In the news

MAKING WAVES

That first ultrasound scan is an exciting time for parents-to-be, letting them see the newest member of their family for the first time and reassuring them that their baby is healthy. But could ultrasound harm the fetus? Pasko Rakic and colleagues at Yale Medical School have recently found that, in pregnant mice, prolonged exposure to ultrasound disrupts neuronal migration during fetal brain development.

It is too early to translate the team's results in mice to humans, as Rakic comments: "We do not have any evidence ourselves that ultrasound waves … have any effect on the developing human brain" (*Reuters*, 7 August 2006). The conditions used in their studies were very different to those seen in the clinic. The ultrasound source was maintained in a fixed position and mice were exposed to the sound waves for 30 mins or more. When a scan is performed on expectant mothers, it is just that — a scan. The ultrasound source is continuously moved and so the fetal brain is typically exposed to ultrasound for only a few seconds.

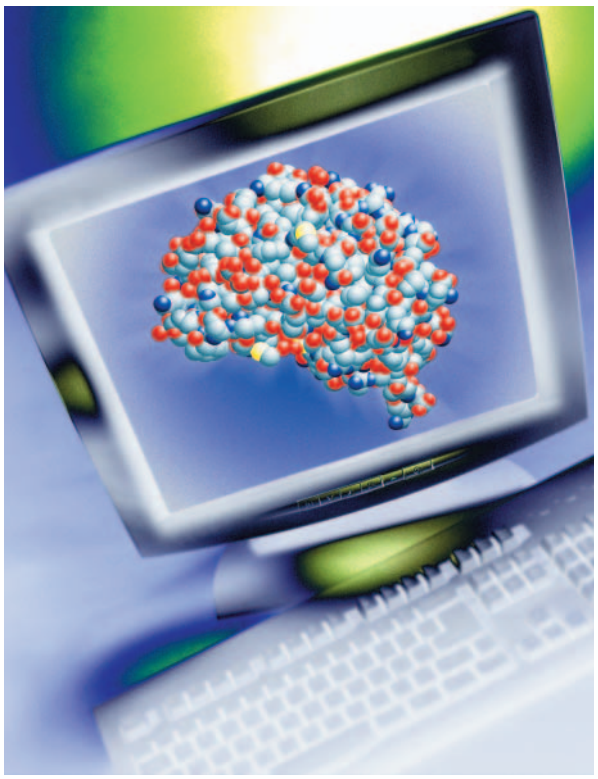
Moreover, the changes induced by ultrasound exposure were small and it is not known whether they were significant enough to affect behaviour. The authors plan to investigate this further in monkeys.

Concerns about the effects of ultrasound on the fetal brain have been voiced before, with exposure to ultrasound being linked to decreased birth weight and delayed speech development, as well as an increased probability of being left-handed. However, the medical value of ultrasound scans is not disputed, as Rakic says: "…the benefits of the ultrasound for diagnosis are so big that I would not hesitate to use it at all" (*New Scientist*, 7 August 2006). Instead, in an age when ultrasound machines can be bought for use in the home, researchers suggest that expectant mothers minimize any risk by only having scans that are medically necessary.

Samantha Barton

NEUROLOGICAL DISORDERS

Mind over machine



The brain is thought by some to be the most powerful computer known. Harnessing these impressive processing powers to control machines, including computers and robots, has been considered to be in the realms of fantasy. However, two reports in *Nature* describing advances in electronic neuronal implants indicate that in the future the mind could be used to manipulate machines, with the potential to improve mobility and communication for those with severe spinal cord injuries.

Currently available neuromotor assistive technologies are limited by low performance. They are typically slow and inaccurate, and can require the user to adapt the neuronal activity in their brain, which requires months of intensive training. However, the work of Hochberg, Santhanam and their respective colleagues suggests that there are solutions to these problems.

Hochberg and co-workers developed a brain–computer interface (BCI) that used a 96-microelectrode array implant to measure neuronal firing patterns directly in the motor cortex. The clinical usefulness of the team's BCI hinged on whether movement signals persist in the motor

NEURODEGENERATIVE DISORDERS

Receptor traffic — parkin rules

Parkinson's disease (PD), a progressive neurodegenerative disorder that causes tremors, stiffness, and impaired balance and coordination, results from the loss of dopamine-producing neurons in the midbrain. Defects in the ubiquitin–proteasome system and protein aggregation in Lewy bodies have typically been associated with the development of PD. A study in *Nature Cell Biology* now indicates that a proteasome-independent ubiquitylation pathway also contributes to the aetiology of this disease.

Parkin encodes an E3 ubiquitin ligase that is inactivated in ~50% of early-onset PD cases. Edward Fon and colleagues showed that, in addition to targeting proteins for degradation, parkin can delay epidermal growth factor (EGF) receptor (EGFR) trafficking by ubiquitylating the endocytic scaffolding protein EPS15, and can promote signalling through phosphoinositide 3-kinase (PI3K)–Akt, an important pathway for neuronal survival.

The ubiquitin-like domain of wild-type parkin, but not of a PD-associated form, binds to the ubiquitin-interacting motif (UIM) of EPS15. This interaction is regulated by EGF, the addition of which transiently increased the formation of a parkin–EPS15–EGFR complex and EPS15 ubiquitylation. The authors propose that intramolecular UIM–ubiquitin binding not only decreases the capability of EPS15 to induce EGFR internalization, but also prevents EPS15 from interacting with parkin, possibly explaining the transient nature of the complex.

cortex long after their communication route to the brain has been disrupted or severed. The participant in the trial was a tetraplegic man (M.N.) who had sustained an injury to the C3 and C4 vertebrae 3 years before he took part in the trial. Amazingly, neuronal firing patterns in M.N.'s motor cortex were similar to those generated in intact monkeys. To correlate these existing neuronal firing patterns with a specific movement, the authors coupled the implant to a computer and recorded activity while M.N. imagined making a range of movements with his hands and arms. By analysing movement-dependent variations in neuronal ensemble activity, the authors decoded the firing patterns, which enabled M.N. through thought alone to control a 'neuronal cursor' to open an e-mail, play video games and manipulate an object using a prosthetic hand, while simultaneously holding a conversation!

In separate research, Santhanam and co-workers addressed the issues of BCI speed and accuracy. The authors began by assessing neuronal activity in the premotor cortex of intact monkeys while they carried out a standard instructed–delay behavioural task. Instead of trying to decode a detailed arm trajectory, the authors determined the desired endpoint of the movement. To optimize performance, they selectively chose which neural activity to decode. Previously reported BCIs typically enable a sustained rate of information transfer of 1.6 bits per second (bps). The software developed by the authors led to significant improvements in both speed and accuracy, enabling information transfer at a rate of 6.5 bps, which translates to a typing speed of about 15 words per minute.

BCIs and neuromotor prosthetics are only in their infancy, and there are still several obstacles to be overcome before they can reproduce the achievements of the cochlear implant, the most successful neuroprosthetic so far. But the results described by these two teams suggest that using the mind to control machines could eventually become a reality.

Samantha Barton

ORIGINAL RESEARCH PAPERS
Hochberg, L. R. *et al.* Neuronal ensemble control of prosthetic devices by a human with tetraplegia. *Nature* **442**, 164–171 (2006) | Santhanam, G. *et al.* A high-performance brain–computer interface. *Nature* **442**, 195–198 (2006)

Overexpression of parkin specifically reduced EGF uptake in COS-7 cells. Consistently, the rate of EGFR internalization was faster in mouse embryonic fibroblasts from parkin-knockout mice compared with wild-type. Small-interfering-RNA-mediated EPS15 knockdown did not further decrease the rate of EGFR endocytosis, indicating that EPS15 is required for the effect of parkin on receptor internalization.

Last, the authors showed that by decreasing receptor internalization, parkin also regulates EGF signalling via the PI3K–Akt pathway. EGF-induced Akt phosphorylation in synaptosomes from parkin-knockout mice was remarkably reduced compared with wild-type synaptosomes. Owing to the positive role of Akt in neuronal survival, these findings are indicative of a novel mechanism through which parkin could prevent neurodegeneration.

In addition, two studies in *Nature* have recently described a role for parkin in the maintenance of mitochondrial integrity in dopaminergic neurons. It will be interesting to determine whether particular parkin mutations affect specific aspects of parkin function. Therapeutic strategies that are aimed at these novel pathways could lead to better and more effective treatments for PD.

Monica Hoyos Flight, Editor
Cell Migration Update

ORIGINAL RESEARCH PAPER
Fallon, L. *et al.* A regulated interaction with the UIM protein Eps15 implicates parkin in EGF receptor trafficking and PI(3)K–Akt signalling. *Nature Cell Biol.* **8**, 834–848 (2006)
FURTHER READING Park, J. *et al.* Mitochondrial dysfunction in *Drosophila PINK1* mutants is complemented by *parkin*. *Nature* **441**, 1157–1161 (2006) | Clark, I. E. *et al. Drosophila pink1* is required for mitochondrial function and interacts genetically with *parkin*. *Nature* **441**, 1162–1166 (2006)
WEB SITE
Edward Fon's laboratory: http://www.mni.mcgill.ca/cfns.html#EdwardFon

COGNITIVE NEUROSCIENCE

Try to remember…

What happens in your brain when you try to commit something to memory? What strategies do you use when studying information? Most of us would find it hard to answer this question, but some people use specific strategies to perform amazing feats of memory. Kirchhoff and Buckner have studied how different strategies affect memory performance, and how brain activation can reflect these techniques.

The subjects of the study were asked to look at pairs of interacting objects — for example, a banana in a truck — and were told that their memory for the images would be tested later. While they studied the images, the activity in their brains was measured using functional MRI, and later they were quizzed on the strategies they had used to remember the information.

Among the participants, encoding strategies varied greatly. Two types of strategy, which the authors call 'verbal elaboration' and 'visual inspection', were correlated with subsequent performance on a retrieval task, whereas 'mental imagery' and 'memory retrieval' strategies were not. In addition, subjects who used the greatest number of different encoding strategies showed the best performance in the test. Further analysis showed that the verbal elaboration and visual inspection strategies independently improved memory performance.

When they studied the strategy-use data together with the brain imaging results, the authors discovered that specific strategies were correlated with activity in different parts of the brain. In particular, the verbal elaboration strategy was associated with prefrontal activity in areas that contribute to verbal processing, whereas the visual inspection strategy was associated with activity in an object-processing area of the extrastriate cortex.

Finally, the authors investigated whether activity in these regions during encoding was directly correlated with memory performance on a subsequent test. As they predicted, activity associated with effective encoding strategies was also correlated with successful recall.

These results shed light on the ways in which people use different strategies — and different parts of the brain — to perform the same task. This is likely to explain a significant part of the individual variation that is seen in functional imaging studies of memory encoding, as well as helping us to understand and perhaps improve memory performance.

Rachel Jones

ORIGINAL RESEARCH PAPER Kirchhoff, B. A. & Buckner, R. L. Functional–anatomic correlates of individual differences in memory. *Neuron* **51**, 263–274 (2006)