term, pallidal stimulation with short-duration PWs results in clinical outcomes comparable to those achieved with longer PWs.

Twenty-two patients with primary generalized dystonia were implanted bilaterally with electrodes in the posterolateral ventral part of the GPi, and the most effective therapeutic stimulation parameters were recorded. After 6 months, 20 patients were assessed while on their normal treatment. Baseline PWs were categorized as short (60–90 μs), medium (120–150 μs) or long (450 μs). Patients then underwent videotaped stimulation sessions with each of the two remaining PWs, in random order and on different days. The stimulation parameters were set 10 h before assessment, with the intensity 10% below the side effect threshold for each PW and all electrodes set at 130 Hz (monopolar stimulation). Median PWs were 60, 160 and 450 μs (mean intensities 4.5 ± 1.3 V, 3.5 ± 1 V and 2.3 ± 0.7 V, respectively). As evaluated with the movement scale of the validated Burke–Fahn–Marsden dystonia rating scale, there was no significant difference in mean dystonia movement score between patients treated with each of the three PW settings.

Use of shorter PWs could increase the battery life of therapeutic devices—thereby lengthening time before device replacement—and reduce charge injection and adverse effects. The authors comment than an optimum combination of frequency, voltage and PW needs to be determined for each patient in the postoperative period. The optimum anatomical target remains to be defined, but could be delineated as the area covered by the narrowest diffusion of current that is efficacious in some select patients.

Original article Vercueil L *et al.* (2007) Effects of pulse width variations in pallidal stimulation for primary generalized dystonia. *J Neurol* [doi: 10.1007/s00415-007-0578-8]

Study demonstrates the safety and tolerability of *in vivo* gene therapy in the human brain

The increase in subthalamic nucleus activity seen in Parkinson's disease (PD) is largely attributable to a reduction in inhibitory gamma-aminobutyric (GABA)ergic input. In a phase I trial, Kaplitt *et al.* examined the safety and tolerability of transferring the gene encoding glutamic acid decarboxylase (GAD)—the enzyme responsible for the synthesis of GABA—into the subthalamic nucleus of patients with PD by use of an adeno-associated virus (AAV) vector.

The study involved 12 patients (mean age 58.2 years) with Hoehn and Yahr stage 3 or greater PD, all of whom underwent unilateral subthalamic AAV–GAD gene therapy. Baseline assessments were conducted within a week of the intervention, and patients were reassessed at 1, 3, 6 and 12 months after therapy. During follow-up, none of the patients had any adverse events related to gene therapy. At 3 months, significant improvements relative to baseline were seen in Unified Parkinson's Disease Rating Scale motor scores for both the off and on states ($P = 0.0015$ and $P = 0.01$, respectively). These improvements were observed primarily on the side of the body contralateral to surgery and persisted up to 12 months. Furthermore, comparison of baseline and 12-month PET scans revealed a marked reduction in thalamic metabolism in the treated hemisphere.

Although not designed to test the efficacy of AAV–GAD gene therapy in PD, the results of this study are encouraging, and indicate that AAV-mediated gene transfer to the brain is safe and well-tolerated.

Original article Kaplitt MG *et al.* (2007) Safety and tolerability of gene therapy with an adeno-associated virus (AAV) borne *GAD* gene for Parkinson's disease: an open label, phase I trial. *Lancet* **369:** 2097–2105

Relationship between topiramate and language disturbance in migraine

Topiramate has shown efficacy as a prophylactic agent in patients with episodic, chronic or medication-overuse migraine. A recent report, however, warns that such patients might experience language disturbances in response to this treatment.

Thirty patients on topiramate (for 3–6 months; 25 mg/day titrated to 75–200 mg/day) were compared with 20 patients treated with other prophylactic agents (for 3–7 months) and 20 with no prophylactic treatment. Both prophylaxis groups experienced substantially reduced headache frequency and conversion from chronic to episodic forms of headache. During treatment with topiramate, however, 8 (26.7%) patients reported experiencing language