locomotor 2.7 years; eye/hand coordination 2.8 years; personal/social 3.1 years

He transferred from special to mainstream education. Coordination problems continued.

He made good academic progress but with behavioural difficulties. Psychometric testing at 12 years showed above average performance and superior language scores with slow handwriting. He passed seven GCSEs and three A levels.

He had early problems with chewing and feeding, difficulties with drawing, buttons and laces, toileting, and in using a knife and fork. Walking and running were abnormal and he could not use a bicycle. He showed slow alternating tongue movements, difficulty with manual gesture imitation, difficulty accessing hip movements, brisk tendon reflexes, and a few beats of clonus at the ankle. The motor picture was dominated by dyspraxia.

From year 2 he was restless with different compulsions—for example, switching lights on and off, scratching his teeth and nose, tooth grinding, hand fiddling, and face and shoulder movements. At 12 years, he had typical complex tics of his head, face and hands, and spasms, sometimes painful, of the jaw, legs, and abdomen. Vocalisations were either unintelligible and/or repeated words—for example, “zip”.

Brain MRI at 12 years was normal.

Three features suggest a good outcome for this child with an otherwise typical presentation with infantile spasms: late age of onset, treatment response, and the lack of pre-existing pathology. Severe language impairment at 2.5 years might suggest a variant of Landau-Kleffner syndrome (acquired epileptic aphasia),² but atypically with very early onset and complete recovery. The recovery period suggests a combination of visual and auditory agnosia and apraxia, which could be regarded as global impairment. Selective cognitive deficits—for example, language impairments with epilepsy—are described, and transient loss of visual function, but not prolonged visual agnosia with infantile spasms. Although subclinical seizures in sleep may have been the cause, sleep studies were not performed.

Language and visual recovery from 3.5 years may indicate earlier cortical storing of visual and language information which was not accessible. Clinical,¹ neurophysiological,³ and surgical⁴ evidence supports this idea. This report supports the hypothesis that epilepsy denies access to information rather than inhibiting its acquisition.

We also propose that the early epileptic encephalopathy (impairments occurring with epilepsy which are not explicable on a structural basis) associated with infantile spasms selectively disturbs cognitive accessing of visual and auditory information temporarily after 6 months of age but permanently before that age.

Apraxia in epilepsy is well recognised,⁵ but Tourette's syndrome is unexpected and may be an accidental association. When investigated, neither were driven by active epilepsy. No primary pathology was found and clinical manifestations, natural history, and imaging are not those of CMV encephalitis despite evidence of infection.

In conclusion, a boy with infantile spasms at 7-8 months developed severe global regression which seemed to be a combination of severe auditory and visual agnosia and apraxia which persisted for more than 2 years

after prompt relief of infantile spasms but continuing mild generalised seizures. He was assessed as severely cognitively impaired. A total spontaneous cognitive recovery occurred from 3.5 years. These impairments seem to have been a pervasive effect of epilepsy (an epileptic encephalopathy), and suggest that if infantile spasms occur before 6 months there is a high risk of permanent impairment but if later there is potential for recovery. During the prolonged phase of “agnosia” information seems to have been acquired but was not accessible. The comorbidity of Tourette's syndrome is unexplained.

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Motor evoked potentials from the external anal sphincter in patients with autosomal dominant pure spastic paraplegia linked to chromosome 2p

Hereditary spastic paraplegia (HSP) is the name given to a heterogeneous group of rare neurodegenerative disorders of the motor system characterised by slowly progressive spasticity and weakness of the lower limbs. About one third of patients with autosomal dominant pure spastic paraplegia (ADPSP) linked to chromosome 2p have lower urinary tract symptoms (LUTS) and additionally most of these patients also experience rectal urgency/urge incontinence (RUI) as well as sexual dysfunction.¹

The direct motor pathway to the external anal sphincter may be studied by transcranial magnetic stimulation (TMS), evoking compound muscle action potentials (CMAPs) with cortical and sacral stimulation.^{2,3}

This study was conducted to evaluate the motor evoked potentials (MEPs) from the external anal sphincter in patients with ADPSP linked to chromosome 2p and to obtain normative data.

After informed consent was obtained 11 definitely affected patients from six different families with ADPSP linked to chromosome 2p and 12 normal controls were included. The median age for the patients was 41 (range 20-64) years, and for the controls 40 (range 21-60) years. Six patients had LUTS and RUI, five of whom previously underwent urodynamic evaluation including measures of the bulbocavernosus reflex (patient numbers A2, C4, C6, K10, and L11 in Neerup Jensen et al¹). Five patients were without LUTS and RUI. Family details, clinical features, and

Figure 1 Cortical and sacral stimulation and CMAP from the external anal sphincter evoked in (A) a control person and (B) in a patient with ADPSP with LUTS and RUI. The stimulation is reproduced in three trials over the vertex and the sacral region.

urodynamic findings have been previously described.⁴⁻¹ The investigator was blinded to the urinary and bowel symptoms. The study was approved by the ethics committee.

Motor evoked potentials (MEPs) were elicited by cortical stimulation using a parabolic shaped coil, diameter 14 cm with a Twintop Magnetic Stimulator, and EMG responses obtained with a Keypoint EMG-machine (Dantec Medical Inc, Denmark). The compound motor action potentials (CMAPs) were recorded from the external anal sphincter using a disposable sphincter electrode (Dantec 13L81, Dantec Medical Inc, Denmark). The position of the electrode was anteroposterior to avoid cancelling of the motor potentials because of bilateral contraction from the right and left side of the external anal sphincter induced by cortical and sacral stimulations.

The cortical stimuli were applied near to the vertex in the area representing the lowest threshold for a motor contraction in the lower limbs measured in the right abductor hallucis (AH) muscle. The motor threshold (MT) was determined as the minimal stimulus intensity applied to the relevant cortical representation evoking at least three motor action potentials of five trials with an amplitude exceeding 50 μ V. In some patients the MEP amplitudes were very small, and therefore MT determination was difficult. To ensure a sufficient stimulus intensity the AH muscle was selected for MT measures. The stimulus intensity was increased to 50% above MT for the AH muscle or to a level sufficient to evoke a reproducible contraction of the external anal sphincter. The patients and the controls were instructed not voluntarily to contract the sphincter (“relaxed MEPs”). The cortical latency (CL) and amplitude of the CMAP were identified. The sacral stimulation was applied to the S2-S4 area using magnetic stimulation (maximum output) and the sacral latency (SL) and the central motor conduction time (CMCT=CL-SL) were calculated. The stimulations were performed in at least three individual trials with two runs to ensure reproducibility. In four patients the motor action potentials were hardly reproducible, and therefore an averaging technique was used in those patients. The results of MEPs

Table 1 Results (median (range)) of cortical and sacral stimulation in patients with ADPSP and normal controls

	Cortical stimulation		Sacral stimulation		
	Latency (ms)	Amplitude (mV)	Latency (ms)	Amplitude (mV)	CMCT (ms)
ADPSP (n=11)	28.0 (24.2-53.2)	0.04 (0.02-0.18)	5.2 (4.0-7.5)	0.15 (0.04-0.39)	22.8 (18.4-48.0)
ADPSP (without LUTS and RUI) (n=5)	26.0 (24.2-28.0)	0.07 (0.03-0.18)	5.8 (4.2-7.5)	0.15 (0.04-0.4)	20.7 (18.4-21.8)
ADPSP (with LUTS and RUI) (n=6)	33.6 (26.8-53.2)	0.03 (0.02-0.05)	5.1 (4.0-5.2)	0.18 (0.08-0.39)	29.0 (22.8-48.0)
Controls (n=12)	24.0 (22.0-29.5)	0.16 (0.04-0.42)	4.7 (3.0-7.8)	0.23 (0.02-0.59)	19.6 (16.5-23.5)

LUTS=Lower urinary tract symptoms; RUI=rectal urgency/urge incontinence; CL=cortical latency; CMAP=compound muscle action potential.

ADPSP with LUTS/RUI v ADPSP without LUTS/RUI:

CL p=0.02; CMAP amplitude p=0.03; CMCT p=0.01.

ADPSP with LUTS/RUI v control persons:

CL p=0.002; CMAP amplitude p=0.01; CMCT p=0.001.

obtained in upper and lower limb muscles are presented elsewhere.⁴

The results are presented as median (range), and the distributions were compared by the Kruskal-Wallis test. The level of significance was taken as 0.05.

Examples of cortical and sacral stimulation and CMAP from the external anal sphincter evoked in a control person and in a patient with LUTS and RUI are shown in figure 1. The results are shown in table 1.

The CL and the CMCT were significantly longer and the amplitude of CMAP at cortical stimulation was significantly lower in the patients with ADPSP with LUTS and RUI compared with the patients without these symptoms. The patients without LUTS and RUI presented no significant differences in CL, CMCT, or amplitude of the CMAP compared with the controls. The patients with LUTS and RUI presented significantly longer CL and CMCT and lower amplitudes of the CMAP than the control subjects. No significant differences in SL or amplitudes of CMAP at sacral stimulation were seen between the patients with ADPSP and the controls.

In this study we found that reproducible CMAPs could be obtained from the external anal sphincter using surface electrodes with cortical and sacral stimulation. Our normative values were similar to former studies.²⁻³ Using TMS we showed that patients with LUTS and RUI presented longer CMCT and reduced amplitudes of the cortical evoked CMAPs, whereas patients without these symptoms showed no differences. As shown in table 1, there is little overlap between the two groups. The number of patients are small, but the results suggest that measurement of MEPs to the external anal sphincter may be a method to be used as a part of the evaluation of patients with supranuclear lesions and sphincter symptoms.

In neuropathological studies axonal degeneration was found to be maximal in the terminal portions of the longest descending and ascending tracts. Dorsal root ganglia, posterior roots, and peripheral nerves were normal.⁵ Axonal degeneration of the corticospinal neurons, however, cannot solely explain the pathogenesis of the disease. Patients without LUTS and RUI presented normal CMCTs and only non-significantly reduced CMAPs, despite the presence of severe spasticity. A reduced CMAP is suggestive of selective large fibre loss in the relevant spinal cord pathways; however, other mechanisms may be involved in the reduced CMAP, including a raised cortical threshold to TMS.

We conclude that MEPs from the external anal sphincter in patients with ADPSP linked to chromosome 2p with LUTS and RUI present longer CMCTs and lower CMAPs at cortical stimulation. These results may in

part be related to the pathogenesis of the disease. MEPs from the external anal sphincter can be relatively easily evoked and may be a new useful method in the evaluation of patients with supranuclear lesions and RUI.

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Call for guidelines for monitoring renal function and haematological variables during intravenous infusion of immunoglobulin in neurological patients

Intravenous immunoglobulin (IVIg) is widely used in the treatment of some neurological conditions thought to have an underlying immune basis. Controlled studies of IVIg have demonstrated benefit in Guillain-Barré syndrome, chronic inflammatory demyelinating polyneuropathy, and dermatomyositis. Treatment with IVIg has also been beneficial in myasthenia gravis, multiple sclerosis,

multifocal motor neuropathy with conduction block, polymyositis, Lambert-Eaton myasthenic syndrome, stiff man syndrome, and Rasmussen's encephalitis.¹

Various complications have been reported in the literature in association with IVIg therapy. These include headache, nausea, fever, rash, aches in the chest or limbs, anaphylaxis especially in association with IgA deficiency, leucopenia, neutropenia, autoimmune haemolysis, renal failure, thromboembolism, aseptic meningitis, and transmission of viral infections—for example, hepatitis C.¹ The therapeutic dose of IVIg in the treatment of neurological disease has been empirically set at 2 g/kg, conventionally divided into five daily doses of 400 mg/kg, although some authors have shown that a 2 day infusion of 1 g/kg is not associated with any higher incidence of side effects than the 5 day infusion.²

Despite the widespread use of IVIg in neurological centres in the United Kingdom, to our knowledge there exists no consensus for advice either on monitoring haematological and renal function in patients pretreatment and post-treatment with IVIg, nor on the merits of shorter infusion periods of IVIg. Both of these factors have considerable cost implications for the National Health Service (NHS).

We have retrospectively examined the records of 21 patients admitted to a regional neurology centre (Hurstwood Park Neurological Centre), over an 18 month period. As several of these patients had multiple courses of IVIg treatment, the records contained 71 courses of treatment, although complete haematological data pretreatment and post-treatment was only available on 35 of these. The conditions treated included Guillain-Barré syndrome, chronic inflammatory demyelinating polyneuropathy, multifocal motor neuropathy with conduction block, and myasthenia gravis. The average age of patients was 51 years (range 22-86 years). Eight patients had indications of possible renal dysfunction (based on one or more abnormal blood urea and creatinine concentration) within 6 months before the first course of treatment. All courses given were at 0.4 g/kg Sandoglobulin (Novartis) for 5 days. A course of treatment was stopped or delayed eight times out of 71 courses: the reasons stated included thrombocytopenia (one patient: platelet count <100×10⁹/l, normal range 150-400×10⁹/l); leucopenia (three patients: white cell count <1.7×10⁹/l, normal range 4-11×10⁹/l); neutropenia (three patients: neutrophil count <1.5×10⁹/l, normal range 2-7.5×10⁹/l); and renal failure (one patient: sodium 134 mM, normal range 132-144 mM, potassium 5.6 mM, normal range 3.5-5.5 mM, urea 20 mM, normal range 2.5-6.7 mM, and creatinine 330 µM, normal