IN THE NEWS

Opening the BrainGate

Neuroscientists have taken another step towards increasing the functional capabilities of people who have been paralysed.

Surgeons at New England Sinai Hospital, Massachusetts, USA, implanted almost 100 electrodes into the motor cortex of the brain of a man who is paralysed from the neck down. The electrodes are connected to a computer, which interprets activation in this area of the brain and translates it into 'action', thereby controlling everyday objects. The technology enables Matthew Nagle to turn a television on and off, switch channels and increase or decrease the volume, play video games and even check emails.

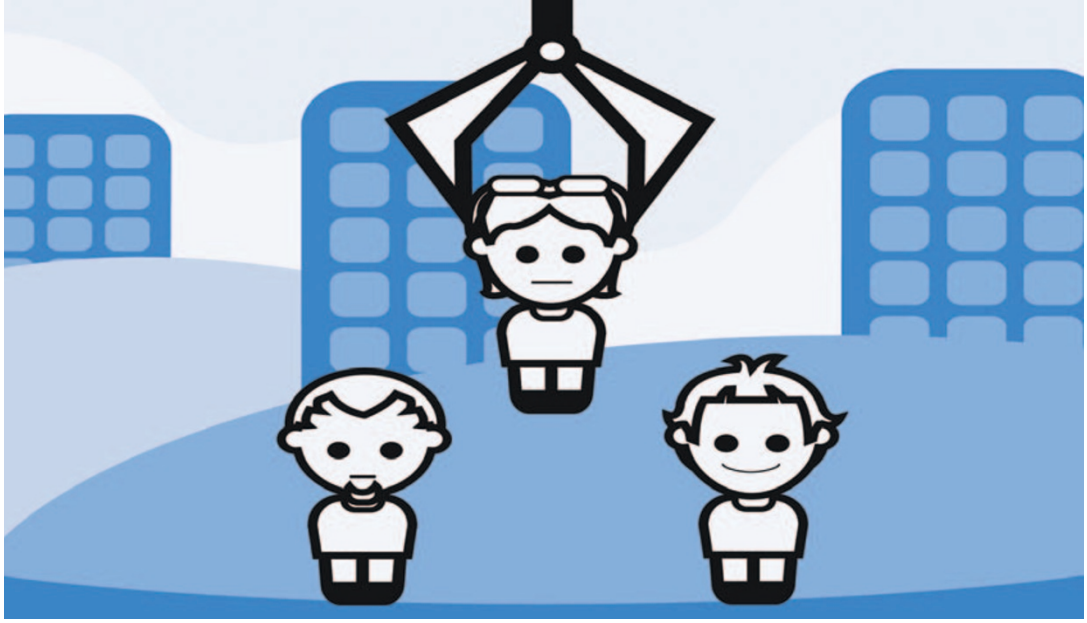
Professor John Donoghue, the neuroscientist responsible for the device, known as 'BrainGate', said, "Eventually, we want him to be able to use it to control the lights, his phone and other devices" (*The Guardian*, 31 March 2005).

Mr Nagle is already able to exert some control over a prosthetic hand and arm, opening and closing the hand and moving the arm to take sweets from one person's hand and transfer them to the hand of another.

Professor Donoghue hopes that similar implants might one day allow people with paralysis to regain limb function, telling *BusinessWeek Online* (15 March 2005), "Our goal is for you to see paralyzed people eating at a restaurant and for you not to know that they are paralyzed."

Dr Richard Apps, a neurophysiologist at Bristol University, UK, commented, "It's quite remarkable. They have taken research to the next stage to have a clear benefit for a patient that otherwise would not be able to move" (*BBC News Online*, 31 March 2005). He added, "Just to be able to grasp an object is a major step forward" (*BBC News Online*).

Sarah Archibald



NEUROGENESIS

Dividing destiny

During development, the mitosis of stem and progenitor cells can give rise to two daughter cells with different fates. It is thought that uneven distribution of crucial intracellular signalling molecules during mitosis has an important role in this asymmetric cell fate determination. Now, a study published in *Neuron* reports a novel mechanism whereby unequal distribution of growth factor receptors during mitosis can result in two daughter cells with different environmental responsiveness and, therefore, different fates.

As the level of epidermal growth factor receptors (EGFRs) can influence the fate choice of cortical progenitor cells (CPCs) — overexpression at mid-gestation pushes cells into the astrocyte lineage at the expense of neuron formation — Sun and colleagues investigated how EGFR might be distributed during mitosis of these progenitors. They observed that, in brain sections from mouse embryos, EGFR expression varied considerably between pairs of daughter cells in 22% of dividing EGFR-positive CPCs.

The authors then plated CPCs in culture so that individual daughter cells could be easily traced and their EGFR expression studied. *In vitro*, some pairs of dividing CPCs showed an asymmetric distribution of EGFR, which resulted in one cell having high levels of EGFR expression ($EGFR^{high}$) and the other having almost none ($EGFR^{low}$). $EGFR^{high}$ daughter cells showed much higher proliferative ability in response to EGF, and could migrate a greater distance towards EGF than their $EGFR^{low}$ counterparts, which indicates that the sibling progenitors with different EGFR levels are functionally distinct.

If the expression of EGFR can affect the cell fate choice of cortical progenitors, do $EGFR^{high}$ and $EGFR^{low}$ daughter cells acquire different fates? Interestingly, most $EGFR^{high}$ daughter cells expressed RC2, the marker for radial glia, and some of these went on to express GLAST, the marker for astrocytes. This was consistent with the observation that, in embryonic mouse brains, EGFR was colocalized with RC2 in CPCs with radial morphology. Contrastingly, $EGFR^{low}$ daughter cells did not express either RC2 or GLAST, but expressed OLIG1 and OLIG2, which are early transcription factors that are involved in neuronal and oligodendrocyte differentiation. When cultured for a longer period of time, many of these $EGFR^{low}$ cells expressed the oligodendrocyte marker NG2.

To understand exactly how astrocytes and oligodendrocytes are generated in culture over time, Sun *et al.* recorded single embryonic CPCs using time-lapse microscopy. At various stages of differentiation, clones were stained for EGFR expression and markers of neurons, astrocytes and oligodendrocytes. In this way, 'family trees' of individual CPCs were constructed and the origin of each progeny traced. This stringent lineage-tracing assay confirms the results of expression studies and indicates that asymmetric distribution of EGFR in CPCs is important for divergence, consistent with the $EGFR^{high}$ and $EGFR^{low}$ daughter cells giving rise to astrocyte and oligodendrocyte lineages, respectively.

These findings provide new insight into how neural cell diversity can be generated. It will be interesting to see whether asymmetric distribution of growth factor receptors is crucial for cell fate determination in other lineages. Furthermore, when one daughter cell inherits an excessive amount of receptors that are important for regulating proliferation, a mechanism for the derivation of cancerous cells might be formed.

Jane Qiu

References and links

ORIGINAL RESEARCH PAPER Sun, Y. *et al.* Asymmetric distribution of EGFR receptor during mitosis generates diverse CNS progenitor cells. *Neuron* **45**, 873–886 (2005)

FURTHER READING Roegiers, F. & Jan, Y. N. Asymmetric cell division. *Curr. Opin. Cell Biol.* **16**, 195–205 (2004)

WEB SITE

Temple's laboratory: http://www.amc.edu/Academic/Research/cnnResearcher.cfm?ID=139

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