LUMEN ET VIRTUS
ISSN: 2177-2789

MAIN CLINICAL MANIFESTATIONS OF SCHIZOPHRENIA AND POSSIBLE APPROACHES: A SYSTEMATIC REVIEW

https://doi.org/10.56238/levv16n48-054

Submitted on: 04/14/2025 **Publication date:** 05/14/2025

Guilherme Bennett Volpato[1], Lívia Iguchi Nishimura[2], Lidiane Indiani[3], Ana Caroline Barreto Cristobal[4], Marcos Vinicius Ribeiro Lobato[5], Nelson Antonio da Silva Neto Segundo[6], Adriana Martins Monteiro de Castro[7], Laura Gabriela Mota Lage Domingues Teixeira[8], Anésia Bezerra da Fonsêca[9] and Marcelo Salomão Aros[10]

ABSTRACT

Objective: The purpose of this analysis was to present current knowledge about the main signs, symptoms, and associated conditions that impact people with schizophrenia. **Methodology:** The investigations were carried out through searches in the PubMed Central (PMC) and Virtual Health Library (VHL) data platforms. Three search terms were used in conjunction with the Boolean operator "AND": Schizophrenia, Signs and Symptoms, Clinical Diagnosis. From this research, 490 works were found, later evaluated according to the selection criteria. Of these, 419 studies came from the PubMed database and 71 from the Virtual Health Library. After applying the inclusion and exclusion criteria, 24 articles from PubMed and 1 from the Virtual Health Library were selected, totaling 25 studies to compose the analysis. **Results:** The investigations highlight the connection between psychotic disorders, such as schizophrenia and depression, evidencing the relevance of continuity in research and interdisciplinary interaction to improve the recognition and treatment of these conditions. The discovery of biological markers and a more detailed analysis of clinical

[1]Doctor from the University Center of Adamantina (FAI).
Email: gui_bennett@hotmail.com
[2]Medical student at the University of Franca - UNIFRAN
E-mail: lin.iguchi@gmail.com
[3]Endocrinologist- USP- SP
Master's student in Health Education- HIAE
E-mail: lidianeindiani@gmail.com
[4]Medical Doctor, Potiguar University (UNP), Natal/RN
Postgraduate student in Psychiatry at IBCMED
E-mail: anacbcristobal@gmail.com
[5]Medical Student at the Federal University of Pará (UFPA) Belém, PA
Email: marcosvrlobato@gmail.com
[6]Family and Community Physician from UFPE
Email: nelsonnsegundo@gmail.com
[7]Medical Degree from the Faculty: Centro Universitário do Espírito Santo (UNESC)
Postgraduate in Psychiatry - ISMD/ BH
E-mail: adrianammonteirodecastro@hotmail.com
[8]Doctor from the University for the Development of the State and the Pantanal Region
Post Graduate in Psychiatry - Faculdade Gaucha
E-mail: dra.lauragabriela@gmail.com
[9]Physician from the Faculty of Medical Sciences of the University of Pernambuco - FCM/UPE
E-mail: anesiafonseca@gmail.com
[10]Advisor
Psychiatrist, professor of the Medicine course at the University of Franca (UNIFRAN) in the discipline of PIESF in Psychiatry

characteristics are essential to develop more effective treatments, with the aim of providing a better quality of life for patients. **Conclusion:** The combination of collaborative strategies between different medical areas and the use of advanced technologies, such as artificial intelligence and machine learning, open up new possibilities for early recognition and customized treatments of schizophrenia. In short, the evolution in the care of these intricate conditions requires an integrated and multidisciplinary approach, aimed at meeting the specific demands of patients and ensuring their overall well-being.

Keywords: Schizophrenia. Clinical evidence. Associated Conditions.

INTRODUCTION

Schizophrenia, defined as a complex neurodevelopmental pathology, is related to the emergence of significant cognitive disabilities and alterations in the initial mechanisms of sensory processing. Classified as a chronic and progressive psychiatric condition, it affects between 4 and 6 individuals per thousand inhabitants. Although its prevalence is similar between the sexes, men tend to manifest the condition at earlier ages compared to women, and the frequency of cases is slightly higher in urban regions compared to rural areas (GASHKARIMOV et al., 2023; JURIŠIĆ et al., 2021; ZHANG et al., 2019). More than 50% of male patients and about a third of female patients experience their first psychiatric hospitalization before the age of 25. The age ranges with the highest incidence are between 10 and 25 years in men, and between 25 and 35 years in women. Women, however, exhibit a bimodal profile of manifestation, with a second peak of incidence in middle age. Around 3 to 10% of women have symptoms after the age of 40, and about 90% of patients on treatment are in the age group of 15 to 55 years (SADOCK et al., 2016).

Evidence points to a higher frequency of schizophrenia in family members of affected patients, when compared to the general population. For example, descendants of a single carrier parent have a 17% chance of developing the condition throughout their lives, a percentage that rises to 35% if both parents are diagnosed (KHAVARI et al., 2020). The likelihood of manifestation of the disorder is directly related to the degree of kinship with the affected individual (e.g., first- or second-degree relatives). In the cases of monozygotic twins, who share the same genetic load, the concordance rate for schizophrenia is around 50%, a value 4 to 5 times higher than that found in dizygotic twins or other first-degree relatives (SADOCK et al., 2016).

Although the genetic mechanisms underlying schizophrenia remain elusive, several genes are implicated in susceptibility to the disorder. Genetic linkage and association studies have identified nine relevant chromosomal regions: 1q, 5q, 6p, 6q, 8p, 10p, 13q, 15q, and 22q. Further investigations of these areas have led to the identification of candidate genes, including the nicotinic receptor alpha-7, DISC1, GRM3, COMT, NRG1, RGS4, and G72. More recently, mutations in the dystrobrevin (DTNBP1) and neuregulin 1 genes have been linked to negative manifestations of schizophrenia (SADOCK et al., 2016).

Despite the estimated genetic preponderance of 80%, multiple environmental factors also contribute to the etiology of schizophrenia. These elements include maternal immune activation, hypoxia, nutritional deprivation, maternal affective deprivation, and exposure to specific toxins. The interaction between such exposures and genetic predispositions

underlies the neurodevelopmental hypothesis, which proposes the combination of genetic vulnerability and environmental factors, especially in the prenatal and juvenile periods (KHAVARI et al., 2020).

Schizophrenic symptoms are classified as positive, including delusions and hallucinations; negative, such as social isolation and anhedonia; and cognitive, including attentional and memory deficits. Difficulties in social cognition pose underlying challenges to interpreting and responding to social stimuli, resulting in impairments in social interactions and reduced social functionality (ADRAQUI et al., 2023).

Studies point to the role of oxidative stress in the socio-cognitive dysfunctions associated with schizophrenia. This redox imbalance, caused by mitochondrial dysfunctions and reduction in antioxidant capacity, is exacerbated by genetic and environmental factors, including maternal immune activation and social stress, increasing the production of reactive oxygen species (ROS) (ADRAQUI et al., 2023).

There are no definitive biomarkers for the diagnosis of schizophrenia, and clinical recognition is based on characteristic symptoms. Prognostic assessment and therapeutic intervention focuses on the analysis of established signs (ANG et al., 2021).

The typical course of schizophrenia involves episodes of exacerbation and remission. After the first psychotic break, the patient tends to recover gradually, presenting prolonged periods of relatively normal functionality. However, relapses are recurrent, with an evolutionary pattern during the first five years after diagnosis, often defining the prognosis. Each relapse worsens the baseline functional deterioration. Longitudinal studies indicate that, after 5 to 10 years from the first hospitalization, only 10-20% of patients have favorable outcomes. More than 50% face unsatisfactory progression, characterized by re-hospitalizations, symptomatological worsening, episodes of mood disorders, and suicide attempts (SADOCK et al., 2016).

Remission rates range between 10% and 60%. It is estimated that 20-30% of patients are able to lead relatively normal lives; another 20-30% have moderate symptoms, while 40-60% remain severely debilitated throughout their lives. Comparatively, patients with mood disorders have better prognosis, although 20-25% face severe difficulties in prolonged follow-up (SADOCK et al., 2016). Evidently, schizophrenia is a severe psychiatric disorder, associated with a substantial impact on the patient's quality of life and social integration. Thus, early diagnoses and interventions favor more positive prognoses (GASHKARIMOV et al., 2023).

The present review aims to synthesize contemporary knowledge about the main clinical manifestations and comorbidities of schizophrenia, offering a critical analysis in the

light of evidence from the current literature, with a view to improving health professionals' understanding of this complex disorder.

METHODOLOGY

This is a systematic review with the aim of analyzing the predominant clinical manifestations of schizophrenia, as well as evidencing the main comorbidities frequently associated with the condition, aiming to promote a greater elucidation of the clinical understanding of the pathology. To conduct this investigation, a guiding question was formulated based on the PVO (Population, Variable and Objective) strategy: "What are the preponderant signs and symptoms of schizophrenia, in addition to the comorbidities frequently associated with the condition?"

The searches were carried out through investigations on the PubMed Central (PMC) and Virtual Health Library (VHL) data platforms. The research was structured using three descriptors combined with the Boolean operator "AND": Schizophrenia, Signs and Symptoms, Clinical Diagnosis. The strategies adopted for consultation in the PMC database were: Schizophrenia AND Signs and Symptoms and Schizophrenia AND Clinical Diagnosis. In the VHL, the strategy consisted of Schizophrenia AND Clinical Diagnosis. As a result, 490 articles were identified, which subsequently underwent rigorous application of selection criteria.

The inclusion criteria included studies published between 2019 and 2024, written in Portuguese, English, or Spanish, that directly addressed the proposed themes, and were review, observational, or experimental articles made available in full. On the other hand, duplicate works, texts available only in abstract format, investigations that did not directly address the main theme, or that did not meet the other established criteria were excluded.

After combining the descriptors applied in the consulted databases, 490 studies were identified: 419 from PubMed and 71 from the Virtual Health Library. With the application of the inclusion and exclusion criteria, 24 articles were selected from the PubMed database and 1 article from the Virtual Health Library, totaling 25 investigations to compose the final sample.

DISCUSSION

Schizophrenia is conceptualized as a multifactorial neurodevelopmental disorder, characterized by significant cognitive changes and dysfunctions in primary sensory mechanisms. It is a psychiatric condition with wide clinical heterogeneity, where different

patients may present a distinct spectrum of manifestations, often disconnected from each other (JURIŠIĆ et al., 2021).

In the context of clinical manifestations, five central negative symptoms are reported in patients, classified into two subdimensions. The Positive and Negative Syndrome Scale (PANSS) demonstrates limitations in the accurate assessment of negative symptoms. The Marder factor, a specific model for negative symptoms, is widely recognized and validated by the United States FDA. Modern instruments, such as the BNSS and CAINS, were created to overcome these limitations; however, the superiority against the PANSS Marder factor is not yet proven. Innovative strategies, such as digital phenotyping, emerge as a promising alternative in the assessment of negative symptoms (MARDER et al., 2023).

Neurobiological studies suggest that deficits in positive reward learning play an essential role in the etiology of negative symptoms, especially anhedonia, which is strongly related to functional limitations. Dysfunction in the neural systems of anticipation and reward is one of the central mechanisms associated with motivational deficiencies in these patients (MARDER et al., 2023).

Among the five main types of negative symptoms are alogia, blunted affect, avoliation, asociality, and anhedonia. The digital phenotyping approach has shown advances in the precise distinction of these symptoms. In addition, disorders related to interpersonal distance are correlated with the negative symptoms of schizophrenia, with difficulties in social cognition being significant underlying factors. Further advances are needed to fully understand these associations (KIRKPATRICK et al., 2023).

Schizophrenic patients face substantial challenges in social cognition, with an emphasis on the domains of theory of mind and emotional perception. Neuroimaging investigations reveal heterogeneous findings, reinforcing the need for more in-depth research. Additional evidence should explore the connections between brain structure and functionality, social cognition, and social outcomes (LEMMERS-JANSEN et al., 2023).

Schizophrenia, due to its multifaceted nature, comprises a wide range of symptoms, including hallucinations, delusions, behavioral changes, cognitive deficits, and negative manifestations. A relevant aspect is apraxia, described as a commitment to qualified actions. Studies indicate that gestural difficulties are prevalent in schizophrenic patients, correlated with positive and negative symptoms, as well as cognitive deficits, motor abnormalities, and changes in brain structure, particularly in the praxis network (WALTHER et al., 2020).

There are correlations between brain architecture and gestural proficiency. The integrity and connectivity of the praxis network directly affect gestural performance, while

changes in neural activation during motor planning impair these behaviors in schizophrenic patients. Differences in resting state functional connectivity are also related to gestural performance, demonstrating disparities between patients and healthy individuals (WALTHER et al., 2020).

Additional neuroimaging studies point to reduced activation of the left inferior parietal lobe during imitative gestures in patients with schizophrenia. This alteration may be analogous to those observed in cases of apraxia associated with brain lesions. Neurostimulation techniques, such as repetitive transcranial magnetic stimulation, have shown potential in improving motor performance in patients, although combined studies are needed to better clarify the impact of this type of intervention (WALTHER et al., 2020).

Praxic deficits in schizophrenia are associated with a variety of factors, including cognitive alterations, motor impairments, and reduced hemispheric laterality. However, such factors do not fully explain the complexity of gestural deficits, requiring an integrated approach in the development of therapeutic strategies (WALTHER et al., 2020).

Catatonia, historically central to psychiatry, is now underestimated, despite its clinical relevance. Identifying its symptoms, often confused with intentional actions, is essential to understand its prevalence. Observed in various disorders, such as schizophrenia, mood disorders, and delusions, its evaluation still faces limitations with instruments such as BFCRS. Modifications in brain motor circuits, similar to those seen in Parkinson's, are frequent, as revealed by neuroimaging studies (WALTHER et al., 2019).

The DSM-V classifies catatonia as an independent psychomotor syndrome, which can vary between excited and delayed forms. The autoimmune subtype, associated with autoantibodies such as those directed to NMDA and GABAA receptors, offers new diagnostic and therapeutic horizons. Patients with catatonic schizophrenia often have GAD65 antibodies, which modulate GABAergic signaling. Immunotherapy has shown efficacy in the treatment of these manifestations, highlighting the relevance of biomarkers in diagnostic and therapeutic improvement (HANSEN et al., 2022).

Anhedonia, defined as the reduced ability to experience pleasure, is a central feature in schizophrenic spectrum disorders. A recent systematic review and meta-analysis quantified self-reported anhedonia in individuals with schizophrenia, comparing them to controls without psychiatric disorders. A total of 146 studies were analyzed, covering more than 13,000 participants. The findings revealed moderate to significant elevations in global anhedonia and in specific domains in this population, with marked effects on all measures investigated. Moderating factors, such as gender, education, intensity of negative symptoms, and pharmacological class of antipsychotics, were identified. Despite the

heterogeneity that exists in schizophrenia-related disorders, self-reported anhedonia remains a constant, underlining its clinical relevance and the need for further study to improve therapeutic interventions (KRZYZANOWSKI et al., 2022).

Auditory verbal hallucinations (HVAs) are predominant symptoms in psychotic disorders, characterized by the perception of voices in the absence of external sound stimuli. Neuroscientific research has identified brain changes underlying HVAs, including hyperexcitability of the auditory cortex and dysregulation in the attribution of internal speech to external sources, suggesting a possible corollary discharge dysfunction. In addition, the coexistence of HVAs and depressive symptoms in patients with schizophrenia is associated with structural changes in brain areas such as the parietal, frontal, and temporal lobes, evidenced by a reduction in white and gray matter volume. Anomalous connections between white matter and gray matter also contribute to the persistence of HVAs, affecting neural connectivity. Functional and structural abnormalities in regions such as the left prefrontal cortex and insula correlate with the severity of HVAs, signaling dysfunctions in neural networks linked to linguistic processing. These findings reflect the complexity of the mechanisms of schizophrenia, underscoring the importance of innovative therapeutic strategies (ROMEO et al., 2022; ZHUO et al., 2021; BARBER et al., 2021).

Very early-onset schizophrenia (VEOS), diagnosed before age 13, shares criteria with adult-onset schizophrenia (OSA) and early-onset schizophrenia (EOS). VEOS is rare and challenging to diagnose due to overlapping symptoms common to childhood and high comorbidity with neurodevelopmental disorders. Studies suggest that VEOS, although it has similarities with EOS and OSA, has identifiable clinical peculiarities. This condition, still little explored, lacks comprehensive epidemiological data. A review consolidated information on their clinical characteristics and comorbidities, promoting the development of individualized diagnoses and treatments (DI LUZIO et al., 2023).

Alterations in thinking and language in schizophrenia are characteristic of formal thought disorders (FTD), a multidimensional construct that involves impairments in cognition, communication, and linguistic processes. Characteristic linguistic phenomena, detected in the risk state, have predictive value in progression to psychosis. Systematic language assessment, combined with advanced analyses based on natural language processing, emerges as a crucial tool for early diagnosis, clinical differentiation, and monitoring of the degree of impairment (EHLEN et al., 2023; ADRAQUI et al., 2023).

On another level, factors such as oxidative stress, neuroinflammation, and NMDA receptor hypofunction contribute to socio-cognitive deficits in schizophrenia. Such processes can induce dysfunctions in neuronal microcircuits and compromise white matter

bundles that interconnect regions of the "social brain". Thus, investigative needs focused on both local microcircuits and large-scale neural networks emerge to decipher the factors that modulate impairment in social cognition (ADRAQUI et al., 2023).

Cognitive deficits, notably in attention, working and episodic memory, represent striking characteristics of schizophrenia, and are largely refractory to conventional treatment. Episodic memory, often the most impaired, reveals difficulties associated with semantic coding and retrieval. This process depends on the interaction between the medial temporal lobe and the frontotemporal systems. Alterations in the dorsolateral prefrontal cortex (DLPFC) are associated with these deficits, indicating it as a critical target for cognitive interventions (GUO et al., 2019).

Suprachiasmatic nucleus (SCN)-mediated disturbances in circadian rhythms affect sleep-wake cycles and are correlated with schizophrenia, and are often characterized by reduced slow-wave sleep and sleep spindles. Such changes reflect dysfunctions in thalamocortical circuits and can act as diagnostic markers (BOIKO et al., 2024; KASKIE et al., 2020).

Circadian rhythm dysfunction emerges as one of the distinctive aspects of schizophrenia, directly associated with the severity of clinical manifestations. Abnormalities in sleep patterns, such as reduced sleep spindle density and slow waves, correlate with cognitive deficits and clinical symptoms, indicating a pressing need for further investigation to elucidate these interconnections (FERRARELLI et al., 2021).

Schizophrenia, as a highly complex and disabling psychiatric condition, has a considerable prevalence globally, accompanied by multiple comorbidities, including abuse of chemical substances, including alcohol, and a marked reduction in life expectancy. However, detailed reviews of gastrointestinal and hepatic pathologies in this population are insufficient, a notable aggravating factor, especially in the context of the COVID-19 pandemic. It is imperative that gastroenterologists, hepatologists, and general practitioners improve their understanding of the specific risks involving schizophrenic patients by ensuring appropriate medical care. Chronic liver diseases, such as nonalcoholic fatty liver, have a higher incidence in individuals with schizophrenia compared to the general population. The adverse metabolic effects attributed to antipsychotics, such as excessive weight gain and dyslipidemia, are important predisposing factors for the development of these conditions. Managing these pathologies properly requires interdisciplinary cooperation, with a special focus on expanded support for patients, aiming at the integral promotion of their physical health and quality of life (GRANT et al., 2022).

Pain, a multifaceted phenomenon with both peripheral and central origins, exerts a significant influence on quality of life. In patients with schizophrenia, changes in pain thresholds are observed, attributed to excess dopaminergic activity in the mesolimbic system, which generates a paradox: while the threshold for acute pain tends to be high, the threshold for chronic pain is lower. Precise modulation of dopamine by antipsychotic agents emerges as a promising therapeutic strategy to normalize such thresholds, although in-depth investigations are needed to fully understand the impact of antipsychotics on pain management in this specific population (NAGAMINE et al., 2023).

Recent evidence reaffirms the multisystemic character of schizophrenia, transcending its traditional classification as an exclusively cerebral disorder. Among its primary manifestations, visual impairments have been highlighted, proving to be fundamental for the delineation of the clinical stage of the disease and, consequently, for the definition of appropriate therapeutic strategies. During the early stages of the condition, symptoms related to visual deterioration often emerge, contributing to the progressive worsening of other clinical manifestations and negatively impacting the quality of life of patients. The retina, considered an embryonic extension of the central nervous system, is possibly involved in the pathophysiology of visual impairments seen in schizophrenia. Ophthalmological investigations indicate that alterations in the initial components of the optic tract are a predominant feature in these patients (JURIŠIĆ et al., 2021).

In short, schizophrenia encompasses a wide spectrum of symptoms, including apraxia and visual deficits, whose etiology is associated with multiple factors, including cognitive changes, motor dysfunctions, and structural changes in the central nervous system. Continuous and in-depth advances in this area are crucial for improving the diagnosis and treatment of schizophrenia (JURIŠIĆ et al., 2021).

CONCLUSION

In summary, the investigations carried out elucidate the intricate relationship and systemic interconnection between different dimensions of psychotic disorders, such as schizophrenia and depression, highlighting the imperative of continuous efforts in the field of scientific research and interdisciplinary collaboration to foster significant advances in diagnostic methods and therapeutic interventions for these conditions. The identification of specific biomarkers, together with an in-depth analysis of the clinical characteristics of these disorders, is a crucial approach for the development of more targeted and effective interventions, with a view to optimizing the quality of life of affected patients.

In addition, collaborative integration between medical specialties emerges as an essential foundation to ensure care that contemplates both the physical and psychological well-being of patients. In parallel, the use of innovative technologies, such as artificial intelligence algorithms and machine learning models, presents itself as a promising resource for the early identification and development of personalized therapeutic approaches in schizophrenia.

Finally, progress in the understanding and management of this complex condition requires a multidimensional and integrative perspective, aimed at meeting the specificities of patients and promoting substantial improvements in their quality of life.

REFERENCES

1. Adraoui, F. W., & et al. (2023). Connecting neurobiological features with interregional dysconnectivity in social-cognitive impairments of schizophrenia. International Journal of Molecular Sciences, 24(9), Article 7680. https://doi.org/10.3390/ijms24097680

2. Ang, M. J., & et al. (2021). Behavioral tasks evaluating schizophrenia-like symptoms in animal models: A recent update. Current Neuropharmacology, 19(5), 641–664. https://doi.org/10.2174/1570159X18666200814171837

3. Barber, L., Reniers, R., & Upthegrove, R. (2021). A review of functional and structural neuroimaging studies to investigate the inner speech model of auditory verbal hallucinations in schizophrenia. Translational Psychiatry, 11(1), Article 582. https://doi.org/10.1038/s41398-021-01670-6

4. Boiko, D. I., & et al. (2024). Schizophrenia and disruption of circadian rhythms: An overview of genetic, metabolic and clinical signs. Schizophrenia Research, 264, 58–70. https://doi.org/10.1016/j.schres.2023.11.008

5. Di Luzio, M., & et al. (2023). Características clínicas e comorbidades na esquizofrenia de início muito precoce: Uma revisão sistemática. Frontiers in Psychiatry, 14, Article 1270799. https://doi.org/10.3389/fpsyt.2023.1270799

6. Ehlen, F., & et al. (2023). Linguistic findings in persons with schizophrenia—A review of the current literature. Frontiers in Psychology, 14, Article 1287706. https://doi.org/10.3389/fpsyg.2023.1287706

7. Ferrarelli, F. (2021). Sleep abnormalities in schizophrenia: State of the art and next steps. American Journal of Psychiatry, 178(9), 903–913. https://doi.org/10.1176/appi.ajp.2021.20070692

8. Gashkarimov, V., & et al. (2023). Técnicas de aprendizado de máquina no diagnóstico e previsão das características clínicas da esquizofrenia: Uma revisão narrativa. Consórcio Psiquiátrico, 4(3), 43–53. https://doi.org/10.54127/ZZHT8313

9. Grant, R. K., & et al. (2022). Gastrointestinal and liver disease in patients with schizophrenia: A narrative review. World Journal of Gastroenterology, 28(38), 5515–5529. https://doi.org/10.3748/wjg.v28.i38.5515

10. Guo, J. Y., Ragland, J. D., & Carter, C. S. (2019). Memory and cognition in schizophrenia. Molecular Psychiatry, 24(5), 633–642. https://doi.org/10.1038/s41380-018-0231-1

11. Hansen, N., & et al. (2022). Catatonic schizophrenia associated with cerebrospinal GAD65 autoantibodies: Case report and literature review. Frontiers in Immunology, 13, Article 829058. https://doi.org/10.3399/fimmu.2022.829058

12. Jurišić, D., & et al. (2020). New insights into schizophrenia: A look at the eye and related structures. Psychiatria Danubina, 32(1), 60–69.

13. Kaskie, R. E., & Ferrarelli, F. (2020). Sleep disturbances in schizophrenia: What we know, what still needs to be done. Current Opinion in Psychology, 34, 68–71. https://doi.org/10.1016/j.copsyc.2019.09.007

14. Khavari, B., & Cairns, M. J. (2020). Epigenomic dysregulation in schizophrenia: In search of disease etiology and biomarkers. Cells, 9(8), Article 1837. https://doi.org/10.3390/cells9081837

15. Kirkpatrick, B., Luther, L., & Strauss, G. P. (2023). Negative symptoms in the clinic: We treat what we can describe. The British Journal of Psychiatry, 223(1), 271–272. https://doi.org/10.1192/bjp.2023.76

16. Krzyzanowski, D. J., & et al. (2022). Trait anhedonia in schizophrenia: A systematic review and comparative meta-analysis. Schizophrenia Bulletin, 48(2), 335–346. https://doi.org/10.1093/schbul/sbab122

17. Lemmers-Jansen, I., Velthorst, E., & Fett, A.-K. (2023). The social cognitive and neural mechanisms that underlie social functioning in individuals with schizophrenia—A review. Translational Psychiatry, 13(1), Article 327. https://doi.org/10.1038/s41398-023-02615-x

18. Marder, S. R., & Umbricht, D. (2023). Negative symptoms in schizophrenia: Newly emerging measurements, pathways, and treatments. Schizophrenia Research, 258, 71–77. https://doi.org/10.1016/j.schres.2023.07.002

19. Nagamine, T. (2023). Pain threshold paradox in schizophrenia: A narrative review based on the latest neuroscience. Psychiatria Danubina, 35(2), 174–179. https://doi.org/10.24869/psyd.2023.174

20. Romeo, Z., & Spironelli, C. (2022). Hearing voices in the head: Two meta-analyses on structural correlates of auditory hallucinations in schizophrenia. NeuroImage: Clinical, 36, Article 103241. https://doi.org/10.1016/j.nicl.2022.103241

21. Sadock, B. J., Sadock, V. A., & Ruiz, P. (2016). Compêndio de psiquiatria (11th ed.). Artmed Editora.

22. Walther, S., & et al. (2019). Structure and neural mechanisms of catatonia. The Lancet Psychiatry, 6(7), 610–619. https://doi.org/10.1016/S2215-0366(19)30190-0

23. Walther, S., & et al. (2020). Gesture deficits and apraxia in schizophrenia. Cortex, 133, 65–75. https://doi.org/10.1016/j.cortex.2020.09.017

24. Wang, Z., & et al. (2022). The causal relationship between sleep traits and the risk of schizophrenia: A two-sample bidirectional Mendelian randomization study. BMC Psychiatry, 22(1), Article 399. https://doi.org/10.1186/s12888-022-04043-5

25. Zhang, Y., & et al. (2019). A review of autobiographical memory studies on patients with schizophrenia spectrum disorders. BMC Psychiatry, 19(1), Article 361. https://doi.org/10.1186/s12888-019-2341-7

26. Zhuo, C., & et al. (2021). Brain imaging features in schizophrenia with co-occurring auditory verbal hallucinations and depressive symptoms—Implication for novel therapeutic strategies to alleviate the reciprocal deterioration. Brain and Behavior, 11(2), Article e01991. https://doi.org/10.1002/brb3.1991