No difference was found between the effects of methylphenidate and atomoxetine on SICI. Both treatments, however, were found to increase SICI in *DAT1* VNTR 9/10 heterozygotes, and to decrease SICI in *DAT1* VNTR 10/10 homozygotes. The findings support previous work linking *DAT1* variation to ADHD risk, and might partly explain the variable response to methylphenidate seen in previous studies.

Original article Gilbert DL *et al.* (2006) Dopamine transporter genotype influences the physiological response to medication in ADHD. *Brain* **129:** 2038–2046

Methylthioadenosine beneficial in multiple sclerosis

Multiple sclerosis (MS) can be diagnosed when only minor CNS damage has occurred. Approximately 40% of patients, however, fail to respond to current immunomodulatory treatments and progress to major brain damage and disability. Early results indicated that the nucleoside methylthioadenosine, which has a strong inhibitory effect on polyamine biosynthesis and has been demonstrated to have pharmacological effects on cellular function, could be an effective treatment in MS.

Moreno and colleagues at the University of Navarra, Spain, carried out a series of tests in rats and humans. They found that methylthioadenosine prevented the acute phase, and reversed the chronic relapsing phase, of experimental autoimmune encephalomyelitis, an animal model of autoimmune CNS inflammation. Administration of the drug to rats inhibited brain inflammation and reduced brain damage. Methylthioadenosine suppressed T-cell activation *in vivo* and *in vitro*, probably by blocking T-cell signaling, leading to prevention of degradation of IκB (inhibitor of kappa B) and impaired activation of NFκB (nuclear factor kappa B). The drug downregulated expression of proinflammatory genes and cytokines and enhanced interleukin-10 production. These mechanisms suggest an important immunomodulatory role for methylthioadenosine, which might also have a role in the CNS innate immune system through modulation of microglial activity.

Unlike current treatments for MS, methylthioadenosine might be suitable for oral administration and is not associated with treatment-limiting side effects. Moreno *et al.* suggest that this drug could be effectively combined with other immunomodulatory agents to halt progression not just of MS, but possibly also other autoimmune diseases, such as type 1 diabetes and rheumatoid arthritis, in which T-cell activation has a critical role. Research is ongoing, and clinical trials in humans are planned for the near future.

Original article Moreno B *et al.* (2006) Methylthioadenosine reverses brain autoimmune disease. *Ann Neurol* [doi: 10.1002/ana.20895]

Individuals exposed to pesticides show increased risk of Parkinson's disease

Evidence suggests that exposure to pesticides might be a risk factor for the development of Parkinson's disease (PD). When administered at high doses, certain pesticide compounds can cause degeneration of dopaminergic cells in the substantia nigra. Ascherio *et al.* tested the association between pesticide exposure and PD in a prospective investigation. The study population comprised 143,325 participants from the Cancer Prevention Study II Nutrition Cohort who did not have a diagnosis or symptoms of PD on enrollment in 1992.

Analyses adjusted for age, sex and smoking status showed that the 5.7% of participants who reported exposure to pesticides before 1982 had a 70% higher incidence of PD 10–20 years after pesticide exposure than those who had not been exposed. The mean age of PD onset was unaffected by pesticide exposure, being approximately 70 years in both exposed and unexposed participants. The exposed population had a slightly lower educational level than the nonexposed population, but other aspects of lifestyle were similar. Data were insufficient to determine how duration of exposure might affect the risk of PD. No significant association was found between incidence of PD and exposure to any of the other environmental pollutants examined.

On the basis of these results, the authors conclude that pesticide exposure does increase the risk of PD. They suggest that future studies should seek to identify the specific compounds associated with this risk.

Original article Ascherio A *et al.* (2006) Pesticide exposure and risk for Parkinson's disease. *Ann Neurol* [doi: 10.1002/ana.20904]