NEUROGENESIS

Two ways to look after your hippocampus

Neuronal turnover in the hippocampus is now accepted to be a remarkably dynamic phenomenon. The survival of hippocampal neurons is exquisitely sensitive to many environmental stimuli, but this brain structure also shows an extraordinary capacity for regeneration. Two recent papers in the *European Journal of Neuroscience* report on the two faces of turnover — neuronal birth and death.

A fascinating observation about hippocampal neurogenesis is that physical exercise, such as running, can stimulate the birth of new neurons. In the first study, Fabel *et al.* explored possible mechanisms behind the effect of exercise and reported on the obligatory involvement of peripheral vascular endothelial growth factor (VEGF).

The circulating levels of VEGF increase after exercise, and the authors wondered whether this factor might mediate the stimulatory effect of physical activity on neurogenesis. They therefore tested the effect of VEGF on rat hippocampal progenitor cells *in vitro* and found that indeed it had a mitogenic effect. However, when looking at whole animals, Fabel *et al.* did not find that exercise induced the transcription of VEGF in the hippocampus, hinting at the possibility that circulating VEGF was the molecule responsible for the effect on neurogenesis.

To test this idea, the authors blocked the action of peripheral VEGF using a viral vector that produced a VEGF antagonist incapable of crossing the blood–brain barrier. They found that such a manipulation abrogated the exercise-induced production of new neurons but, remarkably, did not affect basal neurogenesis in control animals. This result indicates that different, independent mechanisms can control neurogenesis, and that peripheral factors can act separately from the central networks that regulate the production of new nerve cells. The precise way in which VEGF controls exercise-induced neurogenesis remains to be elucidated.

In the second paper, Bredy *et al.* investigated the effect of maternal care on neuronal survival in the rat hippocampus. The origin of this study can be found in the intriguing observation that the density of synapses and the spatial memory of rats differs, depending on the licking and grooming behaviour of their mothers. Rats reared by mothers that lick them with high frequency have higher synaptic density and better memory than rats reared by mothers with low-frequency licking behaviour. Bredy *et al.* asked whether such differences also correlated with the number of hippocampal neurons.

To answer this question, the authors injected one-week-old rat pups with 5-bromo-2-deoxyuridine (BrdU) to label cells that were born at this point of the rat's life, and looked for the labelled cells one day, three weeks or three months later. Crucially, some rats were reared by 'high-licking' mothers and some by 'low-licking' mothers. Bredy *et al.* found no differences in the number of labelled cells 24 h after the BrdU injection, indicating that cell proliferation was not significantly affected by the differences in maternal behaviour. But in rats that were examined three weeks and three months later, the rats in the high-licking group showed a larger number of labelled cells than the rats in the low-licking group. Moreover, the authors found that the labelled cells were mature neurons, and that the dissimilarity in maternal behaviour did not lead to differences in the number of immature neurons. This result indicates that maternal care does not affect neuronal maturation, but rather influences survival.

In fact, Bredy *et al.* also reported an increase in the expression of basic fibroblast growth factor in the high-licking group, pointing to the possibility that this form of maternal behaviour helped to provide an environment that promoted neuronal survival. The authors speculate that such an effect might be responsible for the influence of early maternal care on cognitive function in the adult.

Juan Carlos López

References and links

ORIGINAL RESEARCH PAPERS Fabel, K. *et al.* VEGF is necessary for exercise-induced adult neurogenesis. *Eur. J. Neurosci.* (in the press) | Bredy, T. W. *et al.* Maternal care influences neuronal survival in the adult hippocampus of the rat. *Eur. J. Neurosci.* (in the press)

FURTHER READING van Praag, H. *et al.* Neural consequences of environmental enrichment. *Nature Rev. Neurosci.* **1**, 191–198 (2000)

IN THE NEWS

Fair play

Postal workers and firefighters in the UK have recently walked out in protest at their pay and conditions. Just like humans, monkeys will down tools without hesitation if they feel that they are being ripped off, apparently revealing an innate sense of fair play similar to our own.

The discovery that justice is important to monkeys attracted a lot of attention in the press. The study — carried out at Emory University and published in *Nature* (18 September 2003) — involved training capuchin monkeys to exchange tokens for food. The monkeys were tested in pairs. As *USA Today* (18 September 2003) explains, "When pairs of females were both given cucumber in exchange for their tokens, everything was fine. But then one capuchin saw the other receive a grape while it received only cucumber, the seeds of unrest were sown."

The slighted monkey "often threw away the token, refused to eat the piece of cucumber, or even gave it to the other capuchin," (*The Scotsman*, 18 September 2003). According to Sarah Brosnan, one of the researchers, "refusing a food item of any type is very rare behavior in a capuchin," (*USA Today*).

Quoted in *CBC News* (18 September 2003), Brosnan went on to say that "the findings may help explain why people often forgo a reward if they don't perceive it as fair."

Needless to say, some journalists went to town with their headlines. Perhaps the best one was used by *CBC News*, who went with "Keep your darn cucumbers: angry monkeys." Enough said.

Rachel Jones