IN THE NEWS

Mental gymnastics

"Scientists grow brain in rat's thigh" was the title used by *The Learning Channel News Service* (US, 3 December) to announce a new model of brain hypoxia reported in *Neuroscience Letters*. In the experiment, Nobutumi Kawai and his colleagues (Jichi Medical School, Japan) decapitated newborn rats and waited 90 minutes before grafting the heads onto the thighs of adult rats, hoping that the leg arteries would restore blood supply to the brain.

Remarkably, some nervous tissue survived. "A transplanted brain can develop as normal for at least three weeks", reported the *New Scientist News Service* (UK, 2 December), choosing imagery that will feed the imagination of B-series horror moviemakers: "the mouth of the head will move, as if it is trying to drink milk".

But not everybody seems enthused by what *The Strait Times* (Singapore, 6 December) referred to as "the grisly technique". Denis Azzopardi of Imperial College London, reminds us that there are other well established models of ischaemia, "so I'm not sure that this complicated technique offers an advantage in any way" (*New Scientist News Service*). Besides, at a time of great interest in animal welfare, this experiment might add more fuel to what is already a raging fire. According to a spokesperson of the UK Research Defense Society, "vivisection that provides no obvious research benefit and involves clear animal suffering will only cause public concern" (*New Scientist News Service*).

Whether we ultimately reap any benefits from this approach remains to be seen. In the meantime, we can be sure that this experiment gives a totally new meaning to the phrase 'exercise your brain'.

Juan Carlos López

CEREBRAL CORTEX

Joining the dots (or bars)

The receptive field is one of the most familiar concepts in sensory physiology. For a visual neuron, it is commonly defined as the area of visual space in which stimulus presentation leads to a change in neuronal activity. But stimuli outside the 'classical' receptive field can modulate a neuron's response to stimuli within this area. A new tracing technique promises to shed light on the anatomical connections that mediate this effect.

A good example of the 'non-classical' receptive field is contour integration. A neuron in the primary visual cortex (V1) will respond more strongly to a bar in its receptive field if there is another bar just outside this area that is colinear with the first bar, so that if the two were joined they would make a line. This 'colinear facilitation' is strikingly similar to the psychophysical finding that observers can detect a faint bar more easily if another, colinear bar is presented alongside it.

There is healthy debate about many aspects of V1 function, often centring on whether certain properties are intrinsic to V1 or are imposed upon it by feedback from higher visual areas, such as V2. And colinear facilitation is no exception. Gilbert *et al*. have developed a very precise anterograde tracing technique, and used it to compare intrinsic connections in V1 with those from V2 back to V1. Their results support the idea that intrinsic connections in V1 are more likely to mediate colinear facilitation.

The new technique uses an adenovirus that contains the gene for green fluorescent protein (GFP). When small amounts of virus are injected into the cortex, the virus enters neurons and the gene is transcribed. The GFP that is produced acts as a tracer, labelling not only the cell bodies but also all of the dendrites and axons. Because the label is produced within the neurons, rather than injected directly, there is no saturation at the injection site and it is easy to identify the cell bodies of the labelled neurons. When Gilbert *et al*. injected the adenovirus into specific locations in V1, it labelled intrinsic axonal connections that extended for up to 3.5 mm from the cell bodies at the injection site, corresponding to around 4° of the visual field.

The intrinsic connections were not uniform. Rather, they formed periodic clusters or patches, about every 0.75 mm. The authors found that these clusters corresponded to columns with the same orientation selectivity as the neurons at the injection site, making these connections good candidates for mediating colinear facilitation.

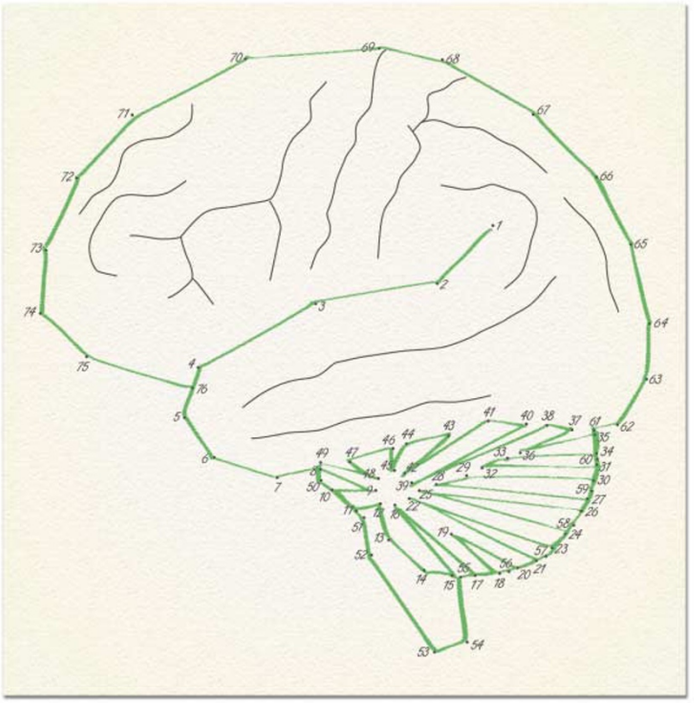
Connections from a single injection site in V2 covered a similar expanse in V1, although the projections were much less dense. However, there was no orientation specificity in these projections. This makes it less likely that feedback from V2 is responsible for contour integration in V1. As the authors point out, feedback from other visual areas, such as V3 or MT, might show orientation specificity — and the adenoviral tracing technique, which allows

NEUROGENESIS

A new target for Hedgehog

Tumorigenesis and embryogenesis share many molecular players and pathways, including the sonic hedgehog (Shh) signalling pathway. In a new study, Kenney *et al.* have identified a downstream target of Shh that is involved in both neurogenesis and tumorigenesis in the cerebellum.

***Nmyc* is a proto-oncogene that is amplified in certain brain tumours, including the cerebellar tumour medulloblastoma. Circumstantial evidence has indicated that Shh and *Nmyc* might be functionally linked — for example, Knoepfler *et al.* recently showed that *Nmyc* is required for normal neurogenesis in the cerebellum, a process that also depends on Shh. Also, blocking Hedgehog signalling has been shown to inhibit medulloblastoma growth. Now, Kenney *et al*. have discovered the**



precise identification of labelled cells and quantification of their projections and geometry, should make it easier to address this question, as well as others relating to the functional anatomy of cortical connections.

Rachel Jones

References and links

ORIGINAL RESEARCH PAPER Stettler, D. D. *et al*. Lateral connectivity and contextual interactions in macaque primary visual cortex. *Neuron* **36**, 739–750 (2002)

WEB SITES

Gilbert's laboratory: http://www.rockefeller.edu/labheads/gilbert/gilbert.html

nature of this functional relationship.

The authors found that Shh upregulates *Nmyc* expression in cerebellar granule neuron precursors (CGNPs) *in vitro*. Using transgenic embryos, they showed that *Nmyc* is upregulated ectopically in the dorsal spinal cord when Shh expression is driven by a *Wnt1* regulatory element. Two further observations indicated that *Nmyc* acts downstream of Shh. Overexpression of *Nmyc* activated G_1 cyclins in CGNPs and stimulated ongoing proliferation, independent of Shh activity. Shh also promoted CGNP proliferation, but its potency was reduced by the addition of a Myc antagonist.

These findings indicate that *Nmyc* is a direct downstream target of Shh that mediates its effects on cell proliferation during cerebellar development and in medulloblastomas. The upregulation of *Nmyc* by Shh seems to be context-dependent, as *Nmyc* is expressed in the cerebellar granule cell precursor layer, but not in the floorplate, which is another key site of Shh expression. This finding represents a significant step in piecing together a signalling pathway that is important to both neuroscientists and cancer biologists.

Heather Wood

References and links

ORIGINAL RESEARCH PAPERS Kenney, A. M. *et al*. *Nmyc* upregulation by sonic hedgehog signaling promotes proliferation in developing cerebellar granule neuron precursors. *Development* **130**, 15–28 (2002)

FURTHER READING Knoepfler, P. S. *et al*. N-myc is essential during neurogenesis for the rapid expansion of progenitor cell populations and the inhibition of neuronal differentation. *Genes Dev*. **16**, 2699–2712 (2002) | Berman, D. M. *et al*. Medulloblastoma growth inhibition by hedgehog pathway blockade. *Science* **297**, 1559–1561 (2002)

IN BRIEF

FUNCTIONAL IMAGING

The neural correlates of feeling sympathy.

Decety, J. & Chaminade, T. *Neuropsychologia* **41**, 127–138 (2003)

The authors use functional imaging to show that watching actors telling sad stories leads to activation of neural structures that are involved in processing emotion. It also activates a 'shared motor representation' network that includes the right inferior parietal cortex, and which is normally activated by both observed and executed actions. If the actors used emotive gestures and facial expressions, there was also a specific increase in activity in the left inferior frontal gyrus. These areas are proposed to form a network that is important for feeling sympathy.

CIRCADIAN RHYTHMS

Rhythmic histone acetylation underlies transcription in the mammalian circadian clock.

Etchegaray, J.-P. *et al. Nature* 11 December 2002 (doi:10.1038/nature01304)

In mammals, the circadian clock is controlled by a transcriptional feedback loop. Clock and Bmal1 drive the expression of *Per1–3*, *Cry1* and *Cry2*, and the Cry proteins in turn block Clock/Bmal1-mediated transcription. Here, Etchegaray *et al*. show that in the mouse liver, the *Per1*, *Per2* and *Cry1* gene promoters exhibit oscillations in histone acetylation that are synchronized with circadian rhythms. The data imply a new role for chromatin rearrangements in circadian rhythmicity.

NEUROTROPHIC FACTORS

Brain-derived neurotrophic factor can act as a pronecrotic factor through transcriptional and translational activation of NADPH oxidase.

Kim, S. H. *et al*. *J. Cell Biol.* 2 December 2002 (doi:10.1083/jcb.200112131)

As brain-derived neurotrophic factor (BDNF) can cause cell death, Kim *et al*. set out to explore the underlying mechanisms. They found that BDNF-induced neuronal death depended on the production of free radicals and the synthesis of new proteins. Microarray analysis revealed that BDNF increased the synthesis of a subunit of NADPH oxidase. The authors obtained evidence for the involvement of this enzyme in the death process, as blocking its activity prevented BDNF toxicity, but not the antiapoptotic action of this neurotrophin.

STEM CELLS

A nucleolar mechanism controlling cell proliferation in stem cells and cancer cells.

Tsai, R. Y. L. & McKay, R. D. G. *Genes Dev*. **16**, 2991–3003 (2002)

The authors identify nucleostemin as a nucleolar protein that is expressed in neuronal and other stem cells, as well as in cancer cells. When stem cells differentiate, the expression of nucleostemin decreases before they exit the cell cycle. Increasing or decreasing the levels of nucleostemin reduces stem cell proliferation, leading to apoptosis. The data point to a new nucleolar mechanism that controls the progression of stem cells through the cell cycle.