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

range 60–120 µM]). Other adverse effects noted which did not delay or stop treatment included tachycardia (one patient), fall in haemoglobin (one), persistent pyrexia (one), nausea and vomiting (four), limb or chest pain (four), rigors (two), and headache (two). It was noted that there was no consensus on the level of leucopenia, neutropenia, raised urea, or creatinine at which treatment was discontinued among the six consultant neurologists at the centre. During a 5 day course, the white cell count was noted to fall below $4 \times 10^9/l$ in 12 patients and the neutrophil count to below $2.0 \times 10^9/l$ in eight patients. Urea and creatinine concentration only became abnormal in one patient (who developed renal failure requiring haemodialysis) whose renal function was mildly impaired before treatment (sodium 133 mM, potassium 4.6 mM, urea 7.0 mM, and creatinine 138 µM). In all patients with noted haematological derangement secondary to IVIg treatment, subsequent blood monitoring 14 days after stopping treatment showed a return to normal values.

The number of patients who had abnormal blood variables during this retrospective study suggests a need to establish guidelines for monitoring haematological and renal variables during IVIg therapy. Furthermore, given the cost implications of an abortive course of IVIg treatment, guidelines for a tolerable level of leucopenia, neutropenia, or urea/creatinine derangement during a standard 5 day course of IVIg also needs to be established. It may well be that neutropenia during IVIg treatment is transient and reversible, as suggested by this study, and if validated, there would be an argument against the need for regular haematological monitoring during IVIg therapy. This argument is supported by the findings of Koffman *et al.*³ who retrospectively reviewed the records of 46 patients with neuromuscular disease receiving standard courses of IVIg (Gamimune N (Bayer) 2 g/kg) compared with 23 patients given placebo infusions of dextrose in water. In this study leucopenia, neutropenia, and lymphopenia were noted in a large proportion of patients treated with IVIg. Despite this no significant side effects—for example, infection—resulted and all haematological derangements were transient.

Furthermore, consensus needs to be established on the effect of IVIg formulation and risk of sucrose nephropathy (sucrose is used as a stabiliser in some IVIg preparations). Some previous case reports have suggested a link between the use of high sucrose formulations of IVIg (for example, Sandoglobulin (Novartis)) and subsequent renal failure compared with the use of lower sugar or glycine based formulations.⁴ However, a recent report by Levy and Pusey⁵ comparing Vigam (BPL; 0.5 g sucrose/g immunoglobulin) and Sandoglobulin (Novartis: 1.76 g sucrose/g immunoglobulin) in various indications has shown no such correlation between concentration of sucrose stabiliser in IVIg and propensity to cause renal failure. In their study of 119 patients given 287 courses of IVIg, eight patients (6.7%) showed a deterioration in renal function regardless of preparation used. On this basis, they concluded that all patients given IVIg should have renal function monitored before, during, and 4–5 days after treatment. This should be compared with the study of Koffman *et al.*³ where none of the 46 patients given the same preparation of high dose IVIg had renal dysfunction.

Our current practice, based on the results of this audit and the literature available, is to check the renal function of all patients before IVIg therapy. Those in whom the renal function is mildly abnormal (normal sodium and potassium, urea 7–8 mM, and creatinine 120–150 µM) have their renal function monitored during and 5 days after IVIg treatment and are currently receiving low sucrose or no sucrose (Octagam (Octapharma)) IVIg formulations. Patients with more seriously impaired renal function are not being considered for IVIg therapy; alternative modes of treatment—for example, plasmapheresis—could be considered for this subgroup. Haematological function is also checked before IVIg therapy; if normal, no further monitoring is carried out during or after IVIg treatment. If there is evidence of mild leucopenia, neutropenia, or thrombocytopenia before IVIg, the full blood count is monitored on a daily basis during treatment and once more 5 days after treatment. Patients with more severe blood derangement (platelets $<100 \times 10^9/l$, neutrophil count $<1 \times 10^9/l$, and leucocyte count $<2 \times 10^9/l$) are not being considered for IVIg therapy and again alternative modes of therapy would be considered.

A consensus statement on the recommended duration of treatment course (1–2 days *vs* 5 days) and the requirements for blood monitoring during IVIg infusion will require further study and collaborative audit across the many neurological centres in the United Kingdom using this form of therapy. We think that the potential cost implications and side effect profile of IVIg justify a call for such a study.

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Neuropsychological effects of pallidotomy in patients with Parkinson's disease

Whether patients with Parkinson's disease develop cognitive impairments or improvements after ventral pallidotomy is still a debated issue.¹ Recent studies produced contradictory findings which may have resulted from methodological factors such as differences in surgical techniques, neuropsychological assessments, duration of follow up, and the lack of evaluations of non-operated controls with Parkinson's disease.¹

We assessed a consecutive series of 27 patients with Parkinson's disease who received unilateral pallidotomy using the microelectrode registration technique.² Sixteen of these patients received a 3–6 month follow up evaluation, and 10 of them received a 12 month follow up evaluation. They were compared with a non-operated control group of 20 patients with Parkinson's disease matched for age, severity of extrapyramidal symptoms, and overall cognitive status who received the same neuropsychological evaluation at baseline and 12 months later. The neuropsychological examination included the Raven's progressive matrices, the Wisconsin card sorting test (WCST), the controlled oral word association test, the Buschke selective reminding test, the Benton visual retention test, the digit span, and the Perdue pegboard.

No significant differences between the pallidotomy and the control groups were found for age (years (SD) pallidotomy group 56.3 (6.9), control group 59.3 (7.9)), sex (pallidotomy group 50% women, control group: 50% women), years of education (years (SD) pallidotomy group 10.7 (2.7), control group: 11.4 (4.1)), baseline levodopa equivalent dosage, and UPDRS total scores (table 1). All patients were right handed.

Sixteen patients with Parkinson's disease who underwent unilateral pallidotomy received a 3–6 month follow up. A repeated measures multivariate analysis of variance (MANOVA) for the neuropsychological variables comparing baseline versus 3–6 month

Table 1 Neurological and neuropsychological findings

	Pallidotomy group		Control group	
	Initial evaluation	Follow up evaluation	Initial evaluation	Follow up evaluation
Mini mental state examination	26.4 (3.4)	25.3 (3.3)	26.3 (3.3)	27.5 (2.2)
UPDRS motor score	15.4 (7.8)	10.8 (5.3)	18.8 (15.8)	15.1 (9.0)
Levodopa dosage	785 (379)	775 (429)	590 (346)	890 (711)
Raven's progressive matrices	39.9 (33.8)	53.9 (36.1)	59.8 (36.5)	62.2 (34.3)
Wisconsin card sorting test	3.7 (2.1)	4.0 (2.5)	4.6 (1.9)	4.9 (1.9)
Verbal fluency	33.0 (8.9)	37.3 (6.4)	38.8 (9.8)	41.0 (13.4)
Buschke total recall	65.4 (22.2)	69.4 (17.5)	76.7 (18.1)	70.5 (15.3)
Buschke delayed	3.3 (3.1)	5.5 (3.0)	6.8 (3.0)	5.8 (2.5)
Benton visual retention test	5.7 (3.0)	7.1 (2.6)	7.7 (2.0)	7.5 (2.1)
Digits forward	5.3 (0.8)	5.0 (1.0)	5.7 (1.1)	5.6 (0.9)
Digits backwards	3.6 (0.8)	3.8 (0.8)	4.2 (1.0)	4.4 (1.0)
Perdue pegboard test*	14.0 (5.5)	17.9 (2.6)	19.3 (5.5)	18.9 (6.4)

Values are means (SD).

* $F(1,28)=8.84$; $p<0.01$.