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Neuropsychiatric symptoms correlated with autoimmune diseases of the nervous system

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Abstract

Autoimmune diseases of the nervous system often cause neuropsychiatric symptoms, which can both herald the disease and indicate its exacerbation. This paper discusses autoimmune diseases of the nervous system in which neuropsychiatric symptoms occur particularly frequently or are especially severe, such as systemic lupus erythematosus, Chronic Inflammatory Demyelinating Polyneuropathy, multiple sclerosis, Hashimoto's encephalopathy, Guillain–Barré syndrome, paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections

(PANDAS), and myasthenia gravis, with particular emphasis on their neuropsychiatric symptoms. In systemic lupus erythematosus, neuropsychiatric symptoms affect 30–40% of patients and may include cognitive impairments, psychosis, headaches, mood disorders, and others. Hashimoto's encephalopathy is a rare but serious disease requiring rapid immunosuppressive intervention, manifesting with cognitive dysfunction, seizures, productive symptoms, mood changes, and more. Multiple sclerosis, in addition to the neurological symptoms typical for disease relapses, also causes symptoms such as fatigue affecting about 80% of patients, depression, anxiety, and cognitive dysfunctions. Myasthenia gravis, besides its typical symptoms, often also features neuropsychiatric symptoms such as chronic fatigue, anxiety, and sleep disorders. Neuropsychiatric symptoms of autoimmune diseases of the nervous system, particularly depression, cognitive impairments, anxiety, psychosis, but also others, significantly reduce patients quality of life, and early identification of these symptoms is crucial not only for improving quality of life but also often for enhancing patient prognosis and reducing neurological complications.

Keywords: multiple sclerosis, lupus erythematosus, autoimmune diseases, neuropsychiatric symptoms, Hashimoto’s encephalopathy

INTRODUCTION

Autoimmune diseases of the nervous system can lead to numerous neuropsychiatric symptoms that may appear before the full manifestation of the disease, heralding its onset, and whose active identification is important for maintaining the patient’s quality of life. The most common autoimmune diseases of the nervous system in which neuropsychiatric symptoms relatively often occur, and which are discussed in this paper, include lupus erythematosus, multiple sclerosis, Hashimoto’s encephalopathy, Guillain–Barré syndrome, paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS), chronic inflammatory demyelinating polyneuropathy, and myasthenia gravis. Among these, chronic inflammatory demyelinating polyneuropathy, Guillain–Barré syndrome, and myasthenia gravis are mainly peripheral disorders, while lupus, multiple sclerosis, Hashimoto’s encephalopathy, and PANDAS are considered central disorders. Autoimmune diseases of the nervous system with neuropsychiatric symptoms not discussed in this article due to space limitations and the desire to maintain clarity of content include central nervous system disorders such as neuromyelitis optica

spectrum disorder, myelin oligodendrocyte glycoprotein antibody-associated disease, stiff-person syndrome, autoimmune encephalitis, paraneoplastic syndromes. The latter may less commonly also involve the peripheral nervous system.

AUTOIMMUNE DISEASES OF THE NERVOUS SYSTEM: OVERVIEW

Autoimmune diseases, including those of the nervous system, result from an abnormal immune response in which the immune system attacks its own cells. The aetiology of these diseases is complex and involves, among other factors, genetic predispositions and triggering factors such as infections or tissue damage. Increasing evidence also points to a link between disturbances in the gut microbiota composition and the development of autoimmune diseases (Bhagavati, 2021).

These diseases lead to neuropsychiatric symptoms through multiple mechanisms – excessively activated immune cells can disrupt the blood–brain barrier (BBB), trigger an inflammatory response in the central nervous system, or even when the BBB is intact, autoantibodies and proinflammatory particles can activate microglia and induce inflammation (Fan et al., 2022). These mechanisms are often uncertain, and attempts to clarify them in relation to specific diseases are discussed further in this article. Neuropsychological symptoms frequently occurring in autoimmune diseases worsen patients quality of life, thus requiring heightened diagnostic vigilance and thorough knowledge of these symptoms.

Tab. 1

LUPUS ERYTHEMATOSUS

Systemic lupus erythematosus (SLE) is among the most common autoimmune diseases, diagnosed in approximately 3.4 million people worldwide, with around 90% being women. SLE is a complex disorder with a multifactorial aetiology, primarily driven by T cell-mediated activation of B lymphocytes, leading to immune complex deposition in tissues and an autoimmune response that can affect diverse organs (Siegel et al., 2024).

Although neurological and psychiatric symptoms typically present in more advanced stages of SLE, they can also manifest as initial symptoms. Overall, neuropsychiatric involvement is estimated to affect 30–40% of patients with SLE (Justiz-Vaillant et al., 2024; Sim et al., 2022). The pathophysiology of nervous system involvement is multifaceted and includes the presence of

autoantibodies that directly target neural tissue, such as anti-ribosomal P, anti-NR2, and brain cytoplasmic ribonucleic acid antibodies. These antibodies cross the BBB and may inflict direct neuronal damage. For example, anti-NR2 antibodies bind to NMDA receptors in the brain, initially activating these receptors but eventually leading to neuronal injury. Indirect mechanisms also contribute; complement components C3a and C5a exacerbate inflammation in affected neural tissue, antiphospholipid antibodies (aPL) increase risks of thrombosis and cerebral infarction, anti-endothelial cell antibodies (AECA) can damage vessel walls, and the BBB may be compromised by antibodies, inflammatory mediators, and neutrophils (Justiz-Vaillant et al., 2024; Sim et al., 2022).

The American College of Rheumatology has identified 19 neuropsychiatric syndromes related to SLE, with more manifestations frequently reported in recent literature. Central nervous system disorders related to SLE, as classified by the American College of Rheumatology, include aseptic meningitis, cerebrovascular disease, demyelinating syndromes, headaches (such as migraine and benign intracranial hypertension), movement disorders (e.g. chorea), myelopathy, seizure disorders, acute confusional states, anxiety disorders, cognitive dysfunction, mood disorders, and psychosis. Peripheral nervous system manifestations described by the American College of Rheumatology encompass acute inflammatory demyelinating polyradiculoneuropathy (Guillain–Barré syndrome), autonomic disorders, mononeuropathies (single or multiple), myasthenia gravis, cranial neuropathies, plexopathies, and polyneuropathies (American College of Rheumatology, 1999).

One of the most common central nervous system symptoms is headache, for which management aligns with that of primary headaches. Cerebrovascular disease is another frequent neurological manifestation of SLE. Due to the relatively high mortality associated with strokes, some studies suggest prophylactic low-dose aspirin use in patients at highest risk, particularly those with antiphospholipid antibody syndrome (APS).

Cognitive dysfunction is another commonly described central manifestation, generally mild in nature. However, there is currently no consensus regarding specific treatments for cognitive impairments in patients with SLE (Carrión-Barberà et al., 2021; Tektonidou et al., 2019). Depression and anxiety disorders are additional very common comorbidities in SLE, affecting approximately 28% and 37% of patients, respectively, with some studies suggesting that these conditions affect the majority of SLE patients. Depression appears to be most frequent in patients with more severe disease course and lower family income. Standard antidepressant treatments often prove ineffective; however, therapies with methotrexate and hydroxychloroquine have shown beneficial effects. Group psychological intervention programs have also demonstrated high efficacy

(Liao et al., 2022; Vicente-Escudero et al., 2024; Duca et al., 2024).

Psychosis, although less common, is an important neurological manifestation of SLE and often occurs early in the disease course. The most commonly prescribed treatments for this condition include glucocorticosteroids and immunosuppressive drugs, along with neuroleptics, anxiolytics, and antidepressants. SLE patients are also at risk of seizures, with aetiologies linked to the underlying disease varying among individuals. Seizures most frequently occur in children and are usually isolated tonic-clonic episodes. Long-term antiepileptic treatment is generally not required; however, if seizures are associated with disease flares and inflammatory activity, the use of glucocorticosteroids and immunosuppressants should be considered. Other possible neurological and psychiatric conditions related to SLE include peripheral neuropathy, acute confusional state, and autonomic disorders. Rare manifestations such as aseptic meningitis, demyelinating disease, myelopathy, cerebral venous sinus thrombosis, posterior reversible encephalopathy syndrome, isolated optic neuritis, progressive multifocal leukoencephalopathy, idiopathic intracranial hypertension, cranial neuropathy, inflammatory demyelinating polyradiculoneuropathy, mononeuritis, myasthenia gravis, and plexopathy have also been reported (Carrión-Barberà et al., 2021).

CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

Another autoimmune neurological disorder frequently associated with neuropsychiatric manifestations is chronic inflammatory demyelinating polyneuropathy (CIDP). The primary clinical features of this disease include muscle weakness and sensory disturbances resulting from demyelination, leading to slowed or even completely blocked nerve conduction. The pathogenesis is not fully understood, but immune-mediated mechanisms, particularly T-cell responses, as well as antibodies and the complement system, are thought to play a central role (Caballero-Ávila et al., 2025).

Regarding the neuropsychiatric consequences of this condition, depression is the most commonly reported, affecting on average 9–12.1% of patients, whereas cognitive function generally remains intact (Querol et al., 2021). However, some studies indicate a slowdown in the speed of performing cognitive tasks (Kozow et al., 2022) and deficits in executive functions (Lochmann et al., 2024). In addition, patients with CIDP frequently experience disrupted sleep (Englezou et al., 2023).

From a purely neurological perspective, these patients often present with tremor and short-

duration, high-amplitude myoclonus (Çetinkaya Tezer et al., 2022).

Furthermore, autonomic nervous system involvement is commonly observed in this disorder, affecting both sympathetic and parasympathetic functions; however, these disturbances are generally mild (Rzepiński et al., 2023).

HASHIMOTO'S ENCEPHALOPATHY (HE)

Thyroid hormones affect the functioning of almost all systems in the human body, including the nervous system. Already in the foetal period, they play a key role in the maturation of neurons, the formation of neural connections and the myelination of nerve fibres. They are also important in regulating mental health – their disorders are associated with the occurrence of neuropsychiatric conditions such as schizophrenia, bipolar disorder, anxiety and depression, as well as an increased risk of developing dementia. Thyroid hormone deficiency may be responsible for neurological deficits, including difficulties in cognitive function, visual processing, motor skills, language and memory (Baksi et al., 2021).

Hashimoto's thyroiditis is currently one of the most common autoimmune diseases. The systemic symptoms associated with this disease are mainly due to damage to the thyroid follicular cells, leading to the development of primary hypothyroidism. The diagnosis is based on clinical symptoms and positive serum antibodies against thyroid antigens: thyroid peroxidase (anti-TPO) and thyroglobulin (anti-Tg). An ultrasound examination may also be helpful, in which attention is drawn to the hypoechogenicity of the organ parenchyma, increased vascularisation, the presence of multiple and scattered micronodules ≤6 mm in size, and cytological examination with the presence of lymphocytic infiltration (Ralli et al., 2020; Klubo-Gwiezdzinska et al., 2022; Kapali et al., 2017).

The primary treatment is levothyroxine replacement therapy to restore normal hormone levels (fT3, fT4 and TSH). Currently, there is no effective treatment that can directly affect the malfunctioning of the immune system in people with Hashimoto's disease and stop the progression of the disease. However, there are scientific reports indicating that in patients with Hashimoto's autoimmune thyroiditis who remain euthyroid, the severity of somatic and mental symptoms is significantly greater than in the control group without thyroid disease. Symptoms related to neuropsychiatric disorders include memory impairment, anxiety, depressed mood, chronic fatigue, insomnia, irritability and apathy. This indicates the possibility of persistent autoimmunity despite normal thyroid hormone function. It has also been observed that higher levels of antibodies characteristic of Hashimoto's disease – anti-TPO and anti-Tg – were associated with a poorer

quality of life, with these individuals more often reporting low mood, memory problems and chronic fatigue. Anti-Tg antibodies in particular were associated with more severe depression, sleep problems and feelings of indifference (Li et al., 2024).

Hashimoto's encephalopathy (HE), also known as steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT), is a rare disease that can occur in adults, the elderly and children. It is estimated to affect approximately 2 people per 100,000. It is diagnosed much more frequently in women – up to 4 to 5 times more often than in men. The typical age at which the first symptoms appear is usually between 41 and 60 years of age (Mocellin et al., 2007; Ferracci et al., 2004).

HE is a poorly understood disease entity. The first case of this disease was described in 1966 in a 49-year-old man who experienced cognitive impairment, hallucinations and stroke-like symptoms. All these symptoms appeared about a year after he was diagnosed with hypothyroidism and started treatment, and they disappeared after he was given corticosteroids (Brain et al., 1966).

The clinical symptoms observed in patients with HE are varied. Two clinical subtypes have been identified: the first is associated with vasculitis, in which symptoms appear suddenly and resemble a stroke, with focal neurological symptoms such as transient hemiparesis, aphasia and ataxia; the second is associated with progressive cognitive decline, behavioural disorders and psychosis. Seizures, tremors, myoclonus, and stupor may occur in both types (Kothbauer-Margreiter et al., 1996).

The symptoms presented by patients with HE most often include disturbances in consciousness, cognitive function and behavioural changes. This can manifest itself in the form of confusion, memory problems, and even more serious conditions such as dementia, stupor or even coma (Dumrikarnlert et al., 2023; Fu et al., 2016).

Seizures occur in approximately 56–80% of patients with HE, and status epilepticus is reported in approximately 12% of cases. Focal and generalised tonic-clonic seizures, myoclonus and non-convulsive status epilepticus have been described (Guo et al., 2020; Aydin-Ozemir et al., 2006; Arya et al., 2013; Chaigne et al., 2013).

Symptoms resembling a stroke may occur, such as sudden paresis, speech disorders, and focal symptoms (Graham et al., 2016).

Neuropsychiatric symptoms are another group of disorders occurring in this condition and include psychosis, auditory and visual hallucinations, delusions, mood disorders, catatonia, anxiety and insomnia (Dumrikarnlert et al., 2023; Ortiz Arce et al., 2022; Hoffmann et al., 2007; Tsai et al., 2021; Monteiro et al., 2022).

Due to the fact that the above-mentioned symptoms may resemble other neuropsychiatric disorders (including rapidly progressive dementia in Creutzfeldt–Jakob disease (CJD), Alzheimer's disease, Lewy body dementia, frontotemporal dementia, corticobasal degeneration, autoimmune encephalitis, including anti-IgLON5 disease), they should be differentiated from these, and the diagnosis of HE should be considered in cases of a faster, less typical course and resistance to standard treatment (Chaudhuri et al., 2023).

Diagnosing HE is difficult because there is no specific test to confirm the disease, and diagnosis is usually based on ruling out all other potential central nervous system disorders. The criteria for diagnosing HE published by Graus et al. included the presence of: encephalopathy with seizures, myoclonus and hallucinations or stroke-like episodes, as well as thyroid disease (subclinical, mild or overt). The diagnostic criteria also took into account the brain magnetic resonance imaging (MRI) – normal or with non-specific changes, the presence of anti-thyroid antibodies in serum, the absence of other neuronal antibodies in serum or cerebrospinal fluid, and the exclusion of alternative causes of encephalopathy in the differential diagnosis (Graus et al., 2016).

Tab. 2

Given the good response of most patients to treatment with glucocorticosteroids, diagnosis is particularly important because early diagnosis and rapid initiation of immunosuppressive treatment are crucial for achieving complete or significant improvement and limiting permanent neurological complications (Dumrikarnlert, C. et al., 2023).

MULTIPLE SCLEROSIS

Multiple sclerosis (MS) is a complex autoimmune disease affecting central nervous system, presenting with inflammation, demyelination, gliosis, and neuronal loss. Initially, for the substantial majority of cases, progression of MS begins as a relapsing-remitting (RR) course, whereas for the remaining 10–15% of patients, the disease is primary progressive (PP). Ultimately, the majority of RRMS patients develop into a secondary progressive course of disease (SPMS). (Portaccio et al., 2024)

The clinical picture of MS differs between patients, encompassing numerous physical debilitations, including changes in sensation, mobility and vision, as well as cognitive symptoms, fatigue, pain, bladder and sexual dysfunctions (Portaccio et al., 2024; Haki et al., 2024; Maristany et al., 2024). These symptoms already significantly influence the patients overall quality of life.

Additionally, comorbidity is common with MS. Apart from frequent prevalent hypertension, hypercholesterolemia and chronic lung disease, over half of MS patients are affected by neuropsychiatric conditions (Margoni et al., 2023; Maristany et al., 2024).

Fatigue is one of the most common symptoms of MS, affecting nearly 80% of patients, which constitutes a four times higher prevalence rate than in the general adult population. It is the highest among neurological diseases (Maristany et al., 2024). In MS, two types of fatigue are distinguished. Primary fatigue is connected to the mechanisms of the disease and is without a known direct cause, whereas secondary fatigue is related to other disease symptoms and side effects of treatment (Yi et al., 2024). Studies indicate that fatigue might affect female patients more often. Furthermore, lower education levels, duration of MS or disability status are other contributing factors. Multidisciplinary non-pharmacological treatment combined with physical exercise and psychological interventions proves to be the most effective. Additionally, studies indicate that diets such as an anti-inflammatory or Mediterranean diet might be beneficial (Yi et al., 2024).

Nearly half of MS patients suffer from depression. The prevalence is up to five times higher than in the general population and exceeds that observed in other neurological disorders (Maristany et al., 2024). Depression is significantly related to fatigue and cognitive impairment, impacting attention span, memory and information processing, leading to poorer outcomes and almost 2 times higher risk for suicide than in the general population (Margoni et al., 2023; Maristany et al., 2024). Prevalence of depression culminates in the fifth and sixth decade of life. In terms of treatment, there are no differences in therapeutic protocols for MS depression compared to those for patients without (Margoni et al., 2023).

Anxiety disorders often co-occur with depression and can exacerbate each other in MS patients, consequently leading to more fatigue, increasing sleep problems and hence to overall reduced quality of life. Approximately one in three MS patients experiences anxiety at some point during their life (Margoni et al., 2023).

Cognitive impairments describe a group of symptoms and can range from deficits in information processing, memory, and learning to visuospatial processing dysfunctions, resulting in being a major cause of disability in MS (Margoni et al., 2023). As opposed to fatigue, studies have shown male patients have a higher risk for cognitive dysfunctions. Additionally, disability levels, MS duration, and older age are named as other risk factors. Higher education levels and cognitive reserve might potentially act as protection (Margoni et al., 2023; Maristany et al., 2024).

Fatigue, depression, anxiety, and cognitive impairments might be the most frequent neuropsychiatric symptoms of MS; however, others, for instance apathy, schizophrenia or bipolar

disorder are also not uncommon (Margoni et al., 2023; Sangster et al., 2024).

GUILLAIN–BARRÉ SYNDROME

Guillain–Barré syndrome (GBS) is one of the best-known specific set of symptoms of the nervous system. The pathophysiology of the disease involves polyneuropathy triggered by a previous infection, e.g. *Campylobacter jejuni*. Molecular mimicry should be considered the exact cause. Antibodies are produced against lipooligosaccharides present on the surface of bacteria, which then cross-react with glycosides on the nerve surface. The main symptoms of this disease are acute, rapidly progressing polyneuropathy with predominant weakness of the lower limbs, as well as deep tendon reflexes. Peripheral neuropathy with sensory disturbances, motor weakness, and diminished or absent reflexes with or without cranial nerve affection occur. In this disease, there is a noticeable increase in the risk of psychiatric disorders. Patients with a history of this disease are at increased risk of developing conditions such as depression, anxiety disorders and chronic fatigue (Bellanti et al., 2024).

Depression is one of the most common mental illnesses. A correlation has been observed between the occurrence of GBS and an increased incidence of depression in these patients. In a comparative study, clinically defined depression was 4.8 times more common in patients with GBS than in the control group, who did not have GBS (Tzeng et al., 2017).

It is also worth mentioning the correlation between the most severe form of GBS and the occurrence of depression. More specifically, the severity of depression is significantly correlated with anxiety disorders, which are themselves correlated with muscle weakness resulting from the clinical course of GBS. A study was conducted on a group of 20 GBS patients and a control group of 10 people. The Montgomery–Åsberg Depression Rating Scale (MADRS) was used for the assessment. As a result of this study, based on the MADRS scale performed on all patients, there is an increased risk of depression in GBS patients, and it was also noted that the severity of depression may be indirectly related to the underlying disease through anxiety disorders caused by muscle weakness. In this regard, it is also worth mentioning the follow-up examination after one month of immunotherapy. Despite significant clinical improvement in GBS-related disorders, there was no proportional improvement in depression (Bahnasy et al., 2018).

An extremely important issue affecting quality of life is chronic fatigue, which is one of the common disorders associated with GBS. Chronic fatigue is a very common symptom of GBS, even at the onset of the disease, where it is not as pronounced as in the later stages of the disorder. In the

acute phase of GBS, fatigue occurs due to the clinical course of the disease and the necessary increased energy expenditure of the patient. It also occurs due to rehabilitation, which is an essential part of the therapeutic process (De Vries et al., 2009). Various studies have shown different percentages of fatigue in GBS patients depending on the patient groups included in the studies. However, it should be noted that each of these studies shows a statistically significant relationship between the occurrence of GBS and subsequent chronic fatigue (Garssen et al., 2006).

Some analyses also show the negative impact of the lack of rehabilitation exercises during the acute phase of GBS, which has a subsequent effect on the severity of fatigue and negatively affects the psychophysical condition of patients. This is a kind of effect of the overlap of the clinical symptoms of the disease and subsequent psychophysical disorders (Bussmann et al., 2007).

PAEDIATRIC AUTOIMMUNE NEUROPSYCHIATRIC DISORDERS ASSOCIATED WITH STREPTOCOCCAL INFECTIONS

Increasingly recognized phenomena drawing growing interest include PANDAS (paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections) and paediatric acute neuropsychiatric syndrome (PANS).

PANDAS is a paediatric-onset syndrome linked to infection with group A β-haemolytic streptococcus (GAS). It primarily affects children between the ages of 5 and 12 years (Grandinetti et al., 2024). The syndrome is characterised by the sudden onset of obsessive-compulsive disorder (OCD) and/or motor tics, accompanied by neurological symptoms such as hyperactivity and choreiform movements. The disease course is episodic, with abrupt exacerbations (Swedo et al., 2012; Pallanti et al., 2023). PANS represents a broader diagnostic category encompassing all cases of acute onset neuropsychiatric symptoms of various aetiologies. Unlike PANDAS, PANS does not require a preceding streptococcal infection. PANS is defined by the sudden, dramatic onset and/or restriction of food intake, together with at least two other neuropsychiatric symptoms. Both PANDAS and PANS are diagnoses of exclusion, meaning symptoms cannot be better explained by other known neurological or autoimmune disorders such as Sydenham's chorea, SLE, or Tourette's syndrome (Swedo et al., 2012; Pallanti et al., 2023; Grandinetti et al., 2024).

Although the PANDAS syndrome was first described in 1998 (Swedo et al., 1998), it continues to generate considerable controversy, with the medical community approaching it cautiously and emphasising the need for further research.

The pathophysiology and epidemiology of PANDAS have not yet been fully elucidated;

however, substantial evidence suggests an autoimmune basis. This includes the presence of autoantibodies in blood and cerebrospinal fluid (CSF), their ability to activate neurons and dopaminergic pathways, associations with other autoimmune diseases, and improvement following immunomodulatory treatment (Chain et al., 2020). Additionally, family histories of individuals with PANDAS indicate an increased prevalence of autoimmune diseases among relatives, reported in approximately 80% of cases (Pallanti et al., 2023).

The clinical presentation of PANS/PANDAS, in addition to the characteristic sudden onset of OCD and/or tics, also includes other neuropsychiatric symptoms. The most frequently reported symptoms alongside OCD (89%) are anxiety (78%), particularly separation anxiety, and emotional lability (71%). Other commonly co-occurring symptoms include depression, severe oppositional behaviors, developmental regression (such as “childlike speech” or stuttering), academic decline, nocturnal enuresis, or increased urinary frequency (Grandinetti et al., 2024; Chain et al., 2020).

Cognitive deficits and difficulties with concentration have also been reported (Swedo et al., 2012). A study conducted at the USF Clinic in 2011 demonstrated reduced performance in Stroop tests, visuospatial memory, and motor speed (finger tapping) (Lewin et al., 2011).

Motor and sensory disturbances may occur in the form of a sudden increase in sensory sensitivity or intense seeking of stimuli. Occasionally, auditory or visual hallucinations can be present, as well as homicidal or suicidal thoughts. During exacerbations, motor and vocal tics (e.g. barking, jumping, compulsive touching) and drastic rituals emerge. Polysomnographic studies from 2025 indicate that over 80% of children with PANDAS fail to achieve full atonia during REM sleep, suggesting involvement of the basal ganglia. Neuroimaging studies have demonstrated significant structural brain changes in children with PANDAS, including enlargement of the caudate nucleus, striatum, and globus pallidus compared to healthy controls. Increased microglial activity in the basal ganglia during the acute phase of the disease has also been observed. Following immunomodulatory treatment, these abnormalities gradually normalized (Swedo et al., 2024).

MYASTHENIA GRAVIS

Myasthenia gravis (MG) (also known as pseudo-paralytic myasthenia or Erb-Goldflam disease) is a rare autoimmune disorder and the most common condition affecting neuromuscular junction transmission (Mishra et al., 2023; Beloor Suresh et al., 2025). The disease is caused by antibodies attacking acetylcholine receptors (AChR) located on the postsynaptic membrane of the neuromuscular junction, leading to receptor destruction, blockade, and impaired nerve conduction.

It may be triggered by infections, thymic abnormalities, stress, and certain medications (Mishra et al., 2023; Beloor Suresh et al., 2025). A characteristic initial symptom is weakness of the eye muscles (ptosis, diplopia), present in over half of patients at diagnosis (Hehir et al., 2022). Other common symptoms include muscle fatigue that worsens throughout the day and improves with rest, as well as bulbar symptoms (slurred speech, swallowing difficulties) affecting approximately 40% of patients. Additionally, typical signs include head drop related to neck muscle weakness. A dangerous symptom is respiratory muscle weakness, which can lead to a myasthenic crisis, a life-threatening condition requiring urgent intervention. It is estimated that such crises occur in 10–20% of patients with generalized MG at least once in their lifetime (Klaus et al., 2022).

This disease is accompanied by numerous neuropsychiatric symptoms that significantly reduce patients' quality of life.

Results from the international MyRealWorld-MG study ($N = 2,074$) indicate that patients with MG, compared to the general US population, experience more frequent, prolonged, and severe shortness of breath. One of the most burdensome symptoms was fatigue; 54.9% of individuals with MG suffered from chronic fatigue, markedly higher than in the general population (versus 6.8% in POPUP, $p < 0.0001$). The findings also highlight a significantly higher psychological burden in MG patients, particularly anxiety symptoms (69.6% of MG patients had moderate to severe anxiety versus 20.3% in controls). Sleep disturbances were also more common in MG patients (53.7% vs. 50.0%, statistically significant difference). All these symptoms were strongly interrelated and increased in severity with disease progression, underscoring the need for a holistic approach (Dewilde et al., 2024).

Changes also occur in brain function and structure. Neuroimaging studies from 2022 observed that patients with MG had significantly reduced gray matter volume in the cingulate gyrus, inferior parietal lobes, and splenium of the corpus callosum compared to the control group. MG patients also exhibited significantly higher serum levels of BDNF (Klaus et al., 2022).

Cognitive impairments frequently occur in the course of MG. Results from a 2022 meta-analysis show that patients with MG perform significantly worse than individuals without MG across a range of cognitive domains. Cognitive deficits were most pronounced in language, visuospatial functions, processing speed, immediate and delayed verbal memory, and response fluency (Hu et al., 2015).

This review confirms that MG is not merely a muscular disease but a multidimensional disorder.

CONCLUSIONS

Autoimmune diseases of the nervous system are complex conditions requiring an interdisciplinary approach, and patients often need care from neurologists, immunologists, psychologist and psychiatrists. The accompanying neurological and psychiatric symptoms frequently correlate with disease severity or may even precede it, providing an opportunity for earlier diagnosis before the most typical symptoms appear. Unfortunately, however, the presence of these symptoms can mislead the physician diagnosing a patient with such a condition. Moreover, thorough knowledge of neuropsychiatric symptoms is especially important because these symptoms significantly negatively impact patients quality of life, and many of them respond to treatment with psychiatric medications, immunomodulatory therapies, or other specific drugs.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organisations which might negatively affect the content of this publication and/or claim authorship rights to this publication

Author contribution

Original concept of study; collection, recording and/or compilation of data; analysis and interpretation of data; writing of manuscript; critical review of manuscript; final approval of manuscript: PRDS, RG, MZ, MG, WMS, MKG.

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Tab. 1. Summary of neuropsychiatric symptoms across the diseases discussed in the article

Disease	**Neuropsychiatric symptoms**
Lupus erythematosus	Headache; cerebrovascular disease (stroke, thrombosis); cognitive dysfunction; depression; anxiety disorders; psychosis; seizures; movement disorders; acute confusional states; peripheral neuropathy; autonomic disorders; mononeuropathies and polyneuropathies; Guillain–Barré syndrome; myasthenia gravis; cranial neuropathies and plexopathies
Chronic inflammatory demyelinating polyneuropathy	Muscle weakness, sensory disturbances; depression; cognitive slowing, executive deficits; tremor, brief high-amplitude myoclonus; disrupted sleep; mild autonomic dysfunction
Hashimoto's encephalopathy	Altered consciousness; cognitive impairment; seizures; myoclonus; ataxia; stroke-like symptoms; speech disturbances; psychosis; auditory/visual hallucinations; delusions; mood disturbances; insomnia; catatonia
Multiple sclerosis	Fatigue; depression; anxiety; cognitive impairments; apathy
Guillain–Barré syndrome	Depression; anxiety disorders; chronic fatigue
Paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections	Anxiety; emotional lability; depression and oppositional behaviors; developmental regression; cognitive deficits; sensory sensitivity or seeking behavior; motor/vocal tics during exacerbations; occasional auditory/visual

	hallucinations; homicidal or suicidal thoughts; sleep disturbances
Myasthenia gravis	Chronic fatigue; anxiety; sleep disturbances; cognitive impairments

Tab. 2. Diagnostic criteria of HE (Graus et al., 2016)

Category	**Requirement/criterion**
Encephalopathy	Altered consciousness, cognitive or behavioural dysfunction, often with seizures, myoclonus, hallucinations, or stroke-like episodes
Thyroid disease	Presence of thyroid disease (subclinical, overt, or previous)
Thyroid antibodies	Positive anti-TPO and/or anti-Tg antibodies in serum
Brain imaging (MRI)	Normal or nonspecific
Neuronal antibodies	Absence of other neuronal antibodies in serum or cerebrospinal fluid. Excludes autoimmune encephalopathies (e.g. anti-NMDAR, anti-LGI1, anti-IgLON5)
Exclusion of other causes	Exclusion of other possible causes of encephalopathy (metabolic, infectious, toxic, neoplastic, neurodegenerative)