IN THE NEWS

Images of victory

On 6 October, Paul Lauterbur and Sir Peter Mansfield, the pioneers of magnetic resonance imaging (MRI), became the latest scientists to be honoured with a Nobel Prize in Medicine. The Nobel committee credited Lauterbur with discovering the possibility of creating a two-dimensional image by introducing variations into magnetic fields, and Mansfield with developing the mathematical analysis of the signals and the technique of echo-planar imaging, which led to the implementation of MRI as a useful clinical tool. *According to The Globe and Mail* (7 October 2003), Mansfield himself acted as a human guinea pig when the time came to test his methods on a live subject.

Although MRI is a boon to many branches of medicine, it has particular implications for neurology and neuroscience. As *The Times* (UK) points out (7 October, 2003), "MRI is especially useful for examining the brain and spinal cord. Nearly all brain disorders produce differences in water content, which show up on the MRI scan."

Of course, for many neuroscientists the ultimate development of MRI is functional MRI, which allows the indirect visualization of changes in neural activity in the human brain. Talking to *The Times*, Lauterbur said, "There is one very interesting area in the observation of processes going on in the brain, to determine parts of the brain that respond to various thoughts and perceptions." The techniques involved in these studies are still being improved, but the fundamentals go back to the seminal work of Mansfield, Lauterbur and others in the 1970s.

Rachel Jones

NEURODEGENERATIVE DISORDERS

Axonal traffic jams

Neurons depend heavily on efficient intracellular transport, perhaps more than any other type of cell. Two papers in *Neuron* provide evidence that proteins with expanded glutamine repeats, such as huntingtin, might interfere with axonal transport, and that this might contribute to the development of neurodegeneration in polyglutamine disorders such as Huntington's disease.

In the first study, Gunawardena *et al*. looked at axonal transport in *Drosophila*. Flies in which the expression of huntingtin had been reduced by tissue-specific RNAi showed accumulation of organelles within larval nerves, which is typical of a deficit in axonal transport. In addition, reduction of huntingtin in the eye caused neurodegeneration in the eyes of adult flies, similar to that caused by overexpression of mutant huntingtin. These results indicate that normal huntingtin might be involved in axonal transport. But similar deficits were produced by expression of a fragment of huntingtin containing the expanded polyglutamine region, pointing towards a toxic gain of function.

Further investigation revealed that the levels of soluble motor proteins in neurons from flies expressing polyglutamine proteins were reduced. Huntingtin is known to interact with huntingtin-associated protein 1 (HAP1), which in turn associates with a component of the axonal transport system, and the authors suggest that the mutant protein might sequester motor proteins. The resulting shortage of motor proteins in the cell could cause the deficits in axonal transport.

By targeting expression of polyglutamine proteins to either the nucleus or the cytoplasm of cells, Gunawardena *et al*. showed that the axonal transport phenotype depended on cytoplasmic expression of the proteins. When expression was restricted to the nucleus, though, it triggered apoptosis in neurons. The authors propose that mutant huntingtin has two distinct pathogenic mechanisms, one that disrupts transport and another that triggers apoptosis, and that they might act together in Huntington's disease.

GLIA

Tight unions

There is much more to the nodes of Ranvier than simply being axonal segments devoid of myelin. The architecture of the region of contact between oligodendrocytes or Schwann cells and the nerve fibre is exquisitely complex, and two recent papers provide new insight on the molecular interactions between the two cell types.

The myelin sheath has been divided in several regions — paranode, juxtaparanode and internode — that have different structural and molecular signatures. The studies of Poliak *et al*. and Traka *et al*. focus on the juxtaparanode, asking what molecular interactions are necessary for its proper assembly. Previous studies had shown that K^+ channels are enriched at the axonal membrane of the juxtaparanode, where they seem to interact indirectly with the protein Caspr2. The new studies provide evidence that the adhesion molecule Tag1, which is expressed by axon and glia at the juxtaparanode, is crucial for the localization of K^+ channels and Caspr2.

Poliak *et al*. generated mice lacking Caspr2 and found that K^+ channels and Tag1 were no longer abundant in the juxtaparanodes of the peripheral and central nervous systems. To study these interactions in more detail, they generated mice lacking Tag1 and found a similar phenotype: K^+ channels and Caspr2 were missing from the juxtaparanode. A series of biochemical experiments helped them to obtain evidence for the direct interaction between Tag1 and Caspr2, and to show that they only interact when they form part of the same membrane and not between cells. Traka *et al*. did not generate *Caspr2*-null mice, but working with a Tag1 knockout, they obtained similar findings: the abnormal localization of K^+ channels and Caspr2 in the mutant, and the interaction between Tag1 and Caspr2 in *cis*, but not in *trans*.

Both studies converge on the idea that Tag1 is crucial for the assembly of the juxtaparanode on two different fronts. First, owing to its association with Caspr2, Tag1 helps to define the molecular composition of the juxtaparanode.