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NEUROPSYCHOLOGICAL PRESENTATION OF WILSON'S DISEASE: DIAGNOSTIC AND COGNITIVE RECOVERY CHALLENGES FOLLOWING DELAYED DIAGNOSIS

PRESENTACIÓN NEUROPSICOLÓGICA DE LA ENFERMEDAD DE WILSON: DESAFÍOS DIAGNÓSTICOS Y DE RECUPERACIÓN COGNITIVA TRAS UN DIAGNÓSTICO TARDÍO

APRESENTAÇÃO NEUROPSICOLÓGICA DA DOENÇA DE WILSON: DESAFIOS DIAGNÓSTICOS E DA RECUPERAÇÃO COGNITIVA APÓS UM DIAGNÓSTICO TARDIO

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Palabras clave: *enfermedad de Wilson; síntomas neuropsiquiátricos; signos extrapiramidales; síndrome disejecutivo; rehabilitación cognitiva.*

Palavras-chave: doença de Wilson; sintomas neuropsiquiátricos; sinais extrapiramidais; síndrome disexecutivo; reabilitação cognitiva.

A B S T R A C T

Wilson's disease (WD) is a rare but managable genetic disorder of copper metabolism often overlooked or misdiagnosed due to its diverse clinical presentation. This case report describes the clinical course of a young adult patient whose initial symptoms were diverse, leading to a delay in establishing the accurate diagnosis of WD. Psychiatric symptoms such as mood changes and impulsivity appeared alongside neurological signs, including tremor, micrographia, speech disturbances, and dystonia. Due to the initial psychiatric interpretation of the symptoms, essential neurological and metabolic examinations were performed with a two-year delay. Following diagnosis and copper chelation therapy, the patient underwent a two-month structured cognitive rehabilitation program. Neuropsychological evaluations were conducted pre- and post-intervention using a comprehensive battery. Post-rehabilitation results showed a significant recovery in verbal memory, though executive deficits persisted. This paper highlights the importance of early recognition of neuropsychiatric symptoms of WD and the necessity of an interdisciplinary approach in the diagnosis of rare conditions that may initially present with nonspecific psychiatric and neurological symptoms. The analysis of the disease progression and the subsequent neurological and cognitive rehabilitation emphasizes the importance of timely treatment in preventing irreversible consequences.

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R E S U M E N

La enfermedad de Wilson (EW) es un trastorno genético poco frecuente pero tratable del metabolismo del cobre, que a menudo se pasa por alto o se diagnostica erróneamente debido a su presentación clínica diversa. Este reporte de caso describe la evolución clínica de una paciente adulta joven cuyos síntomas iniciales fueron heterogéneos, lo que condujo a un retraso en el establecimiento del diagnóstico correcto de la EW. Los síntomas psiquiátricos, como cambios del estado de ánimo e impulsividad, aparecieron junto con signos neurológicos, incluidos temblor, micrografía, alteraciones del habla y distonía. Debido a la interpretación inicial de los síntomas como psiquiátricos, las exploraciones neurológicas y metabólicas esenciales se realizaron con un retraso de dos años. Tras el diagnóstico y el inicio de la terapia quelante del cobre, la paciente participó en un programa estructurado de rehabilitación cognitiva de dos meses. Se llevaron a cabo evaluaciones neuropsicológicas antes y después de la intervención utilizando una batería completa. Los resultados posteriores a la rehabilitación mostraron una recuperación significativa de la memoria verbal, aunque persistieron los déficits ejecutivos. Este trabajo destaca la importancia del reconocimiento temprano de los síntomas neuropsiquiátricos de la EW y la necesidad de un enfoque interdisciplinario en el diagnóstico de enfermedades raras que pueden presentarse inicialmente con síntomas psiquiátricos y neurológicos inespecíficos. El análisis de la progresión de la enfermedad y de la posterior rehabilitación neurológica y cognitiva subraya la importancia del tratamiento oportuno para prevenir consecuencias irreversibles.

R E S U M O

A doença de Wilson (DW) é uma doença genética rara, mas tratável, do metabolismo do cobre, frequentemente negligenciada ou mal diagnosticada devido à sua apresentação clínica diversa. Este relato de caso descreve a evolução clínica de uma paciente adulta jovem cujos sintomas iniciais foram heterogéneos, conduzindo a um atraso no estabelecimento do diagnóstico correto da DW. Sintomas psiquiátricos, como alterações do humor e impulsividade, surgiram em conjunto com sinais neurológicos, incluindo tremor, micrografia, alterações da fala e distonia. Devido à interpretação inicial dos sintomas como de origem psiquiátrica, exames neurológicos e metabólicos essenciais só foram realizados após um atraso de dois anos. Após o diagnóstico e o início da terapêutica quelante do cobre, a paciente participou num programa estruturado de reabilitação cognitiva com duração de dois meses. As avaliações neuropsicológicas foram realizadas antes e após a intervenção, utilizando uma bateria abrangente. Os resultados pós-reabilitação evidenciaram uma recuperação significativa da memória verbal, embora persistissem défices executivos. Este trabalho salienta a importância do reconhecimento precoce dos sintomas neuropsiquiátricos da DW e a necessidade de uma abordagem interdisciplinar no diagnóstico de doenças raras que podem inicialmente manifestar-se com sintomas psiquiátricos e neurológicos inespecíficos. A análise da progressão da doença e da subsequente reabilitação neurológica e cognitiva destaca a importância do tratamento atempado na prevenção de consequências irreversíveis.

Wilson's disease (WD) is a rare autosomal recessive genetic disorder of copper metabolism (Garanaja et al., 2025). It is caused by a mutation in the ATP7B gene, which disrupts the excretion of copper into bile and its incorporation into ceruloplasmin. As a result, toxic accumulation of copper occurs in the liver, blood and other organs, most often in the brain, eyes, kidneys and heart (Chanpong and Dhawan, 2022). The disease was first described by S.A.K. Wilson, who identified its key features as its hereditary nature, the simultaneous occurrence of liver cirrhosis and neurological defects and the predominantly extrapyramidal nature of the symptoms (Bandmann et al., 2015).

The disease usually presents in two main clinical forms, hepatic and neurological, though psychiatric symptoms also occur (Ala et al., 2007; Gromadzka et al., 2024). Understanding these forms is essential, as the condition is very rare in the general population (1 in 30:000 – 50:000) and highly diverse in clinical presentation, which is why it is often overlooked or misdiagnosed (Ala et al., 2007). Poujois and Woimant (2019) found that diagnostic errors occured in 62.5% of referring physicians from various medical fields. Timely confirmation of diagnosis, prompt initiation of treatment and genetic screening of family members are essential (Poujois & Woimant, 2019), as WD, though progressive and potentially fatal without treatment, is manageable when diagnosed early and treated appropriately (Garanaja et al., 2025).

In most cases, the disease initially presents with hepatic symptoms. These can vary widely, ranging from asymptomatic laboratory abnormalities to acute hepatitis, acute liver failure, chronic hepatitis and cirrhosis (Więcek and Paprocka, 2024). Most common non-hepatic presentations are the appearance of Kayser-Fleischer rings in the cornea and brain

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damage (Poujois and Woimant, 2019). Most patients with the neurological involvement do also have liver disease, however it is often asymptomatic (Poujois and Woimant, 2019).

Neurological symptoms represent the second most common form of the disease and are the initial presentation in 40–50% of cases (Ala et al., 2007). Patients who initially present with neurological or psychiatric symptoms are usually older than those with hepatic onset (Ala et al., 2007). Typically, hepatic symptoms develop in the first or second decade of life, whereas neurological or psychiatric symptoms more often appear in the second or third (Schilsky, 2017). In cases of neurological presenation, the time between symptom onset and diagnosis is usually significantly longer – ranging from 2.5 to 6 years. The neurological manifestations of WD are extremely diverse, depending on the site of copper accumulation. Moreover, patients often have multiple co-occuring symptoms, each with a different degree of severity. These symptoms can develop gradually or appear suddenly, with their intensity often fluctuating, sometimes even within the same day (Więcek and Paprocka, 2024). Subtle early signs, such as behavioral changes, decline in academic performance or problems with hand-eye coordination, often accompanied by deterioration in handwriting and micrographia, may precede typical motor neurological symptoms (Ala et al., 2007).

The neurological form of the disease, which is described in more detail below, includes motor disorders, psychiatric disorders and cognitive impairment (Fernando et al., 2020).

Neurological Symptoms

The characteristic neurological presentation often begins with tremor, which progresses to gait instability, speech difficulties (dysarthria) and Parkinsonian-like symptoms (Schilsky, 2017). Other common symptoms include dystonia, which is characterized by facial grimacing, open jaw, excessive salivation and lip retraction (EASL, 2012). Additional Parkinsonian symptoms in WD include a dragging gait, impaired fine moto control of the hands, foot tapping, hypomimia and a characteristic dystonic smile. Epileptic seizures may occur at any stage of the disease (Bandmann et al., 2015). Without treatment, patients may become immobile due to worsening motor control or progressive dystonia, typically remaining conscious but unable to speak (EASL, 2012).

Psychiatric Symptoms

The classical psychiatric presentation of WD is well-documented in the literature, particularly among young adults. Psychiatric symptoms, alongside hepatic and neurological symptoms, are among the most common clinical features of WD. They occur in approximately 66% of patients; about 37% experience a major depressive episode and 20% seek psychiatric evaluation even before the diagnosis is made (Gromadzka et al., 2024). Despite their high prevalence, these symptoms present a significant diagnostic challenge, as the presence of psychiatric symptoms in the absence of overt neurological or hepatic signs can lead to signidicant delays or misdiagnosis (Gromadzka et al., 2024). Since psychiatric symptoms are highly variable and often precede neurological ones (Garanaja et al., 2025), diagnostic errors are common (Poujois & Woimant, 2019).

Psychiatric symptoms in WD span multiple domains. The most frequently reported include mood disorders such as depression (with or without suicidality), bipolar disorder, and anxiety (Gromadzka et al., 2024). Behavioral and personality changes are also common, including disinhibition, restlessness, irritability, antisocial behavior, emotional lability, gullibility, childishness and inappropriate laughter (Ala et al., 2007). Psychosis with delusions, hallucinations or other schizophrenia-like symptoms are less common, though possible. Other psychiatric manifestations may include eating disorders and sleep disturbances. In the advanced stages of the disease, altered states of consciousness may emerge (Gromadzka et al., 2024; Ala et al., 2007).

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Cognitive Symptoms

Cognitive impairment in WD varies in severity and depends on the presence of neurological symptoms. In neurologically symptomatic and untreated patients with progressive disease, cognitive impairment is often global (Bandmann et al., 2015). In treated patients, the most commonly affected area is psychomotor speed, with additional attentional issues such as reduced attention span and challenges with divided attention (Frota et al., 2009). Memory impairments are most pronounced in the encoding phase, while retrieval tends to remain relatively intact, suggesting a deficit in initial processing of information (Hegde et al., 2010). Similarly, Portala et al. (2001) reported that short-term memory is often weakened, while long-term memory abilities are preserved. Regarding executive functions, an impulsive cognitive style and increased number of perseverative responses are commonly observed, along with reduced cognitive flexibility. In verbal fluency tasks, studies have shown a significant disparity between phonemic and semantic fluency, with semantic fluency usually preserved, whereas phonemic fluency is notably impaired. Additionally, patients often perform poorly on tasks requiring grammatical reasoning, even though their vocabulary remains intact (Hegde et al., 2010; Frota et al., 2009). This cognitive profile is consistent with dysfunction of the frontal-subcortical neuronal circuits (Frota et al., 2009).

In neurologically asymptomatic patients, cognitive deficits tend to be minimal or absent. When present, they may include mild slowing of thought and motor speed, as well as subtle impairments in higher-order cognitive functions such as planning, reasoning, and memory (Hegde et al., 2010).

Diagnosis

Due to its clinical variability, the diagnosis of WD requires a multifaceted approach. Given its genetic nature, the first step often involves obtaining family history to identify potential cases of WD in the family, early deaths due to liver disease or early onset of neurological or psychiatric problems. This is followed by screening for hepatic and neurological signs, which includes liver function tests, specific copper metabolism tests, genetic testing, ophthalmological examination, and magnetic resonance imaging of the brain (Schilsky et al., 2023; Garanaja et al., 2025).

The primary genetic marker for WD is a mutation in the ATP7B gene. Diagnosis is further supported by laboratory findings such as low serum ceruloplasmin, reduced total serum copper, elevated liver transaminases, aminoaciduria, and hemolytic anemia. One of the most basic yet reliable diagnostic tools is the 24-hour urinary copper excretion test, which is a straightforward but critical indicator of pathological copper accumulation in the body (Bandmann et al., 2015; Schilsky, 2017).

Because hepatic symptoms may not always be apparent, clinicians must also focus on other indicators. In ophthalmology, the presence of Kayser–Fleischer rings, caused by copper deposition in the corneal membrane, is a significant diagnostic indicator, found in 95% of patients presenting with neurological symptoms (EASL, 2012; Poujois & Woimant, 2019). To evaluate nervous system involvement, a comprehensive neurological examination is essential (Garanaja et al., 2025). Nearly all patients with a neurological presentation of WD exhibit characteristic changes on brain MRI. Long-term exposure to high amounts of copper leads to structural brain damage, including extensive lesions and demyelination in the basal ganglia, thalamus, midbrain, pons, and brainstem, resulting in diffuse white matter degeneration (Fernando et al., 2020; Ala et al., 2007; Poujois & Woimant, 2019). In addition, cortical damage may occur, such as increased numbe of astrocytes in the gray matter (Ala et al., 2007) and cortical atrophy (Garanaja et al., 2025).

Given the possibility of a purely neurological presentation, clinicians should suspect WD whenever MRI abnormalities and Kayser–Fleischer rings are present, even in the absence of hepatic symptoms (Schilsky, 2017).

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Treatment

Once the diagnosis is made, treatment should begin immediately. Management generally involves two phases. The first involves acute removal of excess copper from the body using copper chelators, while the second is a lifelong maintenance, aimed at perseving copper homeostasis (Brandmann et al., 2015).

Additionally, treatment includes management of neurological and psychiatric symptoms (Schilsky, 2017). Improvement of liver function often leads to reduction of neurological and psychiatric symptoms, since copper removal reduces its toxic effects on neurons (Gromadzka et al., 2024). MRI studies have shown that brain lesions can resolve with successful treatment (Bandmann et al., 2015). Approximately one third of patients with psychiatric symptoms show improvement with copper chelation therapy alone (Schilsky et al., 2023). Althoug there is no specific treatment for cognitive impairment in WD, neuropsychological rehabilitation can serve as a helpful supportive measure (Gromadzka et al., 2024).

While the neurological signs of WD are well-documented, there is a scarcity of case reports detailing the recovery of specific cognitive domains following structured rehabilitation. This paper addresses that gap . In the following section, we present a clinical case illustrating the complexity of the diagnostic process in the neuropsychiatric form of Wilson's disease.

CLINICAL CASE

In April 2025, a 23-year-old civil engineering student was admited for rehabilitation following a confirmed diagnosis of Wilson's disease diagnosis with predominant neurological involvement. Medical history was obtained through patient and family interviews, as well as review of previous medical records.

Her difficulties began in November 2022 with a hand tremor and progressively smaller, distorted handwriting. In the following months, she developed leg tremors, drooling and speech difficulties, characterized by slurred articulation and impaired prosody (e.g. rising intonation at the end of sentences). She was previously healthy, with no neurological or psychiatric history. During this period, she enrolled in psychological counseling, which she described as helpful. She consulted a neurologist, who diagnosed unspecified anxiety. No in-depth neurological work-up (e.g. MRI) was performed. She was prescribed escitalopramx, which she soon abandoned, as she did not perceive it as necessary. She was subsequently referred for psychiatric evaluation.

At the psychiatric evaluation, the referral cited functional neurological symptoms and anxiety. During the assesment, she reported that her issues had been ongoing for approximately a year, with significant worsening in recent months. Her primary concern was her inability to write legibly under stress, which was negatively impacting her academic performance. She reported that she had successfully completed the first two years of her studies without difficulty, but had recently begun to fail exams, increasing her distress. In terms of her mental state, she was alert, oriented, displayed coherent speech with mildly accelerated verbal output, which clinitians attributed to anxiety. Her thought processes were organized and she described herself as emotionally sensitive and reactive. Her mood was not assessed as depressive and she denied any suicidal ideation. However, clinitians noted emotional lability and pronounced anxiety, along with somatic symptoms (tremor, hand cramps while writing) which were assessed as functional in origin. The prescribed escitalopram was deemed appropriate and a trial of at least 6–8 weeks was advised before assessing efficacy. Regular psychiatric follow-up and continued psychological counseling were advised.

Over the course of the year, her symptoms gradually worsened, particularly regarding fine motor skills of the hands, tremors, occasional spasms and falls. By May 2024, she reported fatigue, social withdrawal and excessive worriying.

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Around the same time, she began experiencing blurred vision. Reflecting on this period, she described feeling "intoxicated by copper"—dizzy, excessively sleepy and generally unwell. The presence of unexplained symptoms and associated distress led her to thoughts of self-harm.

In response, she sought help at an emergency psychiatric clinic and was subsequntly admitted to a secure ward. According to the admission records, she was referred due to suspected psychotic decompensation following interrupted self-harming behavior. On admission, she appeared confused, responded with latency and exhibited an incongruent smile, raising concerns about possible psychotic processes. Clinitians noted behavioral regression and conversion symptoms. However, during hospitalization, psychotic symptoms were ruled out. Her mood was assessed as mildly depressed, but without a depressive episode; the predominant presentation was anxiety, seen as a result of exceeded adaptive capabilities. Although she reported a range of neurological symptoms, these were considered clinically inconsistent and neurological examination did not detect deviations in her status. She was started on aripiprazole and sertraline, both of which were well tolerated. After initiating treatment, her anxiety gradually subsided and behavior improved. During hospitalization, she repeatedly denied suicidal ideation or intent. In retrospect, she attributed the events leading to her hospitalization to academic stress. A clinical psychological evaluation confirmed a profile of high achievement orientation, behavioral withdrawal and regressive and dissociative mechanisms in response to psychological strain. After admission, she revoked consent for hospitalization and was discharged with legal assistance one week later. She later described feeling frightened, out of place and misunderstood during the hospitalisation. She reported that others seemed to doubt the reality of her physical symptoms, which she found particularly distressing given her significant speech difficulties at the time. She herself felt confused, as she had not yet received a diagnosis. She recalled simply wanting to feel better. Upon discharge, clinitians noted significant clinical improvement; she was described as lucid, oriented, organized, without delusions or acute risk. Her discharge diagnoses included adjustment disorder, mixed dissociative (conversion) disorder, suicidal ideation (transient, upon admission), problems related to upbringing and education and excessive parental protection. Laboratory tests (hematology, biochemistry, immunology) upon hospitalization were within normal limits.

Following discharge, her health condition continued to fluctuate, with alternating periods of improvement and deterioration, though her functionality steadily declined. In July 2024, a brain MRI revealed atrophic changed, though no clear etilogy was found. She began experiencing increasing difficulty with walking, balance and coordination. Basic daily tasks such as showering or dressing independently became challenging. She slept more, felt fatigued and her mood remained low. Her gait became increasingly slow and unsteady, with further deterioration of fine motor skills. Speech issues worsened with the appearance of echolalia.

In January 2025, while visiting family abroad, she experienced multiple epileptic seizures and was urgently hospitalized. Upon admission, clinitians noted a tightened right corner of her mouth, she was unable to speak or swallow. She communicated solely by squeezing their hands. A series of diagnostic tests, including brain MRI, bloodwork and ophthalmologic examination were conducted—all of which strongly suggested a diagnosis of Wilson's disease.

She was subsequently transferred to the neurology clinic in her hometown. On admission, she was awake but mute, though she understood all instructions. She moved spontaneously, saliva was leaking from the right corner of her mouth and there was a slightly rigid, increased tone in her right hand. Several epileptic seizures were observed and antiepileptic therapy was introduced, after which she was temporarily still in a daze, but her condition began to improve. She became more alert, communicative and fully oriented, however pronounced hypofrontality was evident. A variable clinical picture was noted, including cognitive perseveration, echolalia and palilalia, oculomotor disorders, irregular limb tremor, rigidly increased tone, negative myoclonus of the limbs, pronounced bradyhypokinesia on both sides, and individual dystonic joints. Her gait was initially clumsy, but later improved with ongoing treatment. Further diagnostic testing supported the diagnostis. Laboratory findings revealed decreased serum ceruloplasmin levels and elevated 24-hour urinary copper excretion. A head CT scan revealed typical hypodense changes in the basal ganglia, thalami, midbrain, white matter and

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bilateral superior frontal gyri. EEG showed several slow waves over the left temporal lobe, without ictal activity. A Dat-SCAN revealed bilateral presynaptic dopaminergic damage. An examination by an ophthalmologist showed the presence of Kayser-Fleischer rings. She had previously undergone genetic tests abroad, which had identified a pathogenic mutation in the ATP7B gene. This finding was later confirmed, she met the diagnostic criteria for Wilson's disease.

The disease was treated with a copper chelator and urinary copper excretion was regularly monitored, which confirmed adequately elevated copper output. During hospitalization, the patient was included in a neurological rehabilitation process and a slow and subtle improvement in her condition was observed. Upon discharge, problems persisted in the area of fine motor skills, coordination and attentional control. She was able to walk independently, but still required a some assistance with daily activities. Neurologically, parkinsonism, mild dystonia of the upper extremities and negative myoclonus were prominent.

She was also assessed by a clinical psychologist. Given her impaired fine motor skill and double vision, the assessment included verbal tasks not requiring writing or drawing, alongside visuoperceptional tasks. Most of the results were deemed invalid, as she was unable to fully participate due to echolalia, repetitive movements and frequent disengagement. These limitations negatively impacted her performance on tasks assessing processing speed, sustained attention, naming, verbal memory, verbal fluency, and executive planning. Clinically, her ability to maintain attention was found to fluctuate significantly. Her attention span was mildly impaired, while working memory showed moderate impairment. Despite these difficulties, her capacity to generate, maintain, and adapt mental strategies appeared preserved. Her cognitive profile was consistent with a frontal (dysexecutive) syndrome, which gradually improved over time. Her affect was considered appropriate, though dystonia of the lower half of her face occasionally gave the impression of an incongruent emotional expression.

Given her favorable rehabilitation potential, she was transferred to a specialized rehabilitation facility, where she participated in a comprehensive program, including physical therapy, occupational therapy, neuropsychological rehabilitation and speech therapy.

Upon admission to rehabilitation, she was fully oriented, pleasant, and motivated to participate. Motor restlessness was observed; she had difficulty sitting still, frequently getting up and moving around. There was tremor in both hands and feet, becoming more pronounced during periods of anxiety or excitement. During sessions, she was able to establish eye contact appropriately but struggled to maintain it due to fluctuating attention. Social disinhibition was evident in reduced interpersonal distance, using of informal address and asking personally intrusive questions, although she remained polite and well-intentioned throughout. She appeared warm, open and trusting in relationships, which, due to reduced critical judgment, carried some risk. In conversation, she often shifted from topic to topic or interrupted the psychologist, though her narrative remained coherent. Her speech was fluent and intelligible, but with episodes of echolalia and palilalia. These were prominent at admission but improved over time, improving the quality of communication. They were mostly present during episodes of excitement, stress, or anxiety. Thought content was appropriate to context, but with rapid jumps between topics, mainly as a result of distractibility and disinhibition. Insight into her deficits was somewhat limited; she primarily acknowledged the positive aspects of her recovery while often overlooking persisting deficits. Her mood was neutral to slightly elevated, and her emotional expression was responsive and dynamic, though at times inadequately regulated.

In testing situations, she was motivated and applied adequate effort. She understood and followed testing instructions appropriately, yet exhibited test anxiety, frequently checking tasks accuracy. Avoidance behavior emerged with more demanding tasks.

The continuation sheds light on neuropsychological recovery over the course of cognitive rehabilitation.

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STUDY DESIGN

This study is a clinical case report describing neuropsychological findings across different stages of illness and recovery. Neuropsychological assessments were conducted at separate time points during the acute phase and following participation in a structured neurorehabilitation program, allowing qualitative evaluation of cognitive changes over time.

Upon admission, the patient underwent a comprehensive neuropsychological evaluation to assess attention, memory, executive functions and visuospatial abilities. Due to significant tremor, visuoconstructive functions were not assessed. The following psychodiagnostic instruments were administered: Test of Attentional Performance – Mobility Version Attention Battery (TAP-M): Alertness, Selective Attention, Divided Attention and Sustained Attention Test; California Verbal Learning Test (CVLT); Verbal Fluency Test from the Delis-Kaplan Executive Funcion System (D-KEFS); Wechsler Adult Intelligence Scale (WAIS-IV) Subtests: Block Design, Digit Span Forward and Digit Span Backward; Repeatable Battery for the Assessment of Neuropsychological Status (R-BANS) Subtest: Line Orientation; Neuropsychological Assessment Battery (NAB) Executive Function Module Subtests: Mazes, and Judjement; and the Tower of London task. These tests provided a baseline of cognitive functioning across multiple domains. Following baseline assessment, the patient participated in a structured cognitive rehabilitation program for two months.

The post-rehabilitation evaluation repeated similar neuropsychological battery to assess changes in cognitive performance. The R-BANS Line Orientation subtest was not repeated post-rehabilitation, as the patient's baseline performance was within the average range. The Tower of London task was not repeated to avoid practice effects. Instead, two additional subtests from the NAB Executive Function Module (Categorization and Word Generation) were administered. Furthermore, while the initial CVLT and D-KEFS Verbal Fluency assessment used the alternate form, the post-rehabilitation evaluation employed the standard form.

RESULTS

Upon admission, the patient underwent a comprehensive neuropsychological evaluation to assess a baseline of cognitive functioning across multiple domains. The results are summarized in Table 1.

Table 1
Baseline Neuropsychological Assessment

Cognitive Domain	Test / Subtest	Score / Norm	Interpretation
Attention Span – Numbers	WAIS – IV Digit Span Forward	5[a]	Low Average
Attention Span – Words		16	Low Average
Alertness	TAP-M Simple Reaction Time	1	Significantly Impaired
Selective Attention	TAP-M Selective Attention – Errors	7	Impaired

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Cognitive Domain	**Test / Subtest**	**Score / Norm**	**Interpretation**
	TAP-M Selective Attention – Omissions	13	Low Average
Divided Attention	TAP-M Divided Attention – Errors	3	Impaired
	TAP-M Divided Attention – Omissions	2	Significantly Impaired
Sustained Attention	TAP-M Sustained Attention – Errors	50	Average
	TAP-M Sustained Attention – Omissions	8	Impaired
Verbal Memory – Free Recall (Immediate)	CVLT	2	Impaired
Verbal Memory – Free Recall (Delayed)	CVLT	32	Average
Phonemic Fluency	D-KEFS Verbal Fluency	1	Significantly Impaired
Semantic Fluency	D-KEFS Verbal Fluency	1	Significantly Impaired
Planning	Tower of London – Total Move Score	14	Low Average
Set Shifting	D-KEFS Verbal Fluency	1	Significantly Impaired
Strategy generation and Flexible Thinking	NAB Mazes	1	Significantly Impaired
Judgement	NAB Judgement	1	Significantly Impaired
Working Memory	WAIS-IV Digit Span Backwards	3[a]	Low Average
Visuospatial / Construction	WAIS-IV Block Design	1	Significantly Impaired
Visuospatial – Orientation	R-BANS Line Orientation	26 – 50	Average

Note: [a] – Digit Span Forward and Backward scores are shown as maximum digits correctly repeated. All other scores are presented as percentiles.

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Initial neuropsychological testing revealed pronounced psychomotor slowing and several clinically significant impairments in selective, divided and sustained attention; executive function; and both phonemic and semantic fluency. Distractibility also impacted memory, especially learning of new information and short-delayed recall, while long-delayed recall was preserved. Notably, this represents substantial progress compared to her assessment at the time of diagnosis, when she was unable to complete most testing tasks at all.

Following baseline assessment, the patient participated in a structured cognitive rehabilitation program, which primarily focused on attention and executive function, incorporating tasks designed to improve selective, divided, and sustained attention through both computer-based and paper-pencil exercises. Executive function training targeted strategy generation, planning, problem-solving and flexible thinking. In addition, the program included memory exercises addressing learning and recall strategies, as well as timed tasks aimed at enhancing processing speed and psychomotor coordination. Post-rehabilitation results are summarised in Table 2.

Table 2

Post-Rehabilitation Neuropsychological Assessment

Cognitive Domain	**Test / Subtest**	**Score / Norm**	**Interpretation**
Attention Span – Numbers	WAIS – IV Digit Span Forward	5[a]	Low Average
Attention Span – Words		16	Low Average
Alertness	TAP-M Simple Reaction Time	1	Significantly Impaired
Selective Attention	TAP-M Selective Attention – Errors	>62	Average
	TAP-M Selective Attention – Omissions	>14	Average
Divided Attention	TAP-M Divided Attention – Errors	8	Impaired
	TAP-M Divided Attention – Omissions	45	Average
Sustained Attention	TAP-M Sustained Attention – Errors	8	Impaired
	TAP-M Sustained Attention – Omissions	21	Low Average
Verbal Memory – Free Recall (Immediate)	CVLT	84	High Average
Verbal Memory – Free Recall (Delayed)	CVLT	68	Average
Phonemic Fluency	D-KEFS Verbal Fluency	1	Significantly Impaired
Semantic Fluency	D-KEFS Verbal Fluency	5	Impaired
Set Shifting	D-KEFS Verbal Fluency	16	Low Average

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Cognitive Domain	Test / Subtest	Score / Norm	Interpretation
Strategy generation and Flexible Thinking	NAB Mazes	1	Significantly Impaired
Judgement	NAB Judgement	4	Impaired
Categorisation	NAB Categorisation	3	Impaired
Word Generation	NAB Word Generation	2	Significantly Impaired
Working Memory	WAIS-IV Digit Span Backwards	3[a]	Low Average
Visuospatial / Construction	WAIS-IV Block Design	5	Impaired

***Note*:** [a] – Digit Span Forward and Backward scores are shown as maximum digits correctly repeated. All other scores are presented as percentiles.

At discharge, testing still showed psychomotor slowing, sustained and divided attention deficits and executive impairments – particularly in strategy generation, categorisation, cognitive flexibility and everyday judgment. Phonemic fluency remained significantly reduced, while semantic fluency reached the low average range. Other domains, including attention span, selective attention, verbal memory, visual-perceptual abilities and planning in structured situations, were preserved. Clinically, she showed less distractibility, followed instructions more easily, and was better able to stay on task.

In conclusion, despite notable improvements, significant deficits persist that may substantially impact her daily functioning, particularly in her ability to cope with multiple demands simultaneously, plan ahead, solve problems, and adapt to new or sudden changes. These cognitive limitations may also affect her independence and safety, indicating a need for a structured environment, guidance, and partial supervision.

DISCUSSION

This study demonstrates that despite a two-year diagnostic delay, structured neurorehabilitation can lead to cognitive improvements, although frontal dysexecutive symptoms may persist.

The patient, a young adult with no previous psychiatric or neurological history, developed a gradually progressing and complex combination of neurological, behavioral, and cognitive changes. In the initial phase, micrographia, tremor, restless legs, speech difficulties and drooling immediately stood out as signs of an extrapyramidal disorder. This combination of symptoms aligns with the early neurological presentation of WD, in which tremor, dysarthria, gait disturbances and drooling are often observed as initial symptoms (Schilsky, 2017; Bandmann et al., 2015). Particularly, the combination of tremor and dysarthria is a classic warning sign (Bandmann et al., 2015) which was clearly present in this case. In addition, symptoms such as facial grimacing, lip retraction, drooling and speech changes are well-documented early neurological signs of the disease (EASL, 2012).

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Despite clear signs of neurological involvement, the patient's symptoms were initially misattubuted to a mood disorder. The psychiatric manifestations of WD are diverse and span several domains. Many features observed in this case are well-documented in the literature, including mood disturbances, particularly depression (with or without suicidality) and anxiety, as well as behavioral and personality changes such as disinhibition, impulsivity, emotional lability, childish behavior, and excessive trust (Gromadzka et al., 2024; Ala et al., 2007). Due to the initial presence of psychiatric symptoms, the diagnostic pathway was focused toward psychiatric assessment, ultimately delaying recognition of the underlying organic condition, which is a common diagnostic challenge in the neuropsychiatric form of WD (Lorincz, 2010). This early diagnosis illustrates a frequent clinical pitfall, as neurological symptoms such as tremor are in practice often attributed to stress or anxiety (Crawford & Zimmerman, 2018). In this context, it is important to note that micrographia is not typical of anxiety disorders. It's presence, alongside tremor, should have prompted a more thorough neurological work-up on, as both signs are indicators of extrapyramidal syndromes such as Parkinson's or Wilson's disease (Eklund et al., 1996).

One of the clinical pitfalls in this case was the early mention of a functional neuological disorder in the initial psychiatric report. Despite the presence of movement disordes, there was no documentation of basic somatic examinations, such as brain MRI or EEG. As emphasised by Espay and colleagues (2018), a diagnosis of a functional neurological disorder should only be considered after reliably excluding possible organic causes. In clinical practice, however, neurological symptoms are often prematurely interpreted as functional or psychiatric, before appropriate differential diagnostics are conducted (Zimbrean & Schilsky, 2014). Yet, a functional disorder is a diagnosis of exclusion and requires a high degree of clinical certainty that no other pathology underlies the symptoms (Espay et al., 2018). In this case, as in many others, the opposite often occurred, as the diagnosis was mentioned prematurely, without appropriate investigations, leading to poor medical outcomes (Litwin et al., 2018).

As the illness progressed, depressive symptoms with self-harming tendencies and more pronounced neurological signs emerged. Due to concerns about suicidality and psychosis, the patient was hospitalized in a secure psychiatric unit. While such treatment was appropriate in acute presentation, it remains a worrying fact that despite more than a year of symptom progression, no appropriate metabolic diagnostics or more comprehensive neurological assessments had yet been initiated. Despite partial stabilization under the influence of psychopharmacological treatment (aripiprazole, sertraline), such improvement does rule out the presence of an underlying organic etiology. Rather, it may reflect the temporay alleviation of symptoms arising from copper-induced disruption of brain circuits involved in mood regulation. Indeed, research on WD has shown structural changes in the basal ganglia, thalamus, and hypothalamus (Litwin et al., 2018) and disruptions in the metabolism of dopamine, norepinephrine, and serotonin, which likely contribute to the development of mood disorders (Portala et al., 2001). Mood improvement may also have resulted from the removal of stress factors, a reduction in metabolic strain or the spontaneously fluctuating nature of the disease (Lorincz, 2010).

During psychiatric hospitalization, some obseved symptoms, such as "inappropriate facial expression" and a "forced smile", were interpreted as dissociation or psychosis. However, these symptoms could reflect facial dystonia and frontal disinhibition, both characteristic of basal ganglia dysfunction caused by toxic copper accumulation. What was described may have been the result of these neurological processes, which were upon diagnosis confirmed by the clinical psychologist, rather than a psychotic disorder. Similar facial expressions, such as rigid, involuntary smiles caused by facial muscle contraction, often incongruent with emotional context, are a recognized manifestation of WD or other basal ganglia disorders (Machado et al., 2006).

Only after the diagnosis of Wilson's disease was confirmed through MRI and laboratory tests did the full course of the illness become retrospectively clarified. The clinical picture involved extrapyramidal signs, speech disturbances, Kayser-Fleischer rings, disinhibition, regression, depressive symptoms, and somnolence, all characteristic of the neuropsychiatric form of the disease caused by toxic copper accumulation (Gromadzka et al., 2024).

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Following the initiation of appropriate treatment, cognitive deficits became more apparent. As research shows, cognitive impairments in WD are often subtle in the early stages and may be masked by more prominent affective or behavioral symptoms. However, when they are expressed, they most commonly affect psychomotor speed and attention. Patients often show reduced attention span and difficulties with divided attention, which manifests as prolonged reaction times during tasks requiring dual attention (Hegde et al., 2010; Frota et al., 2009). In terms of memory function, early encoding processes are most frequently impaired, while recall remains relatively preserved, suggesting difficulties in the initial processing of information (Hegde et al., 2010). Similarly, Portala and colleagues (2001) reported reduced short-term memory with relatively intact long-term memory function. Executive functioning is also frequently compromised, manifesting as an impulsive cognitive style, an increased number of perseverative responses, reduced cognitive flexibility (Hegde et al., 2010; Frota et al., 2009), as well as impaired planning and decision-making abilities (Lorinz, 2010). In addition, patients often show a significant difference between phonemic and semantic fluency: while semantic fluency is usually preserved, phonemic fluency is significantly impaired. Difficulties in grammatical reasoning are also observed, although vocabulary is often well preserved. The pattern of cognitive dysfunction observed in our case is consistent with these established findings, confirming a frontal dysexecutive syndrom typical of the neurological presentation of WD.

After inclusion in a structured neurorehabilitation program, it became evident that neuropsychological symptoms had a more substantial impact on everyday functioning than motor difficulties. Nevertheless, the patient's preserved social skills, motivation and willingness to participate provided a favorable foundation for further rehabilitation, which was aimed on the development of cognitive strategies, improvement of organizational skills and impulsivity regulation. Despite these strenghts, her actual level of functional independence remained significantly limited, primarily due to fluctuating attention and behavioral disinhibition. This further highlights the importance of early recognition of the disease and its impact on long-term functioning. While WD is largely manageable with timely recognition and treatment, prolonged exposure to elevated copper concentrations in brain tissue, particularly in the basal ganglia and limbic system, can cause irreversible damage, even if treatment is eventually initiated (Bandmann et al., 2015). As a result, lasting neurological or cognitive issues may persist, significantly impairing future quality of life (Dusek & Litwin, 2018; Brewer et al., 1987).

CONCLUSION AND FUTURE DIRECTION

In conclusion, this case highlights the critical importance of early and accurate diagnosis of organic causes in young adults with complex neuropsychiatric symptoms. It illustrates the clinical pitfalls in interpreting behavior where organic and psychiatric symptoms are present and demonstrates how the combination of these symptoms, reinforced by the lack of a holistic approach, can lead to misdiagnoses and delayed treatment. Futhermore, due to its rarity and diverse clinical presentations, WD is often not considered in differential diagnosis, which increases the risk of or oversight. Therefore, in the presence of atypical, progressive, and diverse symptoms, particularly in young individuals without prior psychiatric history, it is crucial to consider diagnostic procedures that investigate potential organic causes early on. While antipsychotic and antidepressant treatment can alleviate acute symptoms, it should be considered supportive rather than definitive treatment in the presence of ongoing unexplained neurological signs and a possible neurological basis should be sought. An interdisciplinary approach, including neurologists, psychiatrists and clinical psychologists, is necessary for the timely recognition and management of rare diseases such as WD, where the prognosis can be significantly improved with early diagnosis.

Patient Consent
The patient provided informed consent for participation in this study and publication of relevant clinical data.

Declaration of Interest Statement
The authors report there are no competing interests to declare.

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Declaration Availability Statement

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

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