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THE MAN WHO COULD NOT WALK BACKWARD: AN UNUSUAL PRESENTATION OF NEUROFERRITINOPATHY

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A fifty-three year old highway maintenance worker was referred to the Movement Disorders clinic because he could not walk backward.

In the months before presentation he had begun to feel unsteady when standing and found that he could no longer do his job (placing traffic cones), because whenever he walked backward he would fall over.

Over the following three years he developed a hoarse voice, mild emotional lability and micrographia. He had no significant past medical history and was taking no regular medications. His mother had been diagnosed with Parkinson's disease aged fifty-five and died two years later. One of his two siblings developed chorea in her early fifties and was diagnosed with neuroferritinopathy (FTL1 460InsA mutation).

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Authors' Roles

Dr Adam Cassidy executed the study, produced the video and wrote part of the manuscript.

Dr Elizabeth Williams executed the study, wrote some of the data analysis software, provided statistical expertise and critiqued the final manuscript.

Dr Paul Goldsmith referred the patient, helped design the study and reviewed and critiqued the final manuscript.

Professor Stuart Baker helped design the study, wrote some of the data analysis software, provided statistical expertise, reviewed and critiqued the manuscript.

Dr Mark Baker designed the study, organized and executed the experiments, analysed the data, performed statistical analysis and wrote part of the manuscript.

The authors have no conflict of interest.

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Neurological examination revealed hypomimia, hypophonia and dysphonia. Cranial nerve examination was normal. There was no visible or palpable tremor of the lower limbs. There was bilateral bradykinesia and mild bilateral upper limb cogwheel rigidity. There was no muscle weakness, tendon jerks were normal and plantar responses were flexor. There was no ataxia. Romberg's sign was negative. On walking forwards there was bilaterally reduced arm swing and instability on turning, particularly when making rapid turns. Tandem gait was normal. Antepulsion was normal but there was marked postural instability on retropulsion (pull test). On attempting to walk backward a few shuffling steps were taken before falling backward (see video).

Brain MRI (gradient echo sequences) revealed a pattern of iron deposition typical of that seen in neuroferritinopathy. Genetic testing revealed the FTL1 460InsA mutation, the commonest of the four mutations of the ferritin light chain identified in neuroferritinopathy¹.

Electromyography (EMG) showed no evidence of leg tremor while seated, either at rest or with co-contraction, but as the patient stood synchronous 9Hz tremor bursts of 40-80ms duration appeared in the EMG bilaterally, therefore fulfilling diagnostic criteria for slow orthostatic tremor (OT)². Raw rectified EMG recorded using adhesive electrodes from right and left *tibialis anterior* (TA) muscles (gain 5000; band pass filtered 30Hz-2kHz; 5kHz digitization) whilst standing is shown in Figure 1A. Frequency domain analysis (see power spectra in Figure 1B) confirmed that the dominant frequency was 8-10Hz. Coherence analysis was performed as previously published³ and confirmed significant unilateral and bilateral EMG-EMG coherence at 8-10Hz (see Figure 1C). As previously described in OT, when the patient walked forwards (1-2 steps/second) the 9Hz EMG bursts disappeared (see Figure 1D), unilateral 8-10Hz intermuscular coherence was reduced and there was no significant bilateral 8-10Hz intermuscular coherence (grey line; Figure 1E). However, although ~8Hz EMG bursts persisted when the patient tried to walk backwards, the bursts became desynchronized (Figure 1 D). Coherence analysis confirmed that bilateral EMG bursts were asynchronous (black line; Figure 1E) but that significant unilateral 8-10Hz coherence persisted.

Direction specific or task specific gait disorders are rare and, because of their often bizarre appearance, frequently dismissed as functional or psychogenic⁴. Problems with forward gait initiation can occur after pallidotomy and can be seen in patients with cerebrovascular disease, progressive supranuclear palsy, corticobasal degeneration, pallidoniroluysian degeneration, Orthostatic Myoclonus (OM)⁵ and OT⁶; problems with forward ambulation can be a feature of dystonia⁴. Transient failure of gait initiation (or transient gait arrest) with shuffling and trembling are also features of Freezing of Gait (FOG) in Parkinson's disease, vascular parkinsonism and neurodegenerative parkinsonian syndromes⁷. FOG has not previously been described in neuroferritinopathy, but could explain the task specific gait disorder we observed, particularly given the presence of other parkinsonian features.

Orthostatic Tremor has not previously been reported in neuroferritinopathy¹. OT is a rare task specific tremor affecting the legs and trunk, which only appears on standing, is associated with a profound and disabling sense of unsteadiness and is relieved by sitting, walking or the use of a support. Two types of OT are recognized: fast OT, characterized by bursts of muscle activity at 13-18 Hz⁸; and slow OT, with EMG bursts at frequencies <12Hz². In both fast and slow OT EMG coherence analysis reveals significant bilateral coupling at tremor frequency between EMG recorded from lower limb, upper limb and axial muscles^{2,9}. Although slow OT can persist when walking backward, EMG bursts remain bilaterally coupled¹⁰. Asynchronous 8-12 Hz EMG bursts (duration <75ms) have been described in OM^{2,5}, a recently recognized phenomenon presenting with forward gait initiation failure, symptoms mimicking OT or both³. However, in contrast to OT (and the

pattern of EMG bursting observed in our patient when walking backward), EMG bursting in OM is paroxysmal and non-rhythmic.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

A. Raw rectified EMG recorded simultaneously from right and left *tibialis anterior* (TA) during stance. B. EMG power spectra obtained from right and left TA and left and right *gastrocnemius-soleus* (GS) during stance (black line) and while the patient was sitting producing a similar level of EMG activity by co-contracting his leg muscles (gray line). Note power spectra show relative EMG power (normalised to total power between 1 and 48Hz). C. Intermuscular (EMG-EMG) coherence spectra obtained during stance (black line) and while seated (gray line). Muscle pairs used to calculate each coherence spectrum are indicated on each plot. D. Raw rectified EMG recorded simultaneously from right and left TA as the patient made the transition from walking forward to walking backward. E. Intermuscular coherence spectra obtained during forward (gray line) and backward (black line) ambulation. Muscle pairs used to calculate each coherence spectrum are indicated on each plot.