In the news

SILENT COMMUNICATION

Whether patients in a vegetative state are conscious and aware of their surroundings is a question that has long troubled families and doctors. Recent functional MRI (fMRI) studies involving a 23-year-old woman who sustained a severe traumatic brain injury have indicated that she might be aware of her surroundings and able to carry out mental tasks, prompting hopes that patients in vegetative states could one day communicate with those around them.

During an fMRI study, Adrian Owen *et al.* gave the patient spoken instructions to imagine walking around rooms at home or playing tennis. Owen described the neural reponses as "indistinguishable" from healthy volunteers, and claims that "her decision to work with us when asked represents a clear act of intent … she was consciously aware of herself and her surroundings" (*The Times*, 8 September 2006). Writing in the same issue of *Science*, Lionel Naccache of the Cognitive Neuroimaging Unit in Orsay, France, agrees that "the fMRI findings indicate the existence of a rich mental life."

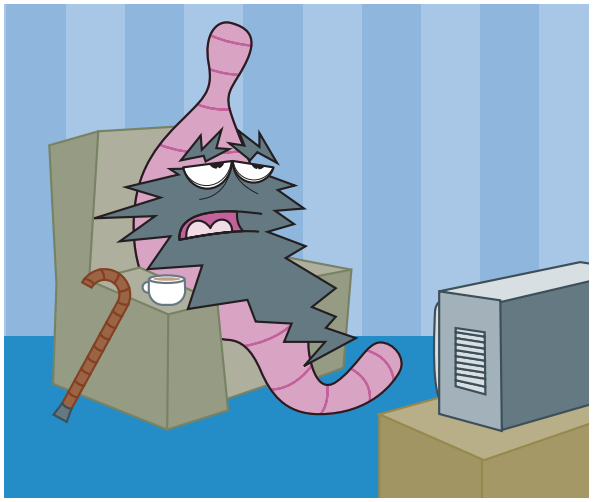
However, Owens himself points out that "all vegetative patients are different: they have damage done to different parts of their brains and their chances of recovery are different" (*BBC News Online*, 7 September 2006). Paul Matthews, at the University of Oxford, goes further: "When patients are in a vegetative state they can react to stimuli but not in a truly meaningful way … Response to stimuli, even complex linguistic stimuli, does not provide evidence of a decision to respond" (*The Times*, 8 September 2006).

Regardless of the precise extent of awareness indicated by this study, as Naccache puts it: "this single case makes a strong argument for the development of fMRI and other neurophysiological tools … to evaluate cognition in such patients", and might help to make decisions about patient care.

Tom Frost

NEURODEGENERATIVE DISEASES

Perils of ageing



A molecular mechanism has now been proposed that explains why Alzheimer's disease (AD), which typically strikes in 50–80-year olds, is linked with ageing. Reporting in *Science*, researchers showed that the transcription factors HSF-1 and DAF-16, which are regulated by a central ageing pathway, have opposing disaggregation and aggregation activities that function together to prevent AD.

AD, like other late-onset neurodegenerative diseases, is correlated with toxic aberrant protein aggregation — specifically, amyloid precursor protein breaks down into $A\beta_{1-42}$ peptides, which aggregate. But why aggregate-mediated toxicity is linked with age has remained unclear.

Cohen, Bieschke and colleagues investigated whether increasing the lifespan (or slowing the ageing) of *Caenorhabditis elegans* would delay the onset of aggregation. If so, then the late onset of AD could be due to a detoxifying activity that becomes compromised with ageing. If not, a stochastic time-related build-up of toxic aggregates to a threshold could explain the late onset of AD.

To distinguish between these possibilities, researchers disrupted the insulin signalling pathway, which is central in the regulation of ageing in worms, flies and mammals. In *C. elegans*, a sole insulin receptor, DAF-2, transduces a signal that

DEVELOPMENT

Glutamate signals growth

The involvement of glutamate in early brain development has been somewhat contentious: although a large body of *in vitro* evidence highlights signalling roles for glutamate during proliferation, migration, differentiation and survival, genetic disruption to glutamatergic activity has little or no effect on brain development. New work by Matsugami and colleagues goes some way to resolving this issue and provides compelling *in vivo* evidence that glutamatergic activity is vital for early developmental events.

The absence of an effect following genetic disruption to glutamate receptors or glutamate release might reflect the compensatory action of other neurotransmitters during development. To overcome this potential confound, Matsugami and co-workers adopted the opposite approach: they overstimulated glutamate receptors in mice by knocking out the glutamate transporters GLAST and GLT1, which normally maintain low levels of extracellular glutamate. These knockout mice had multiple brain defects in the cortex, hippocampus and olfactory bulb after embryonic day (E) 15 and died by E17–18.

By E16, the number of cells in the ventricular zone — a layer of mitotic cells that eventually give rise to all cell types in the mature brain — was decreased in mutant brains compared with wild-type brains. The proportion

The migration pattern of newly generated neurons, darkly stained (BrdU incorporation experiments), was normal in the neocortex of wild-type animals (top panel), but abnormal in the $Glast^{-/-}/Glt1^{-/-}$ E16 neocortex (bottom panel). Images courtesy of T. R. Matsugami, Tokyo Medical and Dental University, Japan.