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BEHAVIOUR

Epigenetically bonded

> trichostatin A induced a marked increase in the mRNA levels of the oxytocin receptor

The tendency of prairie voles to form lifelong pair bonds and to share nesting and pup-raising responsibilities has made them invaluable for understanding the neurobiological basis of long-term social bonding. Previous studies in these mammals have implicated oxytocin, vasopressin and dopamine in triggering affiliative behaviour towards a partner (so-called 'partner preference'). Now, Kabbaj and colleagues show that epigenetic mechanisms also have a role in regulating such behaviour.

J. Vallis/NPG

The authors administered trichostatin A — a histone deacetylase inhibitor — to virgin female prairie voles prior to housing them with a male vole and found that the drug facilitated partner preference in the absence of mating. When they looked for changes in the expression pattern of genes that are known to affect partner preference in the nucleus accumbens (NAc), a brain region involved in pair-bonding, they found that trichostatin A induced a marked increase in the mRNA levels of the oxytocin receptor (*Oxtr*) and a slight increase in the mRNA levels of the arginine vasopressin 1a receptor (*Avpr1a*) after 2 hours of co-habitation with a male (without mating).

To determine whether this increase in gene expression was due to an effect of the drug on the acetylation levels of the gene promoters, the authors carried out chromatin immunoprecipitation experiments. Compared with cerebrospinal fluid-treated control females, the trichostatin A-treated voles exhibited a very high increase in histone H3 acetylation at the *Oxtr* and *Avpr1a* promoters after only 30 minutes of co-habitation with a male. This effect was only observed in the NAc, as no changes were observed in the promoters of these genes (or their mRNA levels) in the caudate putamen, a region associated with the regulation of movement and various forms of learning. Furthermore, when the authors pre-treated the females with oxytocin or vasopressin receptor antagonists via intra-NAc injections, the effects of trichostatin A on partner preference were abolished, confirming that by promoting the expression of these genes and thus stimulating oxytocin and vasopressin signalling pathways in the NAc, it is possible to trigger pair-bonding.

Importantly, Kabbaj and colleagues showed that mating induces a similar epigenetic potentiation of *Oxtr* and *Avpr1a* transcription to trichostatin A, highlighting a role for epigenetic mechanisms in the formation of social bonds. It will be interesting to investigate whether similar changes are involved in human affiliative behaviour and, potentially, other social behaviours.

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ORIGINAL RESEARCH PAPER Wang, H. *et al.* Histone deacetylase inhibitors facilitate partner preference formation in female prairie voles. *Nature Neurosci.* 2 Jun 2013 (doi: 10.1038/nn.3420)