pain and stiff neck 2 months previously, which had spontaneously resolved. An indepth retrospective anamnesis failed to reveal any evidence of tick bites or erythema chronicum migrans, but the patient had undertaken open air activities in a woody countryside at the end of June.

Physical examination showed severe weakness (2/5) in the proximal muscles of both upper limbs. Strength was only mildly reduced in the hands (4.5/5) and was normal in the legs. No sensory deficit was present. Diffuse fasciculations were observed in both shoulders. Deep tendon reflexes were not elicited in the right arm. Of note, Lhermitte's sign was absent. There were no meningeal signs or fever.

Cervical spine MR examination showed abnormally increased signal intensity within the anterior horns of the cord ''grey butterfly'' from C2 to C5 on the T2 weighted images (fig 1B, D), together with increased thickness and strong contrast enhancement of the anterior radicelles of the same dermatoma on post-contrast T1 weighted images (fig 1A, C). Additional abnormal post-contrast enhancement was also observed within the pia mater (fig 1A) and the anterior horns (fig 1C). Brain MR examination was unremarkable.

Neurophysiological studies demonstrated elective involvement of motor nerves at the radicular or motoneuronal level. Needle electromyography showed signs of acute denervation with spontaneous fibrillations in both deltoid and biceps brachii, with a right-sided predominance. Abnormalities were also present in the first dorsal interosseous muscles and in the extensor digitorum communis, but to a lesser degree. Sensory and motor conduction velocities of the ulnar and median nerves were normal, as well as the latency and the amplitude of the F waves.

Standard haematological tests and biochemical assays were normal. Serology was negative for HIV, hepatitis B and C, and syphilis (TPHA and VDRL tests). However, serological tests for Lyme disease (Euroimmun Anti-Borrelia plusV1sE ELISA IgG and Euroimmun Anti-Borrelia ELISA IgM, Lübeck, Germany) were strongly positive in serum for both IgM (IgM ratio of 5.74, normal value <1.0) and IgG (133 relative unit (RU)/ml, normal value <20) antibodies. The IgG and IgM positive samples were confirmed by a commercial western blot assay (Euroline-WB; Euroimmun AG) showing specific patterns (OspC for IgM antibodies, V1sE, p83, p39, p31, 30, OspC and p17 for IgG antibodies).

CSF analysis showed 79 cells/mm^3 with 79% lymphocytes, 12% reactive lymphoblasts and 9% monocytes. The total protein content was elevated (98 mg/dl; normal range 20–55). Considerable intrathecal synthesis of IgM was present (intrathecal fraction at 76%) with a lower synthesis of IgG (intrathecal fraction at 17%). However, several CSF restricted oligoclonal IgG were present. Bb PCR was negative. However, native CSF contained 58 RU/ml of anti-Bb IgG antibodies confirmed by Euroline-WB assay, whereas serum diluted at the same IgG concentration was negative. Such results demonstrated intrathecally restricted production of these antibodies, which is a key feature of Lyme neuroborreliosis.[3]

Intravenous ceftriaxone (2 g daily) was given for 2 weeks and the weakness slowly improved thereafter. The clinical examination normalised 6 weeks after the start of treatment. A follow-up MR examination performed 6 months later demonstrated complete normalisation of the spinal status.

The diagnosis of Lyme neuroborreliosis was therefore biologically supported by the positive blood IgM and IgG serology for Bb, together with the strong intrathecal synthesis of IgM and IgG antibodies seen on analysis of CSF. In addition, the patient's status dramatically improved with ceftriaxone antimicrobial treatment. The clinical presentation was, however, atypical, because of the absence of pain with nocturnal exacerbation, the purely motor involvement with absent tendon reflexes in the upper right limb and the diffuse fasciculations in the shoulders. These atypical signs and symptoms nicely corresponded to the cervical spinal cord imaging showing selective inflammatory involvement of anterior grey matter and spinal roots.

Recently, eight documented cases of early subacute Bb myelitis have been reported.[2] In six of these cases, painful radicular symptoms appeared before spinal cord signs. Most patients exhibited CSF mononuclear pleocytosis and cervical spinal cord lesions on MRI. All but one patient had a favourable outcome with appropriate intravenous antibiotherapy. Absence of encephalitic involvement and cranial nerve palsy, frequent combination with meningoradiculitis and good response to antibiotherapy are key features allowing discrimination between early and late variants of Bb myelitis.

Leptomeningeal enhancement and nerve root enhancement of the cauda equina on post-contrast T1 weighted MR images have been reported in spinal Lyme neuroborreliosis.[4] Enhancement of the cervical nerve roots has also been reported in this condition.[5] Concomitant enhancement of the leptomeninges, anterior horns and anterior radicelles of the cervical spine has never been described to date. The close correlation between clinical and MR features was a prominent feature of this clinically and radiologically atypical case of Lyme neuroborreliosis.

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The vestibulo-ocular reflexes during head impulse in Wernicke's encephalopathy

Ocular motor findings in Wernicke's encephalopathy (WE) include gaze evoked nystagmus (GEN), central positional nystagmus, weakness of abduction, internuclear ophthalmoplegia and horizontal or vertical gaze palsy to total ophthalmoplegia. Another feature of WE is vestibular paresis.[1 2] Previous studies documented hypoactive vestibular responses to both caloric and rotational stimuli, and a short vestibulo-ocular reflex (VOR) time constant. To address differential susceptibility of individual semicircular canals (SCC) according to stimulation frequency, we measured high acceleration VOR of the individual SCC using head impulse manoeuvres, and the low frequency VOR using bithermal caloric and rotatory chair tests in two patients with WE.

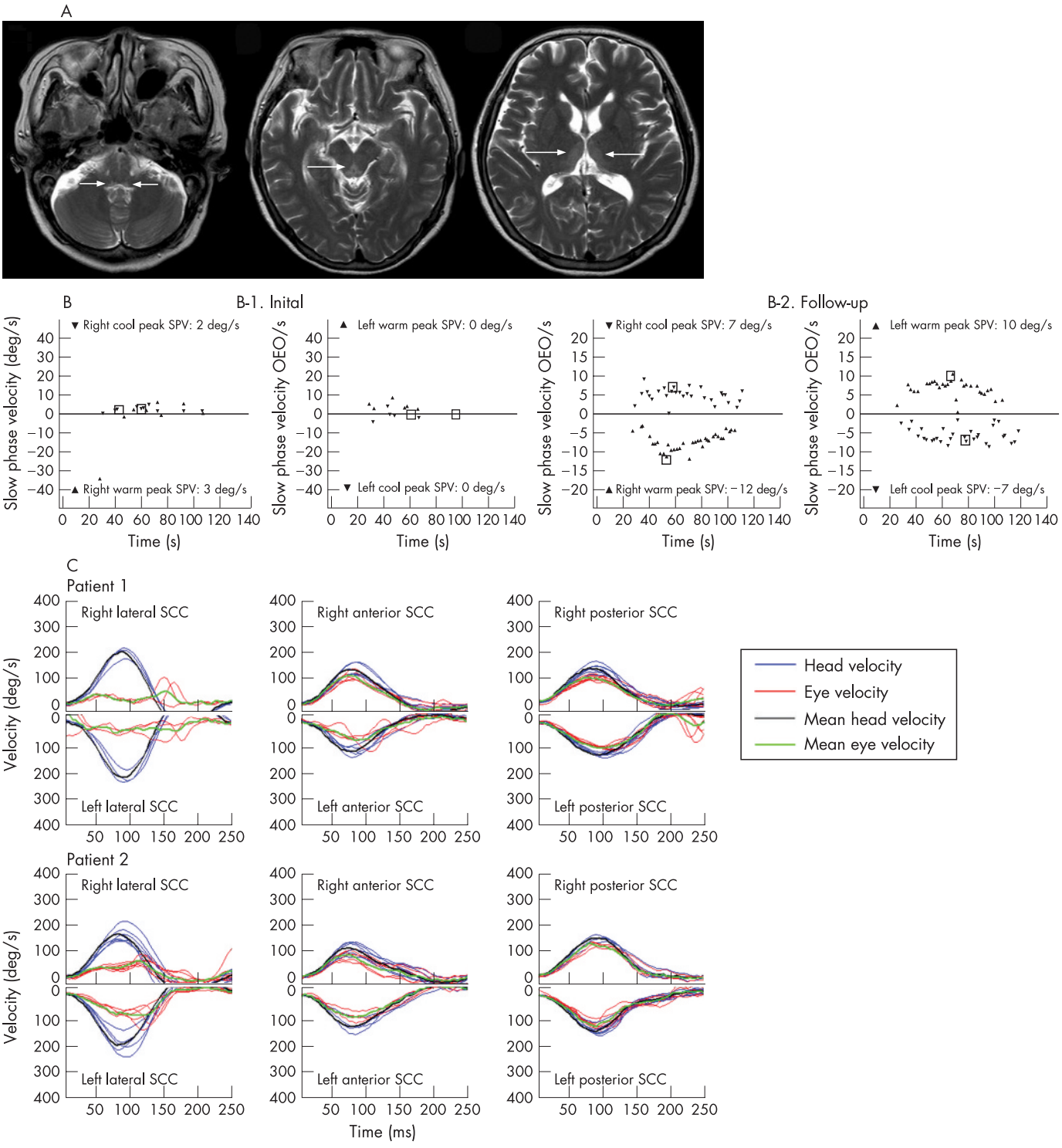
Case reports

Patient No 1

A 63-year-old woman had undergone Whipple's operation because of carcinoma of the ampulla of Vater 1 month previously and had received total parenteral nutrition (TPN). Two weeks after initiation of TPN, she began to suffer from anorexia, vomiting and vertigo which progressed to psychomotor slowing, apathy, forgetfulness and ataxia. On examination, she was awake but not attentive. She was fluent, but comprehension was impaired. The pupils were normal. Horizontal saccades were slowed and limited, and the limited ocular motor range did not improve with oculocephalic stimulation of the VOR. Other findings included horizontal GEN, limb dysmetria and severe truncal ataxia. T2 weighted MRIs showed hyperintense lesions at the periaqueductal gray matter, medial thalami and dorsal medulla (fig 1A). Three days after thiamine supplementation (100 mg intravenously daily), mental status, ataxia and horizontal gaze palsy began to improve.

Patient No 2

A 40-year-old man with diabetes mellitus presented with a 4 day history of progressive vertigo, ataxia, apathy and psychomotor slowing. He had been a heavy drinker for several years. Examination showed decreased alertness, perceptual disturbance and impaired memory. Horizontal saccades were slow and limited to approximately 30° from the primary position in both directions and the ocular motor range did not improve with oculocephalic manoeuvres. He also showed horizontal GEN and bilateral limb dysmetria. He could not stand unaided. Brain MRI was normal. With parenteral thiamine supplementation, mental status, ocular signs and ataxia recovered rapidly. However, memory impairments and GEN remained for 2 weeks after symptom onset.



The gains of the vestibulo-ocular reflex during high acceleration head impulses

Patient	Lateral SCC		Anterior SCC		Posterior SCC	
	Right	Left	Right	Left	Right	Left
1	0.38 (0.20)	0.31 (0.08)	0.84 (0.13)	0.66 (0.10)	0.72 (0.04)	0.80 (0.03)
2	0.44 (0.17)	0.53 (0.14)	0.76 (0.04)	0.70 (0.03)	0.85 (0.03)	0.86 (0.04)
Control	0.82 (0.06)		0.90 (0.09)		0.92 (0.08)	

Figure 1 (A) T2 weighted MRIs of patient No 1. Symmetrical hyperintense lesions are shown at dorsal portions of both the medulla, periaqueductal gray matter and medial portions of both thalami. (B) Bithermal caloric tests in patient No 1 show minimal responses in both ears initially (B-1), which markedly improved 6 months after thiamine replacement (B-2). (C) Head impulses in the plane of each semicircular canal (SCC) reveal severely impaired vestibulo-ocular reflexes (VOR) from both lateral SCCs while the VORs from the vertical SCCs are normal or minimally impaired. Normal data were obtained from 10 healthy subjects (seven men and three women, aged 29–70 years, mean 52.1 (SD 13.6) years) without a history of vestibular or neurological disorders.

Oculography

Saccadic latency was increased to 322 ms in patient No 1 and to 289 ms in patient No 2 (normal 215 (17) ms). The horizontal saccades were hypometric with a mean accuracy of 71% in patient No 1 and 70% in patient No 2 (normal 93 (4)%). Horizontal saccades were slow with a mean velocity of 170°/s for 10° saccades in patient No 1 (normal >186°/s), whereas it was normal (193°/s) in patient No 2. In patient No 1, smooth pursuit was impaired with a gain of 0.4 for a peak target velocity of 10°/s and a frequency of 0.16 Hz (age matched normal 0.69 (0.11)). The gain of rightward smooth pursuit was 0.62 and that of leftward 0.49 in patient No 2 (normal 0.75 (0.07)).

Caloric test, rotatory chair test and pure tone audiometry

Patient No 1 showed no responses during bithermal caloric irrigation of either ear (fig 1B-1). Sinusoidal rotation showed reduced gain and increased phase lead of the VOR. Time constants of pre- and post-rotatory nystagmus were reduced significantly (3.7 s, normal 14.6 (3.7) s). In patient No 2, the caloric responses were slightly decreased, and the gain and phase of the VOR were normal while time constants of pre- and post-rotatory nystagmus were moderately decreased (7.4 s). No patient showed hearing loss on pure tone audiometry.

Head impulse tests

In patient No 1, the VOR gain of each lateral SCC during head impulse was greatly reduced whereas gains of the vertical SCCs were minimally reduced for only left anterior and right posterior SCCs (fig 1C). In patient No 2, head impulse VOR gain of each lateral SCC was significantly reduced while that of vertical SCC was normal. Patient No 1 had a follow-up evaluation 6 months later, and still showed memory dysfunction, GEN, subnormal gain and phase lead of the VOR during sinusoidal rotation, and decreased gain of the VOR during the head impulses in the lateral SCC planes even though the caloric responses improved markedly (fig 1B-2). Time constants of the VOR increased slightly compared with the initial ones.

Discussion

Using the head impulse manoeuvre, we demonstrated differential susceptibility of the vestibular systems to thiamine deficiency. The VOR from the lateral SCCs was selectively or predominantly impaired and the vulnerability of the horizontal vestibular responses differed according to stimulation frequencies. According to previous histopathological studies, vestibular paresis in WE may be accounted for by lesions in the vestibular nucleus (VN).[1] Neuropathological examinations of patients with WE have revealed lesions in the VN, especially in the medial VN (MVN), nucleus prepositus hypoglossi, nodulus and uvula. MVN was most vulnerable to thiamine deprivation,[3] and histological abnormalities in the labyrinthine cristae and vestibular nerves were relatively minor in thiamine deficient pigeons.[4]

The vestibular neurons receiving different primary afferent input are distributed with some topographies across VN.[5] The neurons activated by the saccule, utricle, and anterior and posterior canals are located mainly in the lateral (LVN) and descending vestibular nuclei, while the neurons activated by the lateral canal were found mainly in MVN and LVN. Accordingly, we suggest that different susceptibility of the vestibular systems in our patients may result from selective vulnerability of the neurons in the MVN.

On follow-up evaluation, patient No 1 showed markedly improved caloric responses whereas the responses of rotatory chair and head impulse tests remained unchanged. In view of the selective deficit of high acceleration horizontal VOR during the acute phase in patient No 2, MVN neurons responsible for high acceleration horizontal VOR may be the most vulnerable to thiamine deficiency. A plausible explanation for this selective susceptibility may be high metabolic demands of the neurons responsible for the high acceleration VOR.

Alternatively, lesions of the abducens nucleus may impair conjugate horizontal saccadic, pursuit and vestibular eye movements in WE. However, no restriction in the horizontal ocular motor range, and selective deficit of high acceleration horizontal VOR and smooth pursuit in the presence of preserved saccadic velocities in patient No 2, do not support this assumption.

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Neurofibromatosis type 1 with involvement of the enteric nerves

Gastrointestinal symptoms in neurofibromatosis type 1 (NF1) is increasingly recognised, usually associated with gastrointestinal stromal tumours (GIST). We describe a patient with NF1 who presented with recurrent bowel symptoms and pseudo-obstruction. At laparotomy, a segment of distended transverse colon was resected and histological examination revealed extensive dysplasia of the enteric nervous system different from GIST. These findings indicate that diffuse abnormalities of the gastrointestinal nerves may be symptomatic in patients with NF1 and should be considered as a possible cause of ''functional bowel problems'' in these patients. We suggest that the autonomic nervous system (eg, in the gastrointestinal system) can be involved similar to other peripheral nerves in NF1.

The patient, aged 73 years, had a NF1 diagnosed according to established consensus criteria.[1] She had multiple small cutaneous neurofibromata, axillary freckling and café au lait spots. One large neurofibroma was removed at age 12 years. There was no evidence of skeletal abnormalities, optic gliomas, plexiform neurofibromata or malignant peripheral nerve sheath tumours. There was no family history of neurofibromata. Neurological tests, including examination of ability to sweat, was normal except for slight right-sided clumsiness and facial weakness, as a result of a previous stroke. Remarkably, some years ago she presented with a picture of intermittent abdominal pain, bloating and diarrhoea. CT and coloscopy showed a dilated segment of the distal transverse colon, in keeping with the diagnosis of chronic intestinal pseudo-obstruction. Because of the severity of her symptoms, she was referred for surgery.

At laparotomy, she underwent a transverse colectomy with resection of 21 cm of grossly distended colon. Centrally, the colonic circumference measured 36 cm. This led to some symptomatic improvement. However, she remains with considerable bowels symptoms, including gastroparesis and neurogenic bowel incontinence, confirmed by manometry and pudendus nerve stimulation, showing bilateral pathology. Additionally, she suffered from urinary stress incontinence and reduced bladder capacity, as shown by urodynamic measurements. MRI of the lumbar spine was normal.

Pathological examination of the resected colon showed that in the mesentery and on the serosal surface there were small neurofibromata, measuring up to 0.5 cm in diameter and appearing largely fibrotic on histology. Sections from the resection ends did not show any significant histological abnormality. However, in much of the central area of the colon there was hyperplasia and tortuosity of the nerves, particularly within the myenteric plexus (fig 1A), and also to a lesser extent within the submucosa. These changes were multifocal and associated with Schwann cell proliferation. These areas of hyperplasia were CD34 negative. Within affected areas there was a loss of ganglion cells from the myenteric plexus and the presence of scattered neurons within the inner and outer muscle layers, some of which were binucleate (fig 1B, C). Ganglion cell hyperplasia was not seen in the areas sampled. There was patchy fibrosis and chronic inflammation of the muscularis layers, but no convincing muscle hyperplasia.

Gastrointestinal involvement in NF1 is increasingly recognised and its frequency is estimated at 11–25%.[2] However, the vast majority of these cases are caused by GISTs,[3] which usually occur in the small bowel and frequently present with gastrointestinal bleeding. Although GISTs, as well as ganglioneuromas, are reported in NF1, they were not present in our case, and the areas of hyperplasia were CD 34 negative (in contrast with GISTs). Neurofibromata may also rarely occur in the gastrointestinal nerves but are usually asymptomatic; those present in our case were unlikely to be sufficient to cause the symptoms. The histopathological features in our case most closely resembled those described by Fuller and Williams[3] and Feinstat and colleagues,[4] although the focal ganglion cell hyperplasia in the submucosa was not noted in our case, and are best described as neuronal intestinal dysplasia. Similar lesions have also been described in cases of multiple endocrine neoplasia, type 2b,[5] indicating that separate genetic pathways can lead to this condition.