gene promoters; however, in some patients with schizophrenia, histone methylation at GABAergic promoters is decreased, but can be increased by treatment with antipsychotic agents such as clozapine.

**Original article** Huang H-S *et al.* (2007) Prefrontal dysfunction in schizophrenia involves mixed-lineage leukemia 1-regulated histone methylation at GABAergic gene promoters. *J Neurosci* **27:** 11254–11262

## Brain metabolic patterns correlate with symptom onset in preclinical HD

Neurodegeneration occurs before disease symptoms in patients who carry the Huntington's disease (HD) mutation, but current tests cannot predict the onset of clinical disease. Feigin *et al.* have described a unique pattern of brain metabolism that reflects the HD neurodegenerative process in preclinical HD-gene carrying (p-HD) individuals.

At baseline $^{18}$F-fluorodeoxyglucose PET, p-HD individuals ($n = 12$; mean age 46.8 ± 11.0 years) could be distinguished from controls ($n = 12$; mean age 40.8 ± 14.7 years) on the basis of the expression of an HD-related metabolic covariance pattern (HDRP; $P < 0.01$), which comprised reduced striatal and anterior cingulate activity, and increased activity in the thalamus, cerebellar vermis and the motor and visual regions of the cerebral cortex. Expression of this pattern in p-HD individuals increased during the first 18 months of follow-up ($P < 0.003$) and decreased at 44 months ($P < 0.04$ compared with 18 months). The depressed striatal metabolic activity in the p-HD group declined by a greater amount in p-HD individuals who progressed to HD than in p-HD individuals who did not, and the elevated thalamic activity progressively declined in p-HD patients, to values below those of the controls in individuals who progressed to HD. By use of $^{11}$C-raclopride PET imaging, the authors showed that striatal $D_2$-receptor binding declined from baseline in the HD group ($P < 0.005$) and did not correlate with expression of the HDRP.

The authors conclude that the presence of the HDRP in p-HD individuals characterizes the preclinical period and that declines in thalamic metabolism might predict progression to symptomatic HD. In addition, reductions in $D_2$-receptor binding continue throughout the presymptomatic phase of HD.

**Original article** Feigin A *et al.* (2007) Thalamic metabolism and symptom onset in preclinical Huntington's disease. *Brain* **130:** 2858–2867

## Delaying viral neuroinvasion reduces lethality of West Nile virus

Several cytokines have been implicated in the immunopathogenesis of the flavivirus West Nile virus (WNV). Arjona *et al.* have observed that expression of macrophage migration inhibitory factor (MIF), a mediator of the inflammatory cascade that forms part of the innate immune response, is significantly higher in both the plasma and cerebrospinal fluid of patients with WNV than in that of controls ($P < 0.05$). They have confirmed in WNV-inoculated mice that WNV positively regulates MIF expression and protein production in the early stages of infection, and demonstrated that nullifying MIF by genetic, immunoneutralization or pharmacological approaches significantly increased the survival rate of infected MIF-null mice compared with wild-type mice ($P < 0.05$).

Reduced infection and inflammatory cell infiltration was demonstrated in the brains of MIF-deficient mice compared with wild-type mice 6 days after inoculation with WNV. Notably, the viral burden was not reduced in the spleen. Six days after inoculation, levels of inflammatory cytokines, in particular tumor necrosis factor, were also significantly lower in the brains of MIF-deficient mice than in those of wild-type mice. Brain viral burden and neuroinflammation reached substantial levels in MIF-deficient mice 8 days after inoculation, but even then at levels 14-fold lower than in wild-type mice. Bypassing the blood–brain barrier by intracerebral inoculation of WNV led to similar survival rates for MIF-deficient and wild-type mice, providing support for the investigators' conclusion that MIF facilitates viral neuroinvasion by producing downstream inflammatory cytokines that increase blood–brain-barrier permeability. Blocking MIF in the initial stages of infection could, therefore, represent a new approach to the treatment of WNV.

**Original article** Arjona A *et al.* (2007) Abrogation of macrophage migration inhibitory factor decreases West Nile virus lethality by limiting viral neuroinvasion. *J Clin Invest* **117:** 3059–3066