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Mouse data hint at human pheromones

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On that dream date, something really might be in the air. Results from a mouse study may bolster the evidence for human pheromones, the long-debated chemical signals thought to unconsciously sway our behaviour.

A team at the Fred Hutchinson Cancer Research Center in Seattle, Washington, has identified a class of protein receptor in the lining of mouse noses that may also operate in humans.

Researchers know that certain chemicals in mouse urine can alter the social or sexual behaviour of other mice. These chemicals work partly by binding to receptors in a particular structure in the mouse nose, known as the vomeronasal organ. In humans, however, this organ is thought to be defunct and the role of pheromones is hotly debated.

Finding such receptors in the lining of the nose, rather the vomeronasal organ, is a more direct parallel with humans. Stephen Liberles and Linda Buck report their finding online this week in *Nature* (S. D. Liberles & L. B. Buck *Nature* doi:10.1038/nature05066; 2006). They isolated a group of receptors that can be triggered by at least one known mouse pheromone.

Genes encoding this family of receptors are also found in humans. "It's probably our best bet yet for functional pheromone genes in humans," says Timothy Holy, a neurobiologist at Washington University in St Louis, Missouri.

For their part, Liberles and Buck are cautious about labelling the mouse proteins as pheromone receptors. They have not yet carried out a key test to show that activating or eliminating the receptors alters a mouse's behaviour. But Buck says that her team is "intrigued by the possibility" of their being pheromone receptors, and is embarking on tests to find out.

So far, most evidence for human pheromones has come from behavioural research. In one study, scientists at the University of Chicago showed that women's menstrual cycles changed in length after they sniffed the sweat on pads previously worn in the armpits of another woman (K. Stern & M. K. McClintock *Nature* **392**, 177–179; 1998). Another study showed that newborn babies move towards a pad carrying the smell of their mother's breast rather than a clean pad (H. Varendi & R. H. Porter *Acta Paediatr.* **90**, 372–375; 2001).

But many researchers remain sceptical about the power of human pheromones — or even whether they exist at all. Human behaviour is influenced by so many conscious and unconscious factors that it's hard to measure the subtle changes in behaviour caused by a putative pheromone. "Work on human pheromones seems always to capture both public interest and scientific scepticism," says Holy.

If the receptors discovered in mice are indeed pheromone receptors, this could allow researchers to ask concrete questions about human pheromones. Scientists could, for instance, study people with mutant versions of the receptors to see if they behave differently when exposed to candidate pheromones.

The latest study "makes it harder for the sceptics", says Martha McClintock, who led the University of Chicago experiments. "Hopefully, this will catalyse a lot of research by high-powered scientists."

Neuroscientists already know that genes in neurons in the lining of the nose make more than 1,000 different olfactory receptors for identifying chemical odours. The discovery of this gene family won Buck and Richard Axel the 2004 Nobel Prize in Physiology or Medicine.

To look for other classes of receptor, Liberles and Buck isolated neurons from mouse noses and searched for genes that were active only in those cells and were similar to olfactory receptors. They hit on a family of 15 such receptors, called trace amine-associated receptors, or TAARs. There are six genes that code for similar receptors in humans.

The researchers next searched through a set of other chemicals to find those that activated the TAAR receptors. Three of the chemicals they found are present in mouse urine, which is known to affect the animals' social behaviour. One in particular earns the label of a pheromone because it is produced in the urine of male mice and accelerates the onset of puberty in females.

Experts say there may be other as yet undiscovered sensory receptors involved in detecting mammalian pheromones, perhaps including human ones. A paper in 2000 showed that a gene for one mouse pheromone receptor in the vomeronasal organ is also active in the human nose

(I. Rodriguez *et al. Nature Genet.* **26**, 18–19; 2000). "There might be other unidentified ones out there," says neurobiologist Frank Zufall of the University of Maryland in Baltimore.

Liberles and Buck are now testing whether there are molecules in human urine, sweat and vaginal fluid that can trigger the receptors and that might be human pheromones. They also want to examine whether the neurons manufacturing the newfound receptors are wired up in the brain in a different way from regular, smell-detecting neurons. If so, they might connect to centres that control our behaviour or emotions.

Helen Pearson

"The new study makes it harder for the sceptics."