Two patients experienced infections that required removal of the pulse generator. Serious events during active stimulation included three cases of hypomania, two cases of anxiety, and one case of dyskinesia; all these symptoms resolved after adjustment of the stimulator.

The authors conclude that stimulation of the subthalamic nucleus is effective in patients with refractory OCD but entails a substantial risk of serious adverse effects.

Original article Mallet L *et al.* (2008) Subthalamic nucleus stimulation in severe obsessive–compulsive disorder. *N Engl J Med* **359:** 2121–2134

Can prevention of iron accumulation protect against Parkinson disease?

Iron levels are elevated in the dopaminergic neurons of patients with Parkinson disease (PD), but the mechanism of iron accumulation, and whether such accumulation is a cause or a consequence of the disease, is unknown. A new study by French, US and Chilean researchers has found that levels of the iron transporter divalent metal transporter 1 are increased in the brains of patients with PD compared with controls. The study also found that a mutation that impairs iron transport protects rodents against neurotoxin-induced parkinsonism. A second study has found that neuromelanin pigments in the human brain protect neurons against oxidative damage by sequestering iron metal ions. The two papers suggest possible therapeutic strategies for PD.

Salazar *et al.* found that levels of iron and divalent metal transporter 1 were elevated in the substantia nigra of patients with PD. Divalent metal transporter 1 levels were also elevated in the mitochondrial complex I inhibitor 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced parkinsonism model in mice; divalent metal transporter 1 expression increased after MPTP intoxication in these mice, and the increase occurred alongside microglial activation. Immunolabeling experiments in mice showed that, after MPTP exposure, divalent metal transporter 1 expression increased in the dopaminergic neurons of the substantia nigra and began to be expressed in activated microglia, in tandem with the loss of the dopamine-pathway enzyme tyrosine hydroxylase. Mice with a mutation in divalent metal transporter 1 have impaired iron transport; these *mk/mk* mice were partially protected against MPTP-induced parkinsonism in this study. The *mk/mk* mice that were exposed to MPTP lost 25% of tyrosine-hydroxylase-containing cells, compared with >50% for heterozygous and wild-type mice.

Zecca *et al*. identified and characterized neuromelanin pigments in the substantia nigra, putamen, motor cortex and cerebellum of the human brain. They found that neuromelanin accumulates with age and sequesters iron and zinc, as well as toxic metals such as lead, chromium, and mercury.

The studies suggest that blocking iron transport into dopaminergic neurons might have therapeutic benefit in PD. Boosting neuromelanin production and impairing the formation of free radicals are other possible therapeutic strategies.

Original articles Salazar J *et al.* (2008) Divalent metal transporter 1 (DMT1) contributes to neurodegeneration in animal models of Parkinson's disease. *Proc Natl Acad Sci USA* **105:** 18578–18583
Zecca L *et al.* (2008) New melanic pigments in the human brain that accumulate in aging and block environmental toxic metals. *Proc Natl Acad Sci USA* **105:** 17567–17572