Cystamine is neuroprotective in Huntington's and Parkinson's diseases

Cystamine, a transglutaminase inhibitor, has been demonstrated in two separate studies to have neuroprotective effects in Huntington's disease (HD) and Parkinson's disease. In the first study cysteamine, a reduced form of cystamine, increased levels of the neuronal survival factor brain-derived neurotrophic factor (BDNF) in the brains of HD mice to produce a neuroprotective effect, and also increased serum levels of BDNF in mouse and primate models of HD. In the second study, pretreatment with low doses of cystamine increased levels of four dopaminergic-related markers in aged mice administered the toxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), which causes parkinsonian symptoms.

Borrell-Pagès *et al.* showed that cystamine and cysteamine promoted secretion of BDNF, the transport of which is weakened in HD but which is crucial for survival of the striatal neurons targeted by this disorder. Cystamine produced this effect by increasing heat-shock DnaJ-containing protein 1b (HSJ1b) transcripts (which stimulate BDNF secretion) and also by inhibiting transglutaminase (which negatively affects BDNF sorting). HSJ1b inhibited polyQ-huntingtin-induced neuronal death *in vitro* and, in a nematode model of HD, rescued neuronal dysfunction. In addition, cysteamine increased BDNF levels in the brains of HD mice. Data indicated that BDNF levels in blood, which are low in mouse and primate models of HD but were increased by cysteamine injection, could be a useful biomarker of disease progression, and might also be used to test the effects of neuroprotective agents that alter BDNF levels. The effect of cysteamine on BDNF release was transient, but repeat treatments showed continued efficacy, suggesting that cysteamine could be effectively administered repeatedly at short intervals to treat patients with HD.

Building on their previous research into the effects of cystamine in R6/2 transgenic Huntington mice, Cicchetti's group tested different regimens of cystamine in 16-month-old mice with MPTP-induced parkinsonism. A low (10 mg/kg) dose of cystamine beginning 2 days before and continuing during MPTP lesioning reversed the effects of MPTP; there were major differences in cystamine-treated mice compared with MPTP-treated mice, the former having significantly increased tyrosine hydroxylase-positive striatal fiber levels ($P<0.01$), tyrosine hydroxylase-immunoreactive cell density ($P<0.01$), substantia nigra *Nurr1* messenger RNA levels ($P<0.001$) and density of substantia nigra cells expressing the dopamine transporter ($P<0.001$). Cystamine was not as effective at a higher 50 mg/kg dose. The authors acknowledge that more-specific data on the mechanisms of cystamine neuroprotection in MPTP-treated mice are needed, but the results show promise for low-dose cystamine pretreatment in aged parkinsonian mice, and therefore potential in the treatment of Parkinson's disease.

Original articles Borrell-Pagès M *et al.* (2006) Cystamine and cysteamine increase brain levels of BDNF in Huntington disease via HSJ1b and transglutaminase. *J Clin Invest* **116:** 1410–1424

Tremblay M-È *et al.* (2006) Neuroprotective effects of cystamine in aged parkinsonian mice. *Neurobiol Aging* **27:** 862–870

An association between *Chlamydia pneumoniae* and multiple sclerosis

The bacterial pathogen *Chlamydia pneumoniae* (Cpn) has been identified as a possible etiological factor in the development of multiple sclerosis (MS). To assess the evidence for this hypothesis, a recent meta-analysis investigated studies comparing the presence of Cpn between patients with MS and controls.

Bagos and colleagues identified 26 studies (involving 1,332 patients with MS) fulfilling their inclusion criteria—namely, a cohort, case–control or cross-sectional design study with an outcome measure of detection of Cpn in MS patients. In addition, relevant material had to have been assessed using polymerase chain reaction, Cpn antibodies in cerebrospinal fluid, serum antibodies against Cpn, or measurement of intrathecal production of Cpn antibodies. The study results varied widely, and meta-regression analysis was carried out on study-level covariates in an attempt to determine the cause of this heterogeneity.

The vast majority of studies were considered to be case–control, with all but three of these studies using patients with other neurological disorders as controls. Overall, the frequency of Cpn infection was higher in patients with