

Adaptive motor reorganization in acute intermittent porphyria with cerebellar dysfunction and normal neuroimaging: a case report

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Case Report

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Abstract

Background

Acute intermittent porphyria (AIP) is a rare metabolic disorder associated with heterogeneous neurological manifestations. Cerebellar motor dysfunction may occur despite normal structural neuroimaging, posing diagnostic and therapeutic challenges.

Case presentation:

A 44-year-old woman with confirmed AIP presented with progressive motor impairment, including intention tremor, axial instability, and gait variability, and was unable to complete the six-minute walk test due to neuromotor limitation. At baseline, sit-to-stand performance was 5 repetitions and single-leg stance time (eyes open) was 22 seconds (right) and 16 seconds (left). Brain MRI showed preserved cerebellar morphology. Electroneuromyography showed normal sensory and motor conduction in upper and lower limbs, excluding peripheral neuropathy. A structured sensorimotor program was delivered twice weekly (60 min, light-to-moderate intensity), emphasizing coordination (40%), balance/postural control (35%), and strength (25%). On retest, sit-to-stand increased to 6 repetitions and single-leg stance improved (+ 3.87 s right; +9.25 s left). Serial video documentation demonstrated reduced movement variability and improved axial stability.

Conclusion

Clinically significant cerebellar motor dysfunction may occur in AIP despite normal neuroimaging and peripheral electrophysiology. Structured sensorimotor strategies may facilitate adaptive motor reorganization and measurable functional improvement.

Background

Acute intermittent porphyria (AIP) is a rare inherited metabolic disorder of heme biosynthesis characterized by recurrent neurovisceral manifestations and heterogeneous neurological involvement. In addition to autonomic and psychiatric symptoms, neurological features may include peripheral neuropathy, seizures, and, less frequently, disturbances of motor control [1–3]. Motor dysfunction, when present, may involve disruption of central motor networks, including cerebellar circuits, although this relationship remains incompletely defined [4]. Given that peripheral neuropathy is a recognized neurological manifestation of AIP, careful clinical and electrophysiological differentiation between central and peripheral motor involvement becomes essential. The pathophysiological mechanisms underlying neurological impairment in AIP are incompletely understood, and structural neuroimaging findings are often absent despite clinically relevant dysfunction [5].

The cerebellum plays a central role in the temporal organization, precision, and coordination of voluntary movement through the integration of multisensory afferent input and modulation of motor output. Beyond motor execution, the cerebellum is essential for motor learning and adaptive recalibration through sensory feedback integration. Cerebellar dysfunction typically manifests as ataxia, intention tremor, postural instability, and gait impairment. Importantly, such dysfunction may arise from metabolic or network-level disturbances rather than focal anatomical lesions, resulting in a dissociation between structural neuroimaging findings and clinical presentation. This structure–function mismatch poses diagnostic and therapeutic challenges in patients with suspected cerebellar involvement [6].

In the context of structure–function dissociation, functional motor organization becomes a central focus of clinical assessment. Rather than emphasizing anatomical correlates alone, evaluating how movement is executed and adapted may provide meaningful insights into disease expression and management. Non-pharmacological approaches targeting sensorimotor integration, coordination, and postural control have gained relevance in the management of movement disorders, aiming to reduce motor variability and improve functional efficiency [3] rather than restore normal movement patterns. Such approaches prioritize adaptive compensation within existing neurological constraints rather than structural restitution. However, reports describing functional motor adaptation in patients with metabolic neurological disorders, particularly AIP, are scarce [7].

This case report describes the longitudinal functional evolution of a patient with acute intermittent porphyria presenting with cerebellar motor dysfunction despite normal structural neuroimaging. It highlights objective functional assessment, a structured sensorimotor intervention, and clinically relevant aspects of motor organization and adaptive compensation within a structure–function mismatch framework.

Case presentation

A 44-year-old woman with a confirmed diagnosis of acute intermittent porphyria was referred from a hematology clinic to a multidisciplinary women's health outpatient clinic due to progressive motor complaints. The diagnosis of AIP had been previously established based on positive urinary porphyrin testing in 2017. At the time of referral, she was undergoing neurological investigation for suspected cerebellar dysfunction. There was no history of cerebrovascular events, traumatic brain injury, or other known neurological disorders. She had undergone total thyroidectomy in 2018 and was under stable hormone replacement therapy. Pharmacological treatment remained unchanged throughout the observation period.

At baseline evaluation (September), the patient presented marked motor coordination impairment characterized by intention tremor predominantly affecting axial and upper limb control, impaired postural stability, and gait instability. Tremor amplitude increased during goal-directed movements. Gait was cautious and irregular, with increased step-to-step variability and difficulty increasing walking speed. The patient was unable to complete the six-minute walk test due to inability to sustain increased gait speed,

without evidence of cardiorespiratory limitation. Increased axial rigidity with compensatory co-contraction patterns was observed during dynamic tasks and postural transitions.

Brain magnetic resonance imaging was performed to investigate possible structural correlates of the patient's cerebellar motor dysfunction. The examination included standard axial and sagittal T1- and T2-weighted sequences with gadolinium enhancement. No focal lesions, signal abnormalities, or evidence of cerebellar atrophy were identified. The cerebellar hemispheres and vermis demonstrated preserved morphology and signal intensity without pathological contrast enhancement. These findings confirmed the absence of structural abnormalities despite clinically evident cerebellar motor impairment, reinforcing the proposed structure–function dissociation (Fig. 1).

To further differentiate central from peripheral motor involvement, electroneuromyography (ENMG) of the upper and lower limbs was performed (January 2026). Sensory and motor nerve conduction studies were within normal limits, F-wave latencies were symmetric, and needle electromyography showed normal insertional activity, motor unit morphology, and recruitment patterns without evidence of denervation or neuropathic changes. These findings supported the absence of peripheral nervous system involvement and reinforced the interpretation of predominantly central motor dysfunction.

In the absence of structural abnormalities on neuroimaging and in the presence of clinically relevant motor dysfunction, a structured sensorimotor intervention was initiated based on principles of cerebellar motor control and motor learning. The program was conducted twice weekly for approximately three months, with 60-minute sessions at light-to-moderate intensity. The intervention emphasized coordination-focused tasks (approximately 40%), followed by balance and postural control exercises (approximately 35%), and strength-oriented activities (approximately 25%). Closed kinetic chain tasks, postural transitions, and multisensory cues (tactile, proprioceptive, visual, and vestibular) were systematically incorporated. Manual guidance and external sensory cueing provided by the therapist were used to support motor execution and improve movement consistency.

At baseline functional assessment (October 2025), the patient demonstrated marked impairment in objective functional measures. Static balance time during single-leg stance with eyes open was 22 seconds on the right and 16 seconds on the left. Sit-to-stand performance was limited to five repetitions. The elbow flexion test and six-minute walk test could not be completed due to motor instability, with loss of balance during the walking attempt. Resting heart rate was 52 bpm and blood pressure was 133/83 mmHg. At follow-up reassessment (January 2026), static balance time increased by 3.87 seconds on the right and 9.25 seconds on the left. Sit-to-stand performance increased from five to six repetitions, and the elbow flexion test reached five repetitions. Resting blood pressure decreased from 133/83 to 106/83 mmHg, while heart rate remained stable at 52 bpm. The six-minute walk test was not repeated.

Longitudinal functional assessment using serial video recordings obtained in September, December, and January demonstrated progressive reduction in movement variability, improved axial stability, and increased fluency during gait and postural transitions. In September, movement execution was characterized by marked axial instability and exaggerated co-contraction patterns. By December, partial

reduction in axial oscillation and improved postural alignment during transfer tasks were observed. In January, movement patterns appeared more consistent, with greater trunk control and improved gait initiation. Supplementary video material illustrates movement patterns at baseline (September), intermediate follow-up (December), and later follow-up (January), highlighting longitudinal changes in motor organization (Additional file 1). Although intention tremor persisted, its functional interference decreased over time.

During follow-up interviews, the patient reported subjective improvement in motor control, describing reduced trunk tremor, decreased bodily stiffness, and increased walking tolerance. She noted the ability to walk longer distances with fewer pauses during daily activities and reported a clinically meaningful improvement in perceived quality of life (NAIK et al., 2016; NEELEMAN et al., 2018).

Discussion

This case illustrates a structure–function dissociation, characterized by clinically evident cerebellar motor dysfunction in the absence of detectable structural abnormalities on conventional neuroimaging in a patient with acute intermittent porphyria. Despite normal magnetic resonance imaging and normal electroneuromyography excluding peripheral neuropathic involvement, the patient exhibited classical cerebellar signs, including intention tremor, postural instability, and gait impairment. Similar dissociation patterns have been described in porphyria-related neurological manifestations and are believed to reflect underlying metabolic or neurochemical disturbances rather than focal anatomical lesions [1, 2]. Accumulation of neurotoxic heme precursors, particularly δ -aminolevulinic acid (ALA), has been proposed as a contributor to neuronal dysfunction in acute hepatic porphyrias, potentially affecting central motor circuits even in the absence of structural damage [1, 2].

The longitudinal functional evolution observed in this case suggests adaptive motor reorganization rather than recovery of cerebellar integrity. Improvements in axial stability, reduction in movement variability, and increased gait tolerance occurred without resolution of core neurological signs, indicating enhanced efficiency of motor execution. The persistence of intention tremor alongside reduced functional interference supports the interpretation of compensatory motor strategies rather than reversal of the underlying dysfunction. These changes may reflect adaptive recalibration of internal motor models and improved sensory reweighting at a network level, rather than restoration of intrinsic cerebellar structure. Visual documentation of these longitudinal motor changes is provided in the supplementary video material (Additional file 1), demonstrating progressive improvements in movement consistency and axial control.

The observed functional improvements are consistent with emerging evidence supporting motor adaptation in cerebellar disorders. Intensive coordinative and balance-based training has been shown to improve motor performance and postural control in degenerative cerebellar disease, with both short- and long-term benefits [8, 9]. Randomized and controlled rehabilitation trials further demonstrate that structured task-oriented and balance-focused interventions can enhance gait and functional

independence in individuals with cerebellar ataxia [10, 11]. Systematic reviews also support the role of physiotherapy and postural training in reducing functional impairment in cerebellar disorders [12, 13]. Although acute intermittent porphyria is etiologically distinct from degenerative ataxias, shared network-level dysfunction affecting cerebellar motor circuits may explain the responsiveness to sensorimotor training observed in this case.

The intervention emphasized sensorimotor integration, coordination, and postural control, consistent with principles of cerebellar motor learning. By progressively constraining task complexity and enhancing multisensory feedback, such strategies may facilitate improved movement consistency and reduce excessive axial rigidity and compensatory co-contraction [6]. Importantly, no adverse clinical events or porphyric exacerbations were observed during the intervention period, and hemodynamic parameters remained stable, suggesting that carefully monitored low- to moderate-intensity sensorimotor training may be safely implemented in clinically stable individuals with acute intermittent porphyria under multidisciplinary supervision. Patient-reported outcomes further reinforced the functional relevance of these changes, with the patient describing reduced stiffness, improved walking tolerance, and enhanced quality of life [14].

Limitations include the single-case design and the absence of standardized instrumented gait metrics or validated cerebellar rating scales. Notably, the Scale for the Assessment and Rating of Ataxia (SARA) was not applied, as this case was not originally designed as a prospective experimental study but emerged from routine multidisciplinary clinical care. Additionally, serial biochemical markers of porphyric activity were not systematically correlated with motor performance over time. Nevertheless, the integration of longitudinal observation, video analysis, and patient-reported outcomes strengthens the interpretation of functional motor adaptation. Future studies should explore whether similar structured sensorimotor strategies yield consistent benefits in larger cohorts of patients with acute intermittent porphyria and other metabolic movement disorders [3].

Conclusion

This case demonstrates that meaningful functional improvement may occur in patients with cerebellar motor dysfunction associated with acute intermittent porphyria despite normal structural neuroimaging and absence of peripheral electrophysiological abnormalities. Structured low-to-moderate intensity sensorimotor training focusing on motor organization, multisensory integration, and postural control may facilitate adaptive motor strategies and improve daily mobility. These findings reinforce the clinical relevance of addressing functional motor organization in the context of structure–function dissociation in rare metabolic neurological disorders.

Declarations

Authors' contributions

CBG was a resident in the multidisciplinary women's health program and was responsible for case conception, patient assessment, and implementation of the clinical interventions.

ELCS contributed to physical training supervision and supported patient-centered care delivery.

JBD provided a critical revision of the manuscript

SMSS provided expert consultation and participated in case discussion prior to intervention.

SCS served as residency tutor, supervising and guiding the interventions.

CGCJ was the principal supervisor, conceived the study, and performed data analysis and interpretation.

All authors contributed to case presentation and discussion, critically revised the manuscript, and approved the final version.

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Research Ethics Committee of the State University of Londrina (UEL). Written informed consent was obtained from the patient prior to participation.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images and video materials.

Competing interests

The authors declare that they have no competing interests.

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Availability of data and materials

The datasets supporting the conclusions of this article are included within the article and its additional files.

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Figures

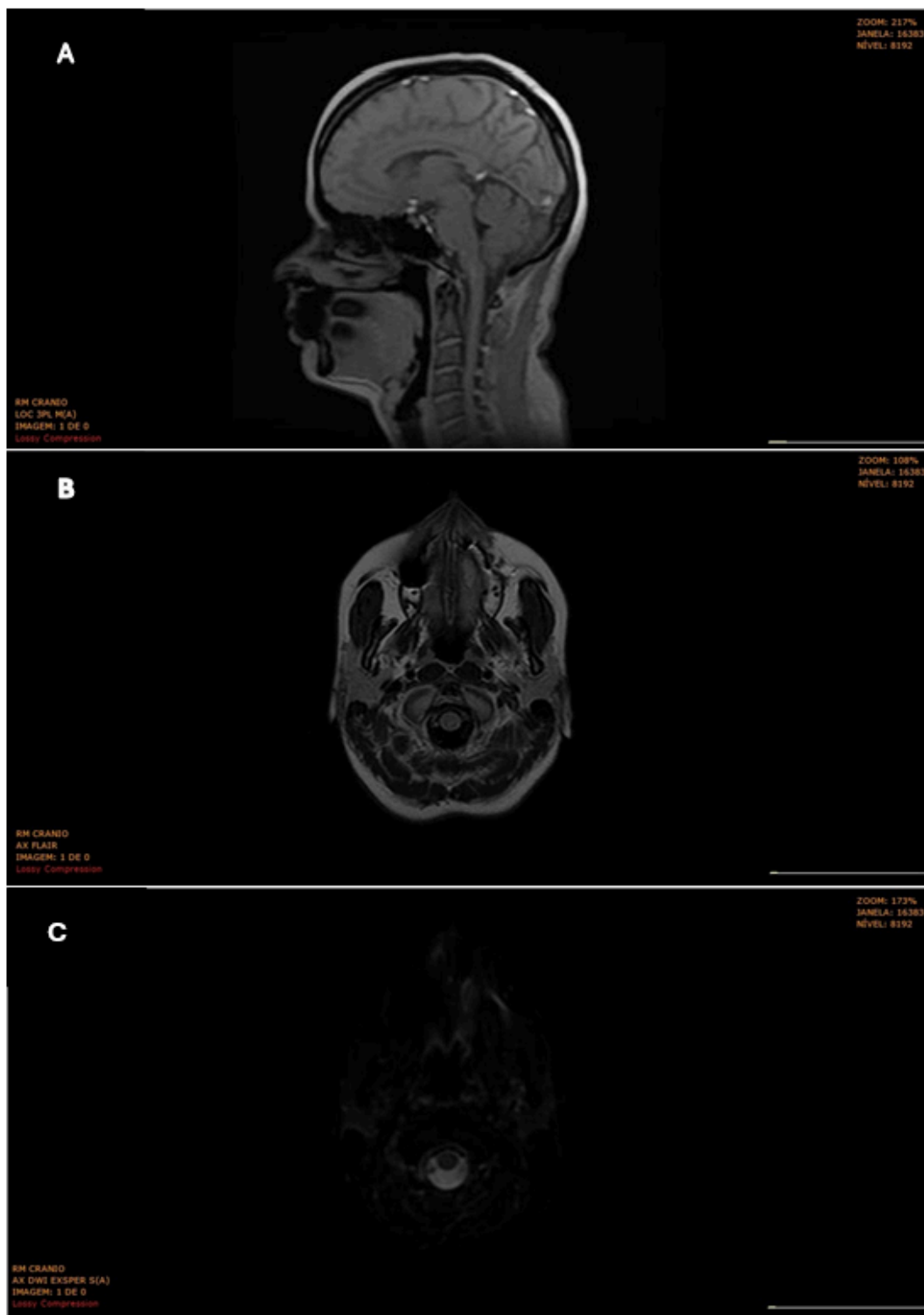


Figure 1

Brain magnetic resonance imaging demonstrating preserved cerebellar morphology. (A) Sagittal T1-weighted image showing normal vermis and hemispheres. (B) Axial FLAIR sequence without focal signal abnormalities. (C) Diffusion-weighted imaging showing no diffusion restriction.

Supplementary Files

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