Nature Reviews Neuroscience | AOP, published online 18 July 2007; doi:10.1038/nrn2202

NEUROGENESIS

New neurons in a whiff

DOI:
10.1038/nrn2202

Hundreds of internet sites offer pheromone-containing perfumes that, it is claimed, can make any man irresistable to women. Whether they work is dubious but, in rodents at least, male pheromones do influence social memory and reproductive behaviour in females. These behaviours are mediated by the hippocampus and the olfactory bulb (OB), two regions in which neurogenesis occurs in adulthood. Mak *et al*. now show that in female mice neurogenesis is stimulated by exposure to pheromones from dominant males.

The authors exposed female mice to soiled bedding from male mice for 7 days, and injected them with 5-bromodeoxyuridine (BrdU) to label newborn cells. They found that BrdU labelling had increased in both the subventricular zone (SVZ), in which progenitor cells are born before they migrate to the OB, and the hippocampal dentate gyrus (DG). Exposure to bedding from castrated males, whose urine does not contain pheromones, did not have this effect. The increased labelling was dependent on an intact olfactory epithelium in the females, indicating that the pheromones increased cell proliferation via the olfactory system. Furthermore, pheromones from dominant males, for which females have a preference, had a stronger effect on SVZ and DG cell proliferation than pheromones from subordinate males.

To establish whether the new-born cells went on to develop into neurons in the OB and the DG, the authors used doublecortin to label neural progenitors. Exposure to male pheromones increased doublecortin labelling in the OB and in the DG, and 4 weeks later the number of cells labelled with BrdU and the neuronal nuclear antigen NeuN (a marker for mature neurons) had increased in both structures, indicating that the new-born cells induced by the male pheromones had matured into neurons.

The authors then tested whether luteinizing hormone (LH) and prolactin (PRL), two hormones involved in regulating the female reproductive cycle, might mediate the effect of pheromones on neurogenesis. Interestingly, male pheromones had no effect on neurogenesis in the DG in females lacking the LH receptor, although they still increased neurogenesis in the SVZ. Conversely, in females lacking the PRL receptor ($Prlr^{-/-}$ females), pheromones stimulated cell proliferation in the DG but not in the SVZ, indicating that LH and PRL specifically mediate pheromone-induced neurogenesis in the DG and the OB, respectively.

The functional significance of the increased neurogenesis was determined in a social-preference task. Females that had been exposed to pheromones from dominant males showed a preference for a dominant male over a subordinate one, whereas exposure to subordinate-male pheromones had no effect on mate preference. This did not occur in $Prlr^{-/-}$ females or in females in which neurogenesis was inhibited with a mitotic blocker.

These findings provide evidence that adult neurogenesis stimulated by pheromone exposure may have a role in mate selection, possibly by increasing memory for dominant-male pheromones. Further research is needed to establish whether the new neurons also function in other hippocampus-mediated forms of memory and behaviour.

Leonie Welberg

PHOTOALTO

ORIGINAL RESEARCH PAPER Mak, G. K. *et al.* Male pheromone-stimulated neurogenesis in the adult female brain: possible role in mating behaviour. *Nature Neurosci.* 1 July 2007 (doi:10.1038/nn1928)

© 2007 Nature Publishing Group