Health, *20*(3), 2307. https://doi.org/10.3390/ijerph20032307

Harvey, P. D., & Strassnig, M. (2019). Cognitive impairment and functional decline in schizophrenia. *Schizophrenia Research: Cognition*, *16*, 1–6. https://doi.org/10.1016/j.scog.2018.11.003

Hasan, A. (2023). Family-based psychosocial interventions in schizophrenia: An updated systematic review. *Schizophrenia Bulletin*, *49*(2), 331–344. https://doi.org/10.1093/schbul/sbac137

Koutsouleris, N., Kambeitz, J., Schmidt, A., Wood, S. J., & Borgwardt, S. (2023). Multimodal neuroimaging markers of disorganization in schizophrenia: A network-based approach. *Nature Communications*, *14*, 2104. https://doi.org/10.1038/s41467-023-37913-3

Kronenberg, G., Harms, C., Sobol, A., & Gertz, K. (2009). Folate deficiency induces neurodegeneration and brain dysfunction in mice lacking methylenetetrahydrofolate reductase. *Journal of Neuroscience Research*, *87*(7), 1605–1615. https://doi.org/10.1002/jnr.21979

Laursen, T. M., Fink-Jensen, A., & Gasse, C. (2021). Excess mortality in schizophrenia: 30-year population-based study. *Acta Psychiatrica Scandinavica*, *144*(6), 550–560. https://doi.org/10.1111/acps.13355

Li, X., & Wang, Q. (2021). Combined pharmacological and cognitive intervention in chronic schizophrenia: A translational perspective. *Translational Psychiatry*, *11*(1), 545. https://doi.org/10.1038/s41398-021-01699-x

Linden, D. (2023). Neuroplastic effects of cognitive behavioral therapy in psychosis: Meta-analytic review. *Neuroscience & Biobehavioral Reviews*, *148*, 105146. https://doi.org/10.1016/j.neubiorev.2023.105146

Marone, A., Dagani, J., & Girolamo, G. (2022). The role of psychosocial interventions in recovery-oriented care for schizophrenia: A systematic review. *European Psychiatry*, *65*(1), 35. https://doi.org/10.1192/j.eurpsy.2022.35

Meis, L. A., Griffin, J. M., Greer, N., & MacDonald, R. (2022). Family-involved psychosocial interventions for adults with schizophrenia: A systematic review. *Psychiatric Services*, *73*(7), 801–809. https://doi.org/10.1176/appi.ps.202100541

Mervis, J. E., Capizzi, R. J., Borodkin, K., & Johnson, J. M. (2017). Targeting the DLPFC with noninvasive brain stimulation in schizophrenia: A meta-analysis. *Schizophrenia Research*, *191*, 38–45. https://doi.org/10.1016/j.schres.2017.04.044

Misiak, B., Stańczykiewicz, B., & Łaczmański, Ł. (2014). The role of homocysteine and B vitamins in the etiopathogenesis of schizophrenia. *Psychiatria Polska*, *48*(6), 1181–1193. https://doi.org/10.12740/PP/27414

Najmi, E., & Akhondzadeh, S. (2022). Early-onset schizophrenia and cognitive decline: A narrative review. *Journal of Clinical Neuroscience*, *100*, 1–9. https://doi.org/10.1016/j.jocn.2022.03.015

Nibbio, G., Vita, A., & Comandini, A. (2020). Cognitive and functional trajectories in schizophrenia and their association over six years. *Psychological Medicine*, *50*(11), 1805–1812. https://doi.org/10.1017/S0033291719002016

Nielsen, J., Leucht, S., & Kane, J. M. (2022). Aripiprazole mechanisms of action: Insights into dopamine partial agonism and clinical implications. *CNS Drugs*, *36*(1), 1–12. https://doi.org/10.1007/s40263-021-00869-4

Ochi, R., Nakamura, T., & Hashimoto, K. (2022). Structural subdivisions of the anterior cingulate cortex in treatment-resistant schizophrenia: A neuroimaging perspective. *Journal of Psychiatry & Neuroscience*, *47*(4), 255– 264. https://doi.org/10.1503/jpn.210113

O'Connor, K., Rossell, S., & Thomas, N. (2021). Cognitive behavioural therapy for hallucinations: Mechanisms and outcomes. *Frontiers in Psychiatry*, *12*, 658307. https://doi.org/10.3389/fpsyt.2021.658307

Olaso-Gonzalez, G., Pérez-Martínez, A., & Navarro-González, I. (2021). Homocysteine and cognitive impairment: Role of folate and vitamin B6 in neurological function. *Nutrients*, *13*(5), 1633. https://doi.org/10.3390/nu13051633

Organization, W. H. (2023). *Schizophrenia fact sheet*. https://doi.org/10.46981/sfjhv2n1-004

Patel, K. R. (2024). Integrated approaches for treatment-resistant schizophrenia. *World Journal of Psychiatry*, *14*(3), 215–229. https://doi.org/10.5498/wjp.v14.i3.215

Penn, D. L., Meyer, P. S., Evans, E., Wasan, A., Bucci, W., & Silverstein, S. M. (2010). A cognitive-behavioral therapy-based intervention for persistent auditory hallucinations: A preliminary study. *Cognitive and Behavioral Practice*, *17*(2), 148–155. https://doi.org/10.1016/j.cbpra.2009.08.003

Perkovic, M. N. (2023). Disorganization symptoms and cognitive impairment in schizophrenia: A meta-analysis. *Schizophrenia Research*, *253*, 28–37. https://doi.org/10.1016/j.schres.2022.11.021

Porter, A., Fei, S., & Damme, K. S. F. (2023). A meta-analysis of multimodal neuroimaging in psychosis classification. *Molecular Psychiatry*, *28*(8), 3278–3292. https://doi.org/10.1038/s41380-023-02195-9

Reynolds, G. P. (2021). Receptor mechanisms in the treatment of schizophrenia. In D. J. Heal & G. P. Reynolds (Eds.), *New Approaches to Psychiatric Drug Development* (pp. 41–56). Springer. https://doi.org/10.1007/978-3-030-79647-3_3

Roffman, J. L., Lamberti, J. S., & Achilles, J. (2013). A randomized, double-blind, placebo-controlled trial of folate plus vitamin B12 for cognitive deficits in schizophrenia. *American Journal of Psychiatry*, *170*(11), 1326–1334. https://doi.org/10.1176/appi.ajp.2013.13020220

Selvaraj, S., & Fatemi, S. H. (2022). Pathophysiology of schizophrenia: Beyond dopamine. *Molecular Psychiatry*, *27*, 270–286. https://doi.org/10.1038/s41380-021-01337-5

Sitko, K., Bewick, B. M., Owens, D., & Masterson, C. (2020). Metaregression of CBT for psychosis across time. *Schizophrenia Bulletin Open*, *1*(1), 23. https://doi.org/10.1093/schizbullopen/sgaa023

Sousa, T., Fernandes, H. M., Firmino, H., Silva, C. F., Marques-Teixeira, J., & Barbosa, F. (2019). Poor emotion recognition is associated with disorganized symptoms in schizophrenia. *Schizophrenia Research*, *210*, 188–194. https://doi.org/10.1016/j.schres.2019.05.034

Tandon, R., Belmaker, R. H., & Gattaz, W. F. (2008). World Psychiatric Association statement on comparative effectiveness of antipsychotics. *Schizophrenia Research*, *100*(1–3), 20–38. https://doi.org/10.1016/j.schres.2007.12.477

Trifu, S., Vladuti, A., & Tudor, R. (2020). Disorganized behavior and self-neglect in schizophrenia: An integrative view. *Journal of Medicine and Life*, *13*(2), 248–251. https://doi.org/10.25122/jml-2020-1009

Tuplin, E. W., & Holahan, M. R. (2017). Aripiprazole as a partial agonist with functional selectivity: A review and update. *CNS Drugs*, *31*(5), 411–417. https://doi.org/10.1007/s40263-017-0439-4

Vita, A., & Barlati, S. (2021). Recovery in schizophrenia: Toward functional outcomes. *World Psychiatry*, *20*(3), 267–284. https://doi.org/10.1002/wps.20874

Yildiz, M. (2021). Cognitive-behavioral therapy in schizophrenia: Updates and clinical applications. *Frontiers in Psychiatry*, *12*, 690301. https://doi.org/10.3389/fpsyt.2021.690301