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Use of the Rehabilitation Treatment Specification System (RTSS) in the management of nitrous oxide (N₂O)-induced spinal cord injury

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SUMMARY

Nitrous oxide (N₂O) is an inhaled anaesthetic gas and a popular intoxicant. Excessive recreational use can cause spinal cord myelopathy. Previous studies have discussed the medical management. However, none have specified the sensorimotor rehabilitation management. This case report documents the investigations, physical rehabilitation and functional outcomes in two cases of N₂O-associated myelopathy. Both presented with lower limb strength and sensorimotor integration impairments resulting in ataxic ambulation. Dorsal column signal abnormality was observed on T2-weighted MRI in one case. Myelopathy was diagnosed based on clinical presentation and both were treated with vitamin B₁₂. Rehabilitation was conceived and specified using the Rehabilitation Treatment Specification System (RTSS). Both cases achieved independent indoor gait on hospital discharge, and full function at 9 months in one case. Appropriate and timely medical management and reasoned rehabilitation provided excellent functional outcomes for N₂O-related myelopathy. By using the RTSS, reasoned rehabilitation efficacy can be tested in the future.

BACKGROUND

The analgesic and intoxicating effects of the colourless inorganic gas nitrous oxide (N₂O) have been known for over 200 years.^{1,2} As an inhaled analgesic, N₂O acts as an N-methyl-D-aspartate antagonist which decreases excitatory neurotransmission throughout the central nervous system via non-competitive glutamate inhibition.³ When prescribed as a mixture with 50% oxygen, it can be safely administered by trained professionals (eg, nurses, midwives, dentists, paramedics) during painful or distressing procedures.⁴ As an inhaled intoxicant without oxygen, N₂O (colloquially sweet-air, nos, noz, nox, hippie-crack⁵) elicits short-lived feelings of euphoria with pleasurable psychedelic and empathogenic effects.⁶

Recreational N₂O intoxication is popular. The UK lifetime-user prevalence rate from a non-probabilistic sample is 38.6%; typical users appear to be male clubbers in their 20s.⁷ The catering industry's development of small 8 g steel recharging canisters for whipped cream dispensers containing pressurised N₂O (bulbs, whippits, nangs) has made them ubiquitous to buy cheaply (50p–£2 per canister⁸) usually in packs of 100. Use from large cylinders (2–10 kg) has become more prevalent recently.⁹ N₂O remains legal to buy in the UK

although this is now under review¹⁰ not least due to recent media concern about the increase in chronic abuse,¹¹ and the alarming increase in use reported in the Netherlands, which has led it to plan for formal controls in 2023.¹² Consuming N₂O directly from the canister is dangerous—the pressure (~200 kPa) can cause barotrauma,¹³ and the temperature of the gas near the outlet (–55°C¹⁴) can cause frostbite injuries.¹⁵ Instead, the gas is typically transferred into balloons via either the whipped cream dispenser or a secondary device (creamers or crackers) easily available that can dispense the canister gas into balloons inserted over the device spout. The preferred recreational use is to inhale or rebreathe the N₂O via the balloon at parties and festivals.¹⁶

Although recreational N₂O use is relatively safe compared with other drugs, acute harm includes falls, accidental injury, confusion⁷ or vomit aspiration.¹⁷ Acute death is rare. A 2016 systematic review of case reports found evidence of 29 case deaths mostly due to acute asphyxiation due to hypoxia with users consuming N₂O with a mask or plastic bag.¹⁸ In the UK, 17 deaths were reported between 2006 and 2012¹⁹ mainly due to accidental asphyxia when N₂O displaces oxygen if used in enclosed spaces.²⁰ Most users inhale low doses per session (1–2 canisters), but overuse exists (~100 canisters), which can lead to persistent neurological sequelae. Chronic clinical toxicity is due to N₂O's interaction with vitamin B₁₂ converting it from an active to an inactive form by irreversible oxidation.²¹ By impairing methylation reactions and DNA synthesis, oxidation results in an accumulation of homocysteine and impaired maintenance of the myelin sheath.²² Thus, B₁₂ deficiency from excessive N₂O use can cause demyelination of the central and peripheral nervous system and a diagnosis of subacute combined degeneration (SACD). If demyelination presents in the spinal cord, the dorsal columns are classically affected, with sometimes the lateral but rarely the anterior columns. The associated diagnostic procedures, neural impairments (progressive vibratory and proprioceptive sensory abnormalities, ascending paraesthesia, ataxic gait, hyporeflexia or hyper-reflexia, and rarely muscle weakness and loss of sphincter control^{23–25}), and medical treatment options have been described in medical case reports and observational studies of SACD of the spinal cord previously.^{22–25–36}

In contrast, *rehabilitative* treatment options for N₂O abuse SACD are not as pervasive in the



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Case report

literature. It is as if patients are expected to recover naturally with cursory reassurance and good luck. One published case study advocates physicians to be cognisant that tailored rehabilitation for a patient's functional and neuropsychiatric impairments can limit the extent of neurological damage,³⁷ and another clinical review advises medical clinicians to refer to physiotherapy if a patient's mobility is affected.³⁸ Yet, rehabilitation treatment is not well specified even in these welcome cases.

This lack of rehabilitation specificity is not unusual in research into rehabilitation treatment efficacy where objective definitions of treatments of interest, or even 'usual care',³⁹ are required. For surgical or pharmacological treatments, it is usual for active treatment ingredients to be obvious and be specified as chemical structures or anatomical results. In contrast, rehabilitation specification is challenging for several reasons. A binary definition of rehabilitation is tenuous because there are non-binary categories of rehabilitation,⁴⁰ rehabilitation ingredients are not obvious, rehabilitation treatments attempt to change multiple interacting patient functions (eg, muscle strength, movement fluidity, participation in occupation) and specific treatment ingredient definitions do not exist, let alone their downstream effect on patient function.⁴¹ To date, the active ingredients of treatment at the macro level of acute inpatient rehabilitation are rarely specified, which equates with the 'black box' approach where little insight into the active treatment ingredients is given which is a typical criticism in the rehabilitation science and clinical communities.⁴² The recently developed coherent framework (the Rehabilitation Treatment Specification System (RTSS)) addresses the black box problem by developing methods that specify, and ultimately measure, the rehabilitative content (ingredients), that via theoretical or observed processes (mechanisms of action), cause a change in desired systems (targets).⁴³ Because of relative rarity of both the clinical condition and the specification of its rehabilitation using the RTSS, the following report of two cases with spinal cord injury post-N₂O overuse is intended to provide an exemplar of holistic medical and rehabilitation management. It was prepared following the Case Report guidelines.⁴⁴

CASE PRESENTATION

The patients were both male. Case 1 was in his early teens (mass 71.7 kg, height 183.0 cm, body mass index (BMI) 21.4 kg/m²) and case 2 was in his 20s (54.1 kg, 173.5 cm, BMI 18.0 kg/m²) on presentation to our large, urban hospital emergency department. Case 1 presented with a 2-day history of gradually worsening lower leg weakness, sensory disturbance in a stocking distribution, reduced balance and mobility. Case 2 presented with a 3-month history of altered leg sensation/weakness commencing with bilateral distal sensory disturbance progressing to pins and needles in a stocking distribution with bilateral leg weakness and reduced mobility.

Neither disclosed any medical history, nor recalled using other recreational drugs except for case 1 who chose to smoke cannabis occasionally. Both confirmed consuming five to six units of alcohol socially per week. History of N₂O consumption was similar for both cases and varied from 50 to 100 canisters per month (usually with large quantities in a single sitting). However, both cases describe an acute escalation in consumption to 100–200 canisters in the week prior to hospital admission. Case 1 was in full-time education, and case 2 worked part time as a football coach. Both cases lived in rented flats; case 1 with his mother, and case 2 with his parents and siblings.

Both patients presented with normal cognition, orientation and fluent speech. The cranial nerves and upper limb examination were normal. There were no cerebellar signs. The sensorimotor lower limb impairments (table 1) included distal lower limb weakness measured using the Medical Research Council ordinal rating scale⁴⁵ and translated into diminished ambulatory function with both cases requiring aids to transfer or walk. Neither case presented with any urinary or bowel dysfunction.

INVESTIGATIONS

Methylmalonic acid (MMA) serum levels were elevated above the normal threshold level of 243 nmol/L,⁴⁶ more so in case 1 (table 1) indicative of vitamin B₁₂ deficiency. Serum folate levels in both cases were unremarkable (3.8 µg/L and 4.9 µg/L for cases 1 and 2, respectively; both within the normal range of 3.1–20.5 µg/L). Other investigations are summarised in table 1.

DIFFERENTIAL DIAGNOSIS

Thorough history taking identified a gradual onset of symptoms over several days, ruling out a vascular cause of neurological dysfunction such as spinal or cerebral stroke. Further neurological assessment and clinical investigations (table 1), along with a history of excessive N₂O intake, led to a diagnosis of SADC of the spinal cord causing sensorimotor myelopathy.

TREATMENT

Case 1

Intramuscular hydroxocobalamin injections (1 mg) were provided daily for 1 week and then on alternate days for a further week. The patient was advised to cease all recreational drug use including N₂O inhalation. Physiotherapy treatment (total with therapist 445 min) was provided in 11 sessions over a 12-day inpatient stay (mean 40.5 min/session). Clinical assessment revealed bilateral lower limb sensorimotor weakness, and a total score of 7 out of 56 on the Berg Balance Scale (BBS—a 14-item ordinal measure that assesses static balance, functional mobility and falls risk⁴⁷) indicated difficulties in functional mobility and balance particularly a reliance on visual sensory cues, and poor

Table 1 Clinical features and investigation findings at initial assessment

Case	Sensation			Motor		Chemistry	Diagnostics		
	LT	Proprioception	Vibration	Strength*	DTR	MMA (nmol/L)	MRI	Neurophysiology	Ambulatory function
1	Impaired/absent LT L1–S2	Symmetrically absent at 1st metatarsal and ankle, intact at knee	Absent below T4	5/5 hip and knee 2/5 ankle	Absent ankle Reduced knee	16930	Dorsal column signal abnormality: T3–T10 levels confirmed subacute combined degeneration	Sensorimotor neuropathy with mild conduction slowing and axonal loss	Mobile 10 m with frame and assistance ×1
2	Impaired/absent LT L1–S2	Symmetrically absent at 1st metatarsal, ankle and knee	Absent below T10	4/5 hip and knee 2/5 ankle	Absent ankle Reduced knee	2629	No intrinsic or compressive cord, cauda equina or neural lesion demonstrated	Not completed	Step round transfer with assistance ×2

All clinical tests shown relate to the lower limbs.

*Strength testing as per Medical Research Council ordinal rating.⁴⁵

†Ambulatory function—assistance ×1 relates to one person (×2 relates to two people) being at touch distance necessary to prevent loss of balance.

DTR, deep tendon reflex; LT, light touch; MMA, methylmalonic acid.

planning of whole body transitional movement and reactions to centre-of-mass excursions. Seeing as the mean (\pm SD) BBS for a sample of ambulatory spinal cord injured-paraplegic participants (American Spinal Injury Association (ASIA) Impairment Scale D (AIS-D))⁴⁸ is 44.8 (\pm 13.0),⁴⁹ case 1's functional mobility and balance deficits at initial assessment were profound, a finding supported by their slow observed average (10m) self-selected gait velocity (0.29 m/s) indicative of a home-only ambulator.⁵⁰ Overall activities of daily living function was moderate (modified Barthel Index⁵¹ 12 out of 20). The aims of physical rehabilitation treatment were safe community ambulation with or without walking aids. Treatment specification was undertaken based on the RTSS⁴³ (table 2) and includes interventions designed to affect volitional rehabilitation behaviour using a behaviour change model that considers three essential conditions: capability, opportunity and motivation (COM-B system).⁵²

Case 2

Intramuscular hydroxocobalamin injections (1 mg) for 1 week were provided which was reduced to alternating days for a further week. He was also prescribed oral paracetamol 1 g four times a day, codeine phosphate 30 mg four times a day and gabapentin 300 mg three times a day for symptom control. Similarly to case 1, the patient was also advised to cease recreational N₂O inhalation. Physiotherapy treatment (370 min) was provided in 12 sessions over a 14-day inpatient stay (30.9 min/session). Assessment revealed similar impairments to case 1: bilateral lower limb sensorimotor weakness (table 1). A combined time of 0/120 s on the modified Clinical Test of Sensory Interaction on Balance (CTSIB-M—a performance measure quantifying postural standing control under four sensory conditions each tolerated for up to 30 s for a maximum score of 120 s^{53 54}) indicated their sensorimotor balance control was profoundly impaired. In fact, case 2's impairments were so profound compared with case 1; they were unable to ambulate at all and required maximal assistance to transfer safely. The aims of treatment were nonetheless the same as in case 1 and remained safe community ambulation with or without walking aids. Treatment specification was undertaken based on the RTSS (table 2).

While folic acid treatment was not indicated to correct abnormal serum folate levels in either of our cases, it should be noted that correcting any diagnosed folate insufficiency should be undertaken only after initial phase B₁₂ replacement to prevent worsening of the neurological spinal cord degeneration.⁵⁵

OUTCOME AND FOLLOW-UP

Cases 1 and 2 improved with treatment and their MMA concentration levels were within the normal range prior to hospital discharge. There were however residual sensorimotor deficits. In case 1, plantarflexor strength was graded at 5/5 on reassessment prior to hospital discharge, but dorsiflexion strength had only recovered to 3/5 bilaterally. Proprioception was no longer impaired at the ankle, but distal impairments remained bilaterally. In addition, there were residual sensory impairments to light touch on the left in an L1–S1 and on the right an L5 dermatomal distribution. He was independently mobile with foot-up splints (due to dorsiflexor fatigue over longer distances) and two elbow crutches up to 45 m but could not ambulate outdoors. Average gait speed increased from 0.29 to 0.41 m/s, an increase of 0.12 m/s, which is a clinically meaningful difference⁵⁶ but still less than the comfortable average gait velocity threshold of 0.49 m/s that delineates community from household-only ambulation.⁵⁰ His sensorimotor recovery translated to a meaningful

improvement in his BBS (47 of 56), and a Barthel score of 17 out of 20 on discharge. The patient was duly referred to local community physiotherapy services available at their discharge residence for treatment as specified.

On discharge, case 2 had residual impaired sensation to light touch bilaterally in an L4–S1 dermatomal distribution. Proprioception at the first metatarsals remained absent bilaterally. He was independently mobile indoors with two elbow crutches up to 60 m and was able to control the knee avoiding recurvatum during stance phases in \geq 90% of gait cycles. Indoor independent gait velocity at discharge was 0.38 m/s. However, he could not ambulate outdoors independently similarly to case 1. His recovery translated to an improved CTSIB-M (71/120 s) revealing residual reliance on visual sensory information, and a Barthel score of 19 out of 20. He too was duly referred for outpatient therapy for treatment as specified; no community therapy options were available at his discharge residence.

Case 1 chose to not participate in further therapy or medical follow-up. In contrast, case 2 attended further physiotherapy and was reviewed in an outpatient medical clinic 3 weeks post-hospital discharge. He was ambulating independently but self-reported mildly impaired balance. While proprioception was intact on clinical examination, he presented with symmetrical, lower limb impaired light touch sensation in a stocking distribution, and could only tolerate the Romberg position (eyes closed)⁵⁷ for 22 s without excessive sway or losing balance.

At a subsequent outpatient medical clinic review at 9 months post-hospital discharge, case 2 reported a full recovery including being able to sprint on a treadmill in his physiotherapy sessions. Repeat neurophysiology tests showed improved conduction velocities and normal sensory studies; however, compound muscle action potentials in the lower limbs remained below the normal range.

DISCUSSION

We observed profound sensorimotor impairment caused by excessive N₂O abuse which led to SACD of the spinal cord in two cases. The cases presented with typical features that collectively confirmed the diagnosis. First, a clinical myelopathy anatomically localised to the spinal cord (confirmed by MRI studies in case 1); second, evidence of vitamin B₁₂ deficiency; and lastly, an absence of identifiable central or peripheral nervous system pathology in keeping with the clinical findings.²³ The lack of confirmatory imaging studies in case 2 is not unusual—a published series of 54 patients with dorsal column injury reported low sensitivity with imaging confirming the diagnosis only in 8 patients (14.8%).⁵⁸ Previous literature has reported excessive N₂O use and vitamin B₁₂ deficiency cases whose main presenting symptoms were weakness, paraesthesia and ataxic gait,^{22 28 32} falls,^{31 33} absent or impaired deep tendon reflexes and diminished vibration sense,^{26 29} hyporeflexia,³⁴ limb proprioceptive abnormalities^{27 30} and wide-based steppage gait,³⁵ not dissimilar to the present cases.

While resolution of symptoms following vitamin B₁₂ therapy is sometimes incomplete in older patients (mean (\pm SD) age 55.9 (\pm 15.5) years), it tends to be complete in younger patients (39.8 (\pm 18.8) years).²³ So it was not surprising that the two young cases presented in this paper progressed in their recovery and made a near full sensorimotor recovery at 9 months, at least in the second case. Because their sensorimotor function returned to near normal, we can presume that the two cases did not re-abuse N₂O while we followed them up. If they had re-abused N₂O inhalation during the follow-up period, then B₁₂ would have

Table 2 Treatment specification based on the RTSS for cases 1 and 2

Description of clinical interaction	Case	Target		Group	Volition type	MOA	Ingredients	
		What/in	what way				Ingredient	Dosing parameters
The PT facilitates stretching, and voluntary performance of dorsiflexion and plantarflexion exercises for strengthening and maintenance of musculoskeletal integrity. The PT teaches patient how to practise for outside of therapy sessions.	1 & 2	Ankle dorsiflexion and plantarflexion strength/increase	O	DV	Muscle fibre hypertrophy		► Verbal description and demonstration of open-kinematic chain dorsiflexion	► N/A
							► Active right, left and bilateral open-chain dorsiflexion with PT	► 1 × max 10 reps each (or until perceives fatigue), in long sitting or (progression) in sitting
							► Verbal description and demonstration of bilateral closed-chain dorsiflexion	► N/A
							► Standing, back to wall ≥10 cm away from heels, feet at shoulder width—controlled leaning back to wall and return to stand with PT	► 3 × 15 reps (or until perceives fatigue), increase distance if no fatigue
							► Verbal description and demonstration of bilateral calf raises	► N/A
							► Active bilateral calf raises with therapist, arm support for balance	► 2 × 10 reps (or until perceives fatigue) in standing
							► Unsupervised seated open-chain active right, left and bilateral dorsiflexion/plantarflexion	► 2 × max 10 reps (daily in long sitting or progression) in sitting
							► Opportunity to practise technique under supervision of therapist	► Until correct technique achieved
							► Positive reinforcement feedback from therapist	► On correct performance of exercise
							► Provision of exercise sheet with images and dosing	► N/A

Continued

Table 2 Continued

Description of clinical interaction	Case	Target			Group	Volition type	MOA	Ingredients		Dosing parameters
		What/in what way						Ingredient		
The PT provides the patient with a resting ankle splint to wear in bed and teaches self-directed plantarflexor stretches with towel	1 & 2	Passive ankle range of movement/maintain 90°	O	DV			Maintained sarcomere length	► Apply ankle-foot resting splint	►	2× daily
								► When supine in bed	►	1 hour (progress to max 4 hours in increments of 1 hour)
								► Passive stretch to calves with towel	►	2× daily per foot for 2 min
								► Long sitting, manipulating towel behind ball of one foot and toes, holding both ends of towel and applying calf stretch with knee straight	►	Progression when 3/5 MRC strength—standing (hands on support), heels lowered over a step, knees straight
Self-application of ankle-foot resting splint/achieve independence	S		S	DV			Learning by doing	► Ankle-foot resting splint	►	N/A
								► Provide opportunity to practise donning/doffing	►	Until independent
								► Verbal reinforcing feedback	►	On each trial
								► Access to ~1 m length rolled-up towel	►	N/A
Self-application of passive ankle stretching technique/achieve independence								► Demonstration of long sitting, placing towel behind foot and toes, and applying calf stretch with knee straight	►	N/A
								► Provide opportunity to practise Physical facilitation and verbal corrective feedback	►	Until independent
								► Verbal education about risk of donning/doffing ankle resting splint (check for skin integrity), and not donning (losing range at ankle)	►	N/A
								► Written instruction on dosing and technique	►	N/A
Independent ankle-foot resting splint programme/perform as directed	R		R	V			Cognitive and affective information processing	► Logging record for nursing care staff	►	Night-shift handover: duration/frequency, skin integrity
								► Verbal explanation of benefits of stretching programme	►	N/A
								► Verbal and written information on technique and dosing	►	N/A

Continued

Table 2 Continued

Description of clinical interaction	Case	Target		Group	Volition type	MOA	Ingredients	
		What/in what way	How				Ingredient	Dosing parameters
The PT rehabilitates the patient's dynamic balance deficits using a bimanual reaching task and changing the context within sessions progressively.	1	Dynamic balance in standing/improve	S	DV	Learning by doing		▶ Football to hold bimanually	▶ Size 5 football
							▶ Parallel bars & chair to sit on for safety	▶ N/A
							▶ Therapist demonstration of technique	▶ N/A
							▶ Patient passes football to therapist up/down, forward/back, left/right directions within reach boundary in reaction to therapist instruction in standing with eyes closed	▶ Maintain—80% success rate without patient touching parallel bars, opening eyes, or therapist touch to prevent loss of balance
							▶ Variation of exercises:	▶ Progression of variations:
							▶ Change foot/ground interface	▶ Progress to foam balance mat if 80% success rate achieved
							▶ Change ball	▶ Increase mass of ball if 80% success rate achieved
							▶ Increase/vari passing tempo	▶ Increase tempo if 80% success rate achieved
							▶ Increase/vari passing distance	▶ Increase passing distance if 80% success rate achieved
							▶ Change body orientation	▶ Receive ball, turn 180° with eyes open before passing ball
The PT rehabilitates the patient's standing balance and proximal joint lower limb strength deficits by facilitating an exercise regime with the patient changing the context within sessions progressively.	2	Knee extension strength/increase	O	DV	Muscle hypertrophy		▶ Change feet configuration	▶ Progress to tandem stand, single leg if 80% success rate
							▶ Change height level when receiving ball	▶ Transfer to step-up for high ball, or squat for low ball
							▶ Leg squats	▶ 3×8 reps (or until fatigue) bilateral, progress—decrease squat height or single-leg squat
							▶ Therapist demonstration of technique	▶ N/A
							▶ Standing with hands on bar, plinth situated behind for safety	▶ N/A
							▶ Bridges in supine	▶ 3×10 reps (or until fatigue), progress to single-leg bridge
							▶ Therapist demonstration of technique	▶ N/A
							▶ Lying on plinth bent knee drop-outs	▶ 3×10 reps (or until perceives fatigue)
							▶ Therapist demonstration of technique	▶ N/A
							▶ Single leg stands	▶ 3×10 reps (or until needs support for balance)
The PT rehabilitates the patient's standing balance and proximal joint lower limb strength deficits by facilitating an exercise regime with the patient changing the context within sessions progressively.	2	Hip add/abductor strength/increase	O	DV	Muscle hypertrophy		▶ Bilateral standing on foam cushion	▶ 3×10 reps (or until needs support for balance)
							▶ Stand-by support from PT	▶ N/A
							▶ High plinth in front, chair behind for safety	▶ N/A
							▶ Learning by doing	▶ 3×10 reps (or until needs support for balance)
							▶ Balance in stance; improve	▶ 3×10 reps (or until needs support for balance)
							▶ Balance in stance; improve	▶ 3×10 reps (or until needs support for balance)
							▶ Balance in stance; improve	▶ 3×10 reps (or until needs support for balance)
							▶ Balance in stance; improve	▶ 3×10 reps (or until needs support for balance)
							▶ Balance in stance; improve	▶ 3×10 reps (or until needs support for balance)
							▶ Balance in stance; improve	▶ 3×10 reps (or until needs support for balance)

Continued

Table 2 Continued

Description of clinical interaction			Target		Ingredients			
			What/in what way	Group	Volition type	MOA	Ingredient	Dosing parameters
The PT teaches the patient to self-monitor exertional fatigue.	1&2	Ability to monitor fatigue/improve performance as directed	S	DV	V	Learning by doing	► Opportunity to practise self-rating exertional fatigue using the NRS–FRS ²	► Until patient reports confidence in using scale
							► Verbal information on importance of managing fatigue	► N/A
							► Education on effect of fatigue on function and quality of life	► N/A
The PT provides the patient with bilateral Boxia splints to compensate for foot drop and to increase gait velocity.	1&2	Replacement of antigravity dorsiflexion function of ankle dorsiflexors	R	V	Habituation to passive support of ankle	Learning by doing	► Provision of bilateral Boxia foot-up splints	► Use in ambulation until ≥3/5 MRC dorsiflexion strength
							► Provide opportunity to practise donning and doffing splints	► Until independent
							► Physical facilitation	► As required
The PT rehabilitates gait and transfer tasks and provides feedback to provide gait re-education.	1&2	Independence with ambulation on level surface/increase	S	DV	Learning by doing	Learning by doing	► Verbal corrective feedback	► As required
							► Provide opportunities to practise ambulatory function within safe exertional fatigue level and balance function independently	► Maximise walking distance or tempo or contexts up to ≥2 exertional fatigue levels above resting state
							► Use walking aid(s)	► Progression—frame to elbow crutches to stick to no aid
							► Provide opportunity to practise whole-body transitions with PT	► With therapist, daily, ≥15 min
							► Provide verbal evaluative feedback	► Intermittent, delayed knowledge of performance at rest intervals
							► Change direction, obstacles	► Turns, cuts, step-overs, introduce uneven ground
							► Include gait initiation and cessation	► Instruct
							► Include reaching activities	► As purpose to ambulation
							► Include head movements	► Include, vary tempo, specify eye contact to targets, introduce walking and reading/talking/carrying objects
							► Provide opportunity to practise bed, chair and toilet transfers	► Until independent
The PT rehabilitates transfer methods for functional independence.	1&2	Bed, chair and toilet transfers/achieve independence	S	DV	Learning by doing	Learning by doing	► Opportunity to practise bed, chair and toilet transfers	► Until independent
							► Verbal performance feedback	► On each attempt
The PT coaches gait re-education due to poor proprioceptive control and episodes of knee recurvatum.	2	Knee recurvatum during gait stance phase/reduce	S	DV	Learning by doing	Learning by doing	► Provide opportunity to self-correct knee recurvatum in gait	► N/A
							► Verbal coaching	► If knee recurvatum observed > 1× every 3 gait cycles
							► Provide opportunity to practise stepping with stable knee	► 3×8 reps each leg, then repeat continuous gait practise
							► In parallel bars for bilateral upper limb support	► N/A
							► PT provides manual support at femoral segment and hip	► 3×8 reps each leg, then repeat continuous gait practise
DV, direct target for volitional; FRS, Face Rating Scale; MOA, mechanism of action; MRC, Medical Research Council; N/A, not applicable; NRS, Numerical Rating Scale; O, organ functions; PT, physiotherapist; R, representation; RTSS, Rehabilitation Treatment Specification System; S, skills and habits; V, volitional.								

been deactivated very rapidly with a commensurate deterioration in neurology and we would have expected to have observed a relapse in balance and ambulation dysfunction.⁵⁹ Re-abuse could be a sign of addiction to N₂O although N₂O inhalation addiction is contentious within the literature.^{18 60 61} While clinical discourse to persuade cessation of use appears to have been successful in these two cases, clinicians should be aware that patients presenting with acute recreational N₂O toxicity should be provided with necessary psychosocial support if difficulties in self-selected cessation of abuse are suspected.³⁸

The positive outcomes overall in the two cases presented here are almost certainly due to the medical diagnostic procedures and subsequent clinical decision to commence vitamin B₁₂ treatment in a timely way with regular monitoring. What is less clear is whether the equally timely and novel specification of rehabilitation interventions using the RTSS led to a more reasoned and tailored physical therapy approach. To our knowledge, this is the first specified rehabilitation report using the RTSS in cases of this type. By acting as a coherent framework for specifying rehabilitation interventions based on the clinician's treatment theory, the RTSS fractionates multidimensional and progressive rehabilitation interventions into entities (treatment components) that are amenable to clinical adoption (including among clinical colleagues) and empirical research.⁴¹ Thus, the specification described herein acts first as a reasoned approach for fellow rehabilitation clinicians to use with these patients downstream of the acute hospital; second, as an example for other clinicians treating similar cases; and lastly, as a record of the specified treatment to inform researchers. It is worth noting though that the treatment specifications provided are examples peculiar to the two cases presented. They are not meant as a prescriptive regime for all patients presenting with sensorimotor system impairments due to recreational N₂O toxicity and functional B₁₂ deficiency. Nonetheless, we contend that in successfully specifying the treatment in this way, the patient's treatment was reasoned and tailored and thus verifies the RTSS's utility.

The impairments (bilateral lower limb sensorimotor) and aims of treatment (restitution of normal ambulatory function) were specified identically between cases. Treatments were also identical based on organ function targets (muscle strengthening and stretching), and skills and habits targets (function balance and ambulation practise tasks). Representation targets were identical too. They were designed to influence cognitive processes when managing the musculoskeletal integrity and injurious falls risks inherently associated with distal lower limb paralysis, and ensure the consequences of failing to voluntarily manage those risks were understood.

However, there were treatment specification differences between cases because case 2 initially presented with impairments so profound that no ambulatory function was possible. Case 2 presented with proximal lower limb joint symmetrical weakness and more widespread proprioceptive loss. Therefore, therapy time was prioritised towards specifying a more widespread and explicit strengthening programme and more rudimentary static balance tasks compared with case 1.

What's more, when case 2 progressed to ambulating, knee recurvatum (KR) was observed during some, but not all, stance phases. KR is a relatively common impairment observed in other neurological pathologies (eg, 30%–50% of ambulatory hemiplegic stroke survivors^{62 63}). In normal continuous gait, coordination between pretibial muscle contraction (which restrains ankle plantarflexion and allows the tibia to move forward over the foot during weight acceptance) and triceps surae/quadriceps contraction (crucial to restraining tibial forward motion during

mid-stance while the femoral segment progresses forward distal to it with extension at the knee) controls knee flexion and forward tibial movement over the stationary foot in stance phases.⁶⁴

While the main cause for gait KR is premature overactivity or spasticity of the plantarflexors which prevents the knee from flexing during loading response in early stance^{63 65} or vasti hypertonia,^{66 67} we reasoned that KR in case 2 was due to dorsiflexion/plantarflexion muscle weakness, poor proprioception and reliance on forward placed walking aids. This is because no muscle hyper-reflexia was observed on assessment at the ankle or knee. The variability of KR observed in case 2 was probably due to instances when knee hyperextension was simply deployed to stabilise the knee in stance by adopting a quadriceps-avoidance strategy sometimes seen in anterior cruciate ligament deficient gait⁶⁸ in combination with plantarflexion weakness during mid-stance.⁶⁹ Our theory therefore was that treatment ingredients targeting muscle weakness and sensory integration (including proprioception) in static balance would ameliorate the KR in case 2. Passive treatment ingredients designed to target KR more directly to support the approach would include issuing of rigid ankle/foot orthotics which were avoided here. Instead, gait re-education was deployed via instructions based on implicit motor learning to avoid KR with delayed knowledge-of-performance feedback.⁷⁰

Specified treatments were not then all identical between cases and support the argument that treatment was tailored for the two cases. This is one of the advantages of the RTSS. Its coherent framework is intended to administer the complexity of rehabilitation practice in the interactions of clinical impairments, dysfunctions and participation in society in order to specify individuals' rehabilitation treatment.⁴³ Yet, the two cases' rehabilitation treatment aims were similar and were focused on ambulation function. Acute adult inpatient physical rehabilitation often includes stressing motor systems toward safe, independent ambulation because ambulatory function is a key milestone for discharge planning. This is important within the goal of reducing acute hospital length of stay (LOS) which is itself dependent on coherent, equitable and resourced rehabilitation services downstream of an acute setting. But the problem with yoking rehabilitation with minimising LOS is that the rehabilitation aim is often achievement of minimal *adaptive* ambulatory function necessary for a safe discharge. The aim instead should be the *restitution*⁷¹ of ambulatory function, especially since stroke⁷² and spinal cord-injured⁷³ neurorehabilitation patients express it as their primary goal. Restitution of ambulatory performance therefore requires rehabilitative progression towards premorbid performance, not merely an assessment of current ambulatory performance.

The RTSS includes accurate specification of rehabilitation progression and was included throughout the two cases described. For ambulatory function, a separate treatment ingredient was included so the two cases were proficient in self-monitoring their exertional fatigue—a common symptom burden for patients with acute spinal cord injury.⁷⁴ That allowed the ambulatory treatment's progression to be specified in both cases by attributing the therapeutic dose of ambulatory practise (distance or time walked) with the patient's increase in self-rated exertional fatigue (using a dual Numerical and Face Rating Scale⁷⁵) during ambulatory treatment ingredients.

Similar separate treatment ingredients were included in our specification designed for the cases to attain skills and habits in managing the risk to their musculoskeletal integrity by applying ankle resting splints and foot-up devices when ambulating. We contend that without the RTSS's coherent framework, there

would be a risk that therapists might not have clinically reasoned tailored treatments as thoroughly, nor been as accurate in specifying it.

In conclusion, the combination of timely medical treatment and specific and clinically reasoned rehabilitation in a structured format using the RTSS provided excellent functional outcomes in both the acute and subacute phases post-injury in two individuals who sustained N₂O-induced spinal cord injury. Stronger conclusions can be drawn when future studies determine the impact of rehabilitation on clinical outcomes at the impairment, activity and participation levels in this patient cohort by virtue of using the RTSS.

Patient's perspective

Case 2 and his next of kin were able to provide their perspective of their assessment and treatment.

Before the hospital admission we had no idea about the possible side effects of the inhaled canisters. Lots of the young people where we live took them at parties and we believed that they were risk free, we had never heard of others experiencing medical complications from taking them.

The profound loss of ambulation was terrifying particularly because there were no initial explanation why these symptoms had occurred.

When we initially went to hospital the doctors weren't sure what was the cause of the weak legs and the inability to walk. After the scans the doctors explained that there was a problem with the nerves in the back and they weren't totally sure if my son's walking would fully recover. They thought that the gas canisters were the cause because of some of the blood test results. We were all shocked that this had happened and it was scary to hear that someone so young might have long term effects that they would have to live with. It was hard for us not to know what the future may hold for him, we felt very worried.

However, the medical assessment and treatment and the inpatient physical therapy rehabilitation delivered enabled meaningful recovery – a recovery that was complete after receiving longer term community physiotherapy. We feel lucky that my son has made a full recovery, it was slow to begin with and he had to work hard in physio sessions in the hospital. Unfortunately it took quite a long time for him to get seen in the physio clinic after leaving hospital, but he's now managing to do everything he could do before the injury. We are thankful for all of the care that my son received.

Learning points

- Rates of nitrous oxide recreational use are rising, meaning that incidents of abuse and associated subacute combined degeneration pathology may also rise leading to profound sensorimotor dysfunction.
- Timely diagnosis and medical treatment to reverse vitamin B₁₂ deficiency in combination with skilled physical rehabilitation led to favourable outcomes.
- Specified treatment from rehabilitation clinicians in the acute phase after neurological pathology in these two cases shows that timely, tailored and theoretically reasoned treatments can be put into practice if the goal is to reconstitute normal movement function.

methodology, validation, investigation, resources, writing (review and editing). JG—conceptualisation, methodology, validation, resources, writing (original draft), writing (review and editing), visualisation, investigation, writing (review and editing). GDJ—conceptualisation, validation, resources, data curation, writing (original draft), writing (review and editing), visualisation, project administration.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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