microglia that cause disinhibition or even excitation of certain spinal cord neurons, the activity of which is normally inhibited by γ -aminobutyric acid (GABA) and glycine neurotransmitters. In a recent study, Coull and co-workers investigated the mechanisms through which activated spinal microglia induce neuronal hyperexcitability and, consequently, neuropathic pain.

Administration of ATP-stimulated microglia to the spinal cords of rats induced neuropathic pain and caused the spinal cord neurons to become excited rather than inhibited in response to GABA. The researchers therefore reasoned that microglia might signal to neurons through a secreted molecule that had previously been shown to induce hypersensitivity of dorsal horn neurons, brain-derived neurotrophic factor (BDNF). When BDNF was administered to the spinal cords of rats, it mimicked the activity of activated microglia and induced a net GABA excitation in approximately 30% of neuronal cells. Blocking BDNF receptor signaling in a rat model of nerve injury prevented allodynia, demonstrating that BDNF is required for neuropathic pain. Finally, transferring activated microglia that could not synthesize BDNF to rat spinal cords failed to cause allodynia, indicating that the signal originating from activated microglia is indeed BDNF.

In summary, BDNF released by microglia is critical for interactions between microglia and neurons in cases of neuropathic pain. This finding holds great promise for the development of therapies that block BDNF signaling and for improving the diagnosis of neuropathic pain.

Kate Matthews

Original article Coull JAM *et al.* (2005) BDNF from microglia causes the shift in neuronal anion gradient underlying neuropathic pain. *Nature* **438**: 1017–1021

RPE cell implantation improves motor symptoms in patients with advanced PD

According to a recent study, implanting human retinal pigment epithelial (RPE) cells into the brains of patients with advanced Parkinson's disease (PD) can improve their motor symptoms. RPE cells produce levodopa and when attached to gelatin microcarriers can be transplanted into the brain and attain prolonged survival.

In this open-label pilot study, RPE cells (~325,000 in total) isolated from postmortem human eyes were attached to gelatin microcarriers and implanted into the putamens of six levodopa-respondent patients (mean age 52.2 years). The implants were well tolerated throughout the 24-month follow-up period, and there were no serious treatment-related adverse events. Motor scores when off antiparkinsonian medications for at least 12h overnight, calculated using the Unified Parkinson's Disease Rating Scale (UPDRS), increased significantly in all patients between baseline and both 12 and 24 months, as did total UPDRS scores ($P=0.03$ by paired sign test for all). Activities of daily living scores, quality of life, length of time for which patients reported noticeable benefit from the medication and motor fluctuations also showed notable improvements over this period.

The authors comment that placebo effects might play a role in this open-label study, and that the results might not be replicable in older patients. It is encouraging, however, that no off-state dyskinesias were observed in any patient throughout follow-up. A second study has begun, to test efficacy with more objectivity and to further assess the safety of this treatment.

Pippa Murdie

Original article Stover NP *et al.* (2005) Intrastriatal implantation of human retinal pigment epithelial cells attached to microcarriers in advanced Parkinson disease. *Arch Neurol* **62**: 1833–1837

Azathioprine therapy inhibits development of new lesions in multiple sclerosis patients

Treatment with azathioprine, an immunosuppressive drug, reduces the rate of relapse in patients with multiple sclerosis (MS); however, it is unknown whether this therapy also inhibits the development of new lesions. Massacesi *et al.* used MRI to investigate whether azathioprine therapy suppresses the number and accumulation of new brain lesions in patients with MS.

This open-label treatment versus baseline study included 14 patients with relapsing–remitting MS (aged 18–55 years), each of whom had shown three or more gadolinium-enhancing lesions during a 6-month period before