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Review

Neuropsychological Diagnostics for Autoimmune Patients—Methodological Frame for Clinicians

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Abstract: Autoimmune syndromes are associated with changes in neuropsychological functioning. Neuropsychological functioning can be altered on cognitive, emotional, and behavioral levels. Understanding and recognizing neuropsychological functions and symptoms are essential for diagnostic procedures in autoimmune patients. These procedures require a solid theoretical foundation and suitable tools for both clinical and scientific settings. The availability of standardized neuropsychological diagnostic tests and batteries with good psychometric properties is the most effective tool for this purpose.

Keywords: autoimmunity; neuropsychological functions; neuropsychological diagnostics

1. Introduction

Long ago, health workers began questioning whether organic damage influences cognitive functions and personality. Psychiatrists and psychologists look for signs of cognitive dysfunctions, damage to executive functions, or personality changes to indicate damage to the central nervous system and/or functional disorders. It is well known that damage to the central nervous system influences behavior, but it is less well understood that damage to the immunological system also affects human behavior. Recent studies and future studies investigate how medical conditions affect human behavior, as well as how human behavior and experiences influence the functioning of the human body.

The immune system and the central nervous system have much more in common than we think. Their connection is bidirectional [1]. For instance, the immune system can improve neuronal survival and contribute to neuronal degeneration through neuroinflammation [2]. Beyond their pathological interactions, immune mediators also play a role in processes such as neuronal guidance, synaptic refinement and maintenance, as well as complex functions including learning, memory, and higher cognitive functions [2]. The immune system plays a crucial role in maintaining healthy neurocognitive function [1–3]. Contemporary literature highlights the immune system's involvement in psychiatric conditions such as schizophrenia, bipolar disorder, and depression. This emerging understanding highlights the immune system's crucial role in brain function and its potential influence on mental health [4–6].

On the other side, stress can significantly impact the immune system, affecting susceptibility to illness and overall health [7].

This manuscript aims to give a methodological framework for neuropsychological evaluation for autoimmune patients. A comprehensive neuropsychological evaluation is a collaborative effort involving psychologists and other professionals. The presented framework and recommended instruments are just one suggestion on how neuropsychological evaluation for autoimmune patients could be done. This manuscript should be considered as a screening review of practical recommendations.

2. Two Ways in Which Autoimmune Conditions Can Influence the Central Nervous System

Neuropsychological evaluations are conducted for a wide range of targeted populations, disorders, and states; the organization and methodology of the evaluation differ, so we need to establish the specific group being evaluated.

The foundation of every autoimmune condition lies in the presence of antibodies directed against the body's components, with neuroinflammation at its base. The spectrum of immune-mediated disorders is expanding as our understanding of diverse disease mechanisms increases. Antibody-mediated disorders of the central nervous system represent a distinct subgroup of immune-mediated neurologic disorders characterized by the presence of autoantibodies directed against specific neuronal or glial target antigens. These disorders are characterized by their expression in the central nervous system and exhibit distinctive MRI (Magnetic Resonance Imaging) characteristics [8]. The intracellular, cell-surface, or synaptic location of different autoantibody targets helps predict the clinical characteristics of the disorder. This subgroup includes encephalitis, myasthenic syndromes, cerebellar ataxias, and other conditions.

We need to differentiate letter subgroup from systemic autoimmune disorders and organ-specific autoimmune disorders with non-specific neuropsychological syndromes [8]. Psychoneurological manifestations in patients with systemic or organ-specific autoimmune/inflammatory disorders can be related to neural antibodies, but mostly, we have separate autoimmune disorders and conditions. This heterogeneous group includes Hashimoto's thyroiditis, Sjögren's Syndrome, Systemic Lupus Erythematosus, Rheumatoid Arthritis, Inflammatory Bowel Disease, Crohn's Disease, antiphospholipid syndrome, and many other syndromes, states, and disorders [8].

Three distinct subgroups of immune-mediated responses emerge, depending on the role of autoantibodies (Table 1).

Table 1. Division of the immune-mediated disorders due to autoantibodies [8].

1.	Autoantibodies target specific neuronal or glial antigens (neuronal autoantibodies) *Encephalitis, Ataxia, Parkinsonism*	Severe clinical syndromes involving multiple neurologic domains.
2.	Autoantibodies targeting neuromuscular structures *Myasthenia gravis*	Severe clinical syndromes involving multiple neurologic domains.
3.	Autoantibodies targeting different tissue antigens (Systemic Autoantibodies) *SLE, Sjogren, Hashimoto*	Mild to severe clinical syndromes with non-specific neuropsychological symptoms.

Neuropsychological diagnostics and its methodology for severe clinical syndromes involving damage to multiple neurologic domains are inherently more complex, which extends beyond the scope of this report. This report focuses on neuropsychological diagnostics for patients with systemic and organ-specific autoimmune disorders and suspected similar conditions (such as Irritable Bowel Syndrome or Ulcerative Colitis), where psychoneurological syndromes can be associated with systemic and organ-specific autoantibodies.

3. Neuropsychological Methodology and Diagnostic Procedures

Neuropsychology is a scientific discipline that examines the relationship between behavior and the functions of the central nervous system. Neuropsychological evaluation encompasses diagnostics, therapy, and research [9].

Behavior is a consequence of the activity of the central nervous system. This is observable and measurable in neuropsychological diagnostics. Neuropsychological diagnostics require standardized procedures and instruments to assess cognitive, social-emotional, adaptive, and academic functioning [10].

Neuropsychologists analyze all aspects of behavior related to cognitive, emotional, and executive functions using standardized procedures [9].

4. Neuropsychological Functions

Behavioral neuroanatomy of the cerebral cortex encompasses five distinct functional areas: primary sensorimotor areas, unimodal associative areas, heteromodal associative areas, paralimbic areas, and limbic areas. Heteromodal, paralimbic, and limbic areas connect regions in distributed and integrated multimodal representations of different functional systems [11]. These areas enable activities for regulating tone and states of alertness, as well as for receiving, processing, and storing information, and for programming, regulating, and controlling [9].

Human behavior has three components: cognition, emotionality, and executive functions. All three components are interwoven in every behavior, but we attempt to observe them separately during neuropsychological evaluations.

4.1. Cognitive Functions

Cognitive functions include receptive functions, memory and learning, thinking, and expressive functions.

Receptive functions include sensation and perception. Perception enables our ability to know our reality and integrates sensory information into psychologically meaningful data. Perception includes sensory data and cognitive structures that manage data processing. Sensations are experiences provoked by the direct action of physical and chemical processes on sensory organs, which inform the central nervous system, which registers, analyzes, codes, and integrates this information. Humans rarely experience sensations; sensory data are part of neurobehavioral systems that build on earlier knowledge [9].

Memory and learning have a central role in all human cognitive functions and are key subjects of observation and investigation. Memory is the ability to register, retain, and use information through experience or active learning. It encompasses attention, repetition, coding, finding, and recall. Memory is categorized into sensory, short-term, and long-term memory. It is evaluated through visual, auditory, and tactile modalities, using tasks that assess both short-term and long-term memory.

Sensory memory retains information for a very short period and can be divided into iconic and echoic memory. The psychological background of sensory memory is still unresolved.

Short-term memory retains information through repetition, and by directing attention, we encode and store this information. Wechsler tests include subtests specifically designed to evaluate short-term memory [12]. Short-term memory is also recognized as working memory, which is widely evaluated using various instruments as a critical measure of cognitive functioning. Within working memory, we retain and manipulate information from sensory and long-term memory through two systems: one for processing speech and the other for processing visual-spatial information [9].

Long-term memory, with its unlimited capacity for storage and processing of information, can be divided in multiple ways. For neuropsychological evaluation, the most significant division is between automatic memory and memory that requires deliberate effort. The latter involves organization, planning, and problem-solving, and is sensitive to stress and changes in bodily systems [4].

Thinking, as the most complex mental activity, encompasses all cognitive processes, including calculating, reasoning, judgment, concept creation, and abstraction. These processes should be evaluated as part of a neuropsychological evaluation in clinical settings. Problem-solving varies in complexity. It can be both abstract and concrete, encompassing executive functions [9].

Level of Awareness, Attention, and Activity Level

Variables of Mental Activities that are involved in all cognitive functions and behavior [9,13].

Awareness refers to the ability to recognize oneself and the environment. Activity level depends on the speed of motor and mental responses, which are evaluated using various diagnostic instruments [12]. The organization and efficiency of neural networks influence processing speed. Evaluating processing speed and reaction time is often prioritized, even before assessing memory.

Attention is directed psychological and psychomotor activity to specific content, the ability of selective perception, accentuation of important elements of psychological activity, and the process that controls and organizes the stream of psychological activity [9,13]. Evaluation of memory is incomplete and lacks validity without assessing attention (capacity for selective perception) and perception, because these functions are prerequisites for memory ability.

4.2. Emotionality and Personality

The American Psychological Association (APA) defines emotion as a complex reaction pattern, involving experiential, behavioral, and physiological elements, by which an individual attempts to deal with a personally significant matter or event [14].

Personality is the enduring configuration of characteristics and behavior that comprises an individual's unique adjustment to life, including major traits, interests, drives, values, self-concept, abilities, and emotional patterns [14].

Emotions and personality are complex psychological constructs that rely on cognitive and executive functions.

4.3. Executive Functions

This is a complex psychological construct that explains purposeful, adaptive, goal-oriented, problem-solving, and coping behavior in new and complex situations [15]. All cognitive activities involve executive functions, which can be understood as a broader concept encompassing various behaviors. Executive functions can be viewed as a supervisor, encompassing a higher level of cognition [15].

Luria [16] presents an integrative model of executive functions, in which regulative functions influence human behavior and facilitate goal-oriented behavior. These higher-order processes enable the synthesis of external stimuli, the formation of goals and strategies, readiness for action, and the verification of plans and actions. Based on this concept, a methodology for evaluating executive functions was developed.

Cognitions and emotions are intertwined and inseparable, so executive functions have a regulative and supervisory role over cognition, emotions, and behavior [15].

Miyake et al. [17] explain executive functions in terms of inhibition, working memory, and flexibility, with each component connecting cognitive and emotional functioning.

Executive functions are closely linked to overall personal functioning, expressive functions, learning ability, social relationships, work achievement, and many other aspects.

Expressive Functions

Expressive functions involve communication and activity, including speech and praxis (e.g., drawing, writing, facial expression, movements) [9]. The ability to communicate depends on reading skills, which are essential for verbal-symbolic communication.

5. Neuropsychological Diagnostics

When various neurological etiologies emerge, a more comprehensive assessment is needed [10]. Patients should be referred to a neuropsychological evaluation. Screening tests that are usually provided are primarily sensitive to severe impairment in quality of life or cognitive abilities. A more profound understanding and evaluation are needed.

Neuropsychological evaluations are comprehensive examinations comprising multiple components and involve more than the administration of a few tests [10].

Patients often experience impaired quality of life and report numerous symptoms that seem unrelated; however, when referred to neuropsychologists—healthcare providers with specialized training in the brain-behavior relationship who perform comprehensive evaluations in addition to providing certain forms of treatment [10]—their condition can be understood more clearly. They can be provided with information and adequate treatment.

During diagnostic procedures, psychologists need to assess neuropsychological functions, provide understanding, and differentiate psychiatric (the Term psychiatric refers to pathological effects; the term psychological refers to every possible effect) and neurological symptoms, being aware of neuropsychological symptoms that may have endocrinological, metabolic, or other origins. The task is to perform differential diagnostics to distinguish between various psychoneurological states and different localizations of damage within the central nervous system or other systems. Exclude psychiatric symptoms that form disorders from neuropsychological states probably provoked by other damages to organ systems, or are just consequences of trauma, loss provoked by life experiences, and/or impaired quality of life.

Psychologists should be part of a multidisciplinary team for diagnostic purposes. The aim of their work is not to establish a specific diagnosis. Results from the evaluations often reveal symptoms that sometimes form syndromes but rarely indicate disorders. The neuropsychological evaluation is tailored to meet the individual patient's needs, as in the case of an autoimmune patient.

5.1. Autoimmune Disorders and Neuropsychological Manifestations

Neuroinflammation is a critical component in autoimmune disorders, affecting the brain's structures and functions. Recent findings provide extensive data on changes in neuropsychological functions and symptoms that precede, emerge, and follow autoimmune disorders. Medical research and scientific studies on animal models have contributed to the understanding of the connection between neuroinflammation and neurocognitive functions [18,19].

To better understand the scope of this issue, it is crucial to recognize the prevalence of neuropsychological functional changes and symptoms in autoimmune patients. The literature contains a wide range of data on this topic.

5.1.1. Neuropsychological Symptoms in Different Autoimmune Conditions

One of the most fundamental human functions is the cognitive component of executive functions, including working memory, speed of information processing, efficiency of information processing, and flexibility. Literature is replete with data showing changes or deterioration of these functions in autoimmune patients [6,20–22].

Different cognitive abilities are highly sensitive to neuroinflammation and stress [6,22]. The organization and efficiency of neural networks influence processing speed. Processing speed and reaction time are highly sensitive to neuroinflammation and tend to deteriorate in autoimmune patients [6,22].

Emotional and Personality changes emerge because of direct damage to the central nervous system, as a secondary reaction to systemic changes in the body, or as a reaction to trauma and loss. Changes in emotions and personality can result from immunological factors, brain damage, or the traumatic impact of autoimmune disorders on patients. Fluctuations in emotional reactions (diminished or exaggerated) are frequently observed and can correlate with psychiatric symptoms that often emerge. Changes in emotional functioning are often the first sign of Central Nervous System disorder [9,23].

Systemic Lupus Erythematosus (SLE), an inflammatory autoimmune disorder that affects multiple organs, including the central nervous system, is often accompanied by neuropsychological changes. Cognitive dysfunction is present in up to 80% of patients, and depression affects up to 39% [20]. Headaches and mood changes are common, while seizures, cerebrovascular disease, and anxiety have a prevalence of up to 10%. Psychosis, peripheral neuropathy, and acute confusion states are present in up to 5% of cases and are frequently associated with corticosteroid use [20,23,24].

Hashimoto's chronic autoimmune thyroiditis frequently includes psycho-neurological disorders [21]. The term Hashimoto's Encephalopathy refers to a neuroendocrine syndrome that is steroid-responsive, with glucocorticoid therapy yielding positive outcomes [21]. Clinical symptoms of Hashimoto's Encephalopathy often mimic neurological and psychiatric disorders, with cognitive dysfunction appearing in 36 to 100% of cases.

Neuropsychiatric manifestations are linked to antiphospholipid syndrome, ischemic attacks, and strokes accompanied by identifiable brain lesions, cognitive dysfunctions (prevalence of 11 to 60.5%), as well as depressive and psychotic symptoms [25].

Patients with rheumatoid arthritis exhibit higher rates of depression, anxiety, and cognitive impairment compared to the general population [26].

Inflammatory bowel disease can be preceded by depression and anxiety, with psychiatric symptoms potentially serving as etiological factors in some cases. These symptoms may also emerge after the onset of the disorder [27,28].

5.1.2. Differentiation between Symptoms and Patients

The relationship between organic and functional disorder becomes crucial, as there is often no definitive evidence that symptoms have an organic cause, leading them to be incorrectly classified as functional or psychological. Disorders of the central nervous system, as well as autoimmune disorders, frequently begin with behavioral changes. Systemic Lupus Erythematosus (SLE) has the highest prevalence of neuropsychiatric symptoms, ranging from 20% to 70% [20]. When a patient experiences one or more neuropsychiatric conditions, it is classified as a disorder attributed to the subgroup of Neuropsychiatric Lupus [29]. In some cases, depression precedes lupus symptoms by up to 18 months [20], which does not necessarily imply that the patient has a major depressive disorder, though this misclassification often occurs. Neuropsychological evaluations are essential for differentiating between patients with autoimmune disorders presenting neuropsychological symptoms, patients with psychiatric disorders, patients with autoimmune disorders without neuropsychological manifestations, and patients with autoimmune disorders in comorbidity with psychiatric disorders. This differentiation is important for understanding the patient's condition and guiding appropriate treatment. All patients can be categorized into three overlapping groups based on these distinctions (Figure 1).

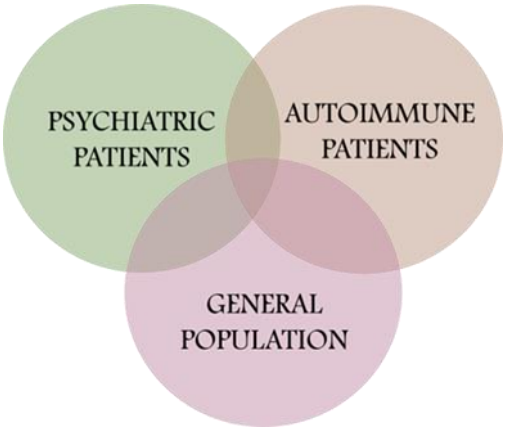

Figure 1. Overlapping of patient groups.

5.1.3. Implementing Neuropsychological Evaluation for Autoimmune Disorders

Neuropsychological diagnostics for autoimmune disorders should include standardized procedures, such as comprehensive batteries of diagnostic instruments, conducted by certified psychologists. These procedures should assess the neuropsychological functions of the central nervous system that are influenced by changes in immunological, endocrinological, and/or metabolic processes. Damage to a single neuropsychological function can cause multiple symptoms, while damage to multiple functions may result in a single symptom. Every symptom can have multiple causes. It is possible to distinguish between organic causes and those resulting from learned behavior, and in some cases, brain damage can be located. This includes evaluating a wide range of psychobiological, psychiatric, and neurological symptoms, with a focus on differentiating between them.

These assessments capture damage at a single point in time, underscoring the need for longitudinal investigations to gain a deeper understanding of this phenomenon. They capture consequences and give information about subtle changes in neuropsychological functioning. They never provide a final diagnosis, but valuable data to support it.

There are many differences between scientific investigations of the phenomena and the practical application of neuropsychological services to individual patients. The investigation of different neuropsychological functions and symptoms is extensive; however, variability in diagnostic instruments across studies limits the comparability of results [30,31]. Scientific and medical research require clear definitions of objectives and standardized, comparable diagnostic tests and batteries, as well as individual neuropsychological evaluations.

6. Diagnostic Instruments and Techniques in Neuropsychological Evaluation

Neuropsychological diagnostic procedures are provided by licensed psychologists specializing in the neuropsychological evaluation of autoimmune patients, in addition to the skills of clinical psychologists, who require expertise in the functions and pathology of the central nervous system, immune system, and endocrine system. Schaefer et al. [10] expect a clinical neuropsychologist to be a doctoral-level health care provider, but in practice, different countries and medical institutions have diverse rules and expectations, if any.

A comprehensive assessment by a neuropsychologist typically begins with a review of the medical record, including medical and psychiatric history, laboratory results, and neuroimaging reports, followed by a clinical interview that includes behavioral observations. Then, a wide range of neuropsychological instruments is administered. The procedure is done face-to-face in an outpatient clinic or a private office in a hospital. Everything can last up to ten hours [10], and the procedure is tailored to each patient's needs.

The clinical setting differs significantly from scientific research. Tests used to evaluate neuropsychological functions in clinical practice often differ from those employed in research studies [9,32]. Clearly defining the goals of neuropsychological evaluation, whether clinical or scientific, is essential, as these goals guide the selection of appropriate tests.

Diagnostic instruments for both clinical and scientific practice should be selected based on their psychometric properties, including validity, reliability, responsiveness, global availability, years of successful use, and the presence of adequate revisions.

Psychometric properties refer to the characteristics that assess the quality and effectiveness of psychological tests. Reliability is the extent to which test scores are accurate; a test is considered reliable only if it produces similar results across multiple testing instances, numerous test editions, or multiple raters grading the participant's

responses. The most commonly used statistical measure for reliability is Cronbach's alpha. Validity means that the information yielded by a test is appropriate, meaningful, and useful for decision making—the purpose of mental measurement [33]. Responsiveness refers to the ability of the test to detect changes in conditions, which is also considered an aspect of validity [34].

Tests must also be standardized for the target population. In clinical practice, many applicable procedures lack robust psychometric characteristics, yet skilled clinicians often rely on them when better alternatives are unavailable. Non-standardized procedures and techniques, such as projective methods, can also provide valuable insights. Clinicians need to pay attention and choose the best instruments from the available options.

The following are test methods and selection of instruments that meet the above-mentioned criteria. Listed instruments are used in practice and for scientific purposes. Exact properties of each instrument and battery, and their comparison, are not listed; it is beyond the scope of this manuscript.

7. Fixed and Flexible Testing

We have two approaches to testing: one involves specific tests selected by a clinician, and the other utilizes standardized batteries [9,15]. Schaefer et al. [10] differentiate flexible and fixed batteries. A flexible battery form means an approach that permits selection on a case-by-case basis.

Using comprehensive tests or batteries is often preferable, as they offer a more complete neuropsychological profile. Alternatively, multiple individual tests, each targeting a specific function, can be combined to achieve the same goal. At the same time, it is important to isolate individual tests from batteries to be used in scientific investigations, allowing researchers to focus on specific functions or symptoms of interest.

7.1. Fixed Testing

Batteries (fixed batteries) are complex tests to evaluate various functions. One of the oldest and most widely used is the Luria-Nebraska Battery [9,35]. It was developed based on the neuropsychological diagnostic procedures used by Aleksandar Romanovich Luria. This is a standardized battery of neuropsychological tests designed to provide information valuable for the diagnosis and treatment of brain damage and dysfunction [9,35]. The battery has two forms: Form 1 includes 11 subtests, while Form 2 includes 12 subtests. These subtests assess major functional domains, including motor, perceptual (auditory, tactile, visual), language (receptive speech, expressive speech), academic (reading, recognition, spelling, writing, arithmetic), memory, and intellectual functioning. Provides an objective scoring system and standardized procedures to Luria's flexible and qualitative approach [35,36]. Items are scored objectively and reliably and evaluated for systematic effectiveness across populations. It has high discriminative value in differentiating between healthy individuals and those with brain dysfunction [9,36].

The Halstead-Reitan Neuropsychological Test Battery (HRNB) is also recommended as a compilation of neuropsychological tests designed to evaluate the functioning of the brain and nervous system in individuals aged 15 years and older. It is effective in identifying impairment associated with head trauma, tumors, cerebrovascular accidents, infections, degenerative diseases, learning disabilities, and specific neurological disorders [10,37].

The Neuropsychological Assessment Battery [38] exemplifies a battery with similar properties as mentioned above.

In practice, clinicians are not strictly required to use the exact recommended tests; the choice of diagnostic instruments depends on their properties and the clinician's judgment. When a clinician chooses a battery, the procedure, timing, application rules, easy scoring, and explanation of the results are already well-organized. Comprehensive results that a clinician gains from battery testing still do not have any meaning for the state of the patient. The clinician's expert opinion is needed.

7.2. Flexible Testing

The clinician chooses standardized instruments, administers them in a standardized manner, and scores are interpreted by comparing them to an appropriate normative group. Tests and norms are selected based on the evaluation's goal, the patient's medical history, their current state, and data collected during the interview, also to match the patient's gender, age, education, and ethnicity.

Without a battery, a clinician must have a well-planned evaluation procedure in place. Typically encompasses three areas: cognitive, emotional (including personality), and executive functions. For every function, the best recommendation is to have two separate tests.

7.2.1. Complex Intelligence Tests

Neuropsychological diagnostics often includes tests that evaluate intelligence and conceptual thinking, as executive functions overlap with intelligence [39]. Many intelligence tests evaluate executive functions. Results on Intelligence tests are used as a neuropsychological measure [9].

The Stanford-Binet Test is the oldest intelligence test still in use and has its sixth version (SB6) today. This was the first modern intelligence test developed in France in 1905. It was standardized and revised in 1916. by Lewis Terman from Stanford University, and the Stanford-Binet Intelligence Scales were created. This standard measure of general and specific intellectual abilities is among the most frequently used intelligence instruments in neuropsychological evaluations. SB6 measures cognitive factors, including fluid reasoning, knowledge, quantitative reasoning, visual-spatial processing, and working memory [40].

Among the most widely used intelligence tests in clinical neuropsychological diagnostics are the Wechsler's scales [9]. The Wechsler-Bellevue scale for measuring intelligence was first introduced in 1939 [12] and has since undergone numerous revisions to its items, norms, and standardizations, adapting to the evolving needs of different countries and periods. Today, the Wechsler Adult Intelligence Scale (WAIS-V) [41] is available, along with textbooks for its neuropsychological application.

Wechsler scales not only assess intelligence as a global and complex construct, reflecting the ability to behave purposefully, reasonably, and efficiently, but also evaluate specific abilities within the five-factor model: Verbal Comprehension, Visual-Spatial Ability, Fluid Reasoning, Working Memory, and Processing Speed [12]. Results from each subscale and factor can be analyzed separately and applied independently in scientific studies, providing a detailed neuropsychological profile of the individual. The neuropsychological explanation of these results can be based on the Cattell-Horn-Carroll theory and Luria's neuropsychological view [12,41], offering valuable insights into neuropsychological functioning and symptoms.

In addition to Wechsler's scales, many other intelligence tests are available, each based on different theories and assessing different intellectual abilities, like Raven's Standard Progressive Matrix, and Mill Hill's dictionary scales, revised Beta Army Test, Kohs block design test, Wisconsin Sorting Card Test, and others [9]. These are chosen by their psychometric properties, longevity, and availability.

7.2.2. Memory and Learning Tests

A separate category consists of tests designed for memory evaluation, distinct from memory subtests included in neuropsychological batteries and intelligence scales. Among the most recognized are Wechsler's Memory Scales (WMS), which assess general information, orientation, mental control, short-term memory, logical memory, associative learning, and visual reproduction; the Rey Auditory Verbal Learning Test (RAVLT), which evaluates short- and long-term memory, verbal memory, the ability to learn new information, and learning strategies; and the Benton Visual Retention Test which is one of the most frequently used tests for visual memory, visual perception, and visuoconstructive abilities [9].

7.2.3. Visuoperceptive and Visuospatial Tests

Neuropsychological diagnostic instruments can be divided into specialized categories based on the functions they assess. One category comprises instruments for examining visuoperceptive, visuospatial, visuoconstructive, auditory, and tactile functions. One of the oldest and most widely used tests for assessing visuoperceptive and visuospatial constructive functions, as well as visual memory, is the Rey-Osterrieth Complex Figure Test (RCFT), which has been in use since 1941 [42]. Another well-known test is the Bender Visual-Motor Gestalt Test (Bender-Gestalt 2), which evaluates visual-motor perception and can differentiate between organic and functional disorders [43]. Certain executive functions can be assessed using Wechsler's scales for Visual Spatial Abilities [12,41].

7.2.4. Attention Tests

Attention and concentration are evaluated through subtests, including short-term memory of numbers, arithmetic tasks, coding tests, mental control tasks, and crossing-out tests, which are available as part of Wechsler's scales [9,12].

The Conners Continuous Performance Test Third Edition (Conners CPT 3) measures attention-related problems by indexing the respondent's performance in areas of inattentiveness, impulsivity, sustained attention, and vigilance. The Conners Continuous Auditory Test of Attention (Conners CATA) assesses auditory processing and attention-related problems, providing information about inattentiveness, impulsivity, and sustained attention, as well as auditory processing and mobility of attention [44].

7.2.5. Expressive Functions Tests

A separate category comprises tests for verbal functions, speech, reading, writing, and expressive functions (primarily focused on examining the consequences of aphasia). To name a few for English-speaking patients: Gary Oral Reading Test-fifth edition (GORT-5), Test of Written Language, fourth edition (TOWL-4), Test of Auditory Processing skills, fourth edition (TAPS-4).

7.2.6. Behavior and Executive Functions Tests

When assessing adaptive and maladaptive behavior and overall functioning in individuals, psychologists primarily use the Achenbach System of Empirically Based Assessment (ASEBA). ASEBA assesses competencies, strengths, adaptive functioning, and behavioral, emotional, and social problems throughout the lifespan [45]. It has been translated into 90 languages. It has multicultural norms. Research conducted on the ASEBA by scholars worldwide has yielded over 5500 published reports.

The Strengths and Difficulties Questionnaire (SDQ) is a questionnaire used to identify behavioral and emotional symptoms in children, adolescents, and young adults with neuropsychiatric disorders. It can be used as a screening questionnaire and in research projects. It is very easy to apply and shows good validity and responsiveness. Captures emotional and behavioral symptoms, detects changes in symptomatology, and identifies the transdiagnostic dimensions across disorders [46].

The Behavior Rating Inventory of Executive Functions-Adult (BRIEF-A) version is a valuable instrument for measuring interrelated higher-order cognitive abilities involved in self-regulatory functions that organize, direct, and manage cognitive activities, emotional responses, and overt behaviors [47].

In the above-mentioned instruments, collecting data relies on observing patients' behavior; significant others also provide data, as do the patients themselves.

7.2.7. Emotional and Personality Evaluation

The degree of change in a person's experiences and behaviors, particularly those related to emotional reactions and regulation, determines the consequences and reactions triggered by the onset of an autoimmune disorder, trauma, or any aberrant experience. The structure and dynamics of personality reflect the underlying mechanisms associated with specific disorders.

The most widely used personality inventory in clinical settings is the Minnesota Multiphasic Personality Inventory [48]. This inventory has undergone numerous structural and psychometric revisions to adapt to evolving social and psychological conditions. However, its extensive number of items and the inability to interpret or use subtests separately make it time-consuming and impractical for scientific research.

A more recommended alternative is Leslie Morey's Personality Assessment Inventory (PAI), which demonstrates good psychometric properties and allows separate application and interpretation of each subscale. Its construct validity and control scales provide clinicians with valuable information about invalid protocols, enabling them to oversee response patterns. The PAI's subscales cover most of the known psychiatric symptoms, personality distortions, quality of life, somatic symptoms, as well as treatment and thought processes. Each item within the subscales is carefully selected to address every component of the targeted clinical syndrome [49].

Projective techniques are widely used in clinical practice as valuable tools for the differential diagnosis of organic and psychotic disorders and symptoms. The projective Mosaic technique (PTM) was designed to diagnose a range of conditions, including neurosis, organic brain damage, psychotic states, and personality disorders. The interpretation of results relies on projective theories and the clinician's expertise [50].

Among the most widely used personality scales with strong psychometric properties, global usage, and longevity are Beck's scales, including the Beck's Depressive Inventory (BDI), Beck's Hopelessness Scale (BHS), and Beck's Anxiety Inventory (BAI) [51].

For evaluating anxiety as both a state and personality trait, Spielberger's scales (STAI) [52] are often used in clinical and scientific settings. Additionally, Hamilton's scale (HAM-A) is used [53].

7.2.8. Symptom Checklists

The Symptom Checklist-90 (SCL-90), designed to assess psychological problems and significant psychiatric symptoms, demonstrates satisfactory internal consistency and reliability. However, its discriminant validity has been criticized as problematic [54].

The Cornell index was developed as a comprehensive personality inventory designed to assess the entire medical state of the patient, encompassing all known psychological aspects of the medical disorder. However, the

Cornell Index was withdrawn from regular use due to a lack of adequate revisions [55]. Since then, a comprehensive inventory of psychobiological symptoms associated with various bodily systems has not been developed. While it remains possible to use this instrument, its outdated nature and problematic result interpretation limit its utility.

Symptom checklists such as the Multidimensional Fatigue Inventory (MFI) evaluate five dimensions of fatigue. However, they exhibit insufficient factorial validity, though their internal validity (reliability) has been deemed acceptable [56,57].

The Short Health Survey (SF-36), a widely used symptom checklist, measures global quality of life. It is frequently employed in scientific research, with various studies confirming its acceptability as a measure of both physical and mental health [58,59].

Pain questionnaires, such as the McGill Pain Questionnaire (MPQ), provide quantitative data that can be statistically analyzed. This instrument is sufficiently sensitive to detect differences among various pain relief methods [60,61].

Quality of life assessments help measure an individual's overall well-being, including physical health, psychological state, and social relationships. Quality of life questionnaires can be used as screening methods. The McGill Quality of Life Questionnaire (MQOL)—Expanded [62] or the World Health Organization Quality of Life Instrument [63] can provide valuable information to practitioners.

8. Instruments for Targeted Symptoms

Literature provides data on neuropsychological symptoms that are most likely to emerge in autoimmune patients. For the clinician, it is beneficial to connect specific symptoms with instruments that evaluate them (Table 2).

Table 2. Often mentioned symptoms by autoimmune patients and the instruments that tackle them.

Emerging symptoms	Instruments
Different health symptoms (headache, sweating, pain, etc.)	Cornell Index, MFI, SF-36, MQOL, MPQ, SOP (subscale PAI)
Fatigue	MFI, Cornell Index, SOP (subscale PAI)
Memory difficulties	WAIS-V (memory scales), WMS, RAVLT, SB6, BRIEF-A
Problems with the speed of processing information	WAIS-V (scales that address processing speed)
Experience of brain fog	WAIS-V, Conners CATA, Conners CPT, RCFT, BRIEF-A, MMPI, PAI, ASEBA, Cornell Index
Difficulties with concentration and focus of attention	WAIS-V (mental control tasks, crossing-out tests, and others), Conners CATA, Conners CPT 3, BRIEF-A
Depressive and anxious symptoms	MMPI, PAI, BDI, BAI, STAI, HAM-A, BRIEF-A, SCL-90
Experience that the body is changing in an unusual way, psychotic symptoms	MMPI, PAI, ASEBA, Cornell Index, PTM

9. Conclusions

Neuroinflammation plays a crucial role in autoimmune disorders, impacting the brain's structures and functions. Recent findings provide extensive data on changes in neuropsychological functions and symptoms that precede, emerge, and follow autoimmune disorders.

To better understand the scope of this issue, it is crucial to recognize the prevalence of neuropsychological functional changes and symptoms in autoimmune patients. The literature contains a wide range of data on this topic.

Clinicians using heteroanamnestic and autoanamnestic data are coming to the understanding that it is important to refer autoimmune patients to neuropsychological evaluation. Neuropsychological evaluation is a team effort, involving licensed psychologists.

Neuropsychological diagnostic procedures are time- and money-consuming efforts. However, they contribute to a better understanding of the connection between the central nervous system and human behavior, providing high-quality data. This data can improve patients' quality of life and influence the provision of the best treatment.

From neuropsychological diagnostics, it is not possible to conclusively determine the presence or absence of damage to the central nervous system or any other systemic damage. It does not provide a conclusive diagnosis.

Instead, these assessments indicate whether there are signs of dysfunction in the areas being tested. The focus should be on the sequelae of brain injuries or systemic changes, identifying and describing the strengths and weaknesses of the patient or targeted group.

Autoimmune patients can be provided with practical assessment tools that provide them with valuable data for improving their quality of life, facilitate adequate treatment, and aid researchers in investigating targeted phenomena.

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