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ANIMAL BEHAVIOUR

The nexus of sex and violence

In mice, brain neurons that respond during either mating or aggression exhibit spatial overlap, and some even respond during both. This may help to explain the relationship between sex and violence in human behaviour. SEE ARTICLE P.221

CLIFFORD B. SAPER

The close relationship between sex and violence has been an enduring theme in literature, theatre and music since the dawn of 'civilized' culture. A particularly graphic depiction of the connection can be found in Anthony Burgess's book *A Clockwork Orange*, which famously mixes the two in a mélange of 'ultraviolence'. Although fascinating, the intertwined nature of these two opposites of social interaction and the underlying neurobiological basis have remained a puzzle. On page 221 of this issue, Lin and colleagues[1] identify some of the basic circuitry for these behaviours in the hypothalamus — a primitive part of the brain that has been highly conserved throughout mammalian evolution.

It has long been known[2] that, in cats, electrical stimulation in certain regions of the hypothalamus elicits attack behaviour. Studies[3,4] in rats have also identified a network of brain sites in which stimulation can produce aggression, including the ventromedial nucleus of the hypothalamus (VMH).

Meanwhile, investigators have identified[5] VMH neurons that express receptors for sex hormones, and have shown[6] that electrical stimulation of the VMH can produce sexual behaviours in rats. Moreover, after mating or aggression, neurons in the ventrolateral VMH (VMHvl) and several other brain areas, including parts of the amygdala, express cFos — a protein that is expressed by many brain neurons that have recently undergone activation[7]. It remained unclear, however, whether both behaviours activate the same neurons, or separate cell populations that overlap spatially. Lin and co-workers[1] attempted to sort this out.

The authors sequentially exposed male mice to another male and, 15–20 minutes later, to a female — situations that would trigger first aggression and then sexual behaviour. They then analysed neurons for two types of cFos messenger RNA: heteronuclear mRNA, which would have been produced more recently, while the female mouse was present; and cytoplasmic mRNA, which would have matured from heteronuclear mRNA generated earlier while the male mouse was present. Although neurons expressing both types of mRNA spatially overlapped in the VMHvl, they largely belonged to distinct populations. However, a proportion (20–30%) of these cells showed cFos expression during both encounters.

To better define the time course of the neuronal response, Lin *et al.* recorded the firing of individual VMHvl neurons in male mice during encounters with both sexes. Whereas some 40% of the VMHvl neurons were excited by male intruders, about half of these were activated only during close encounter and attack. By contrast, roughly one-third of the VMHvl cells were excited by a female intruder, but the level of excitement in around two-thirds of these neurons tended to decrease as the sexual encounter progressed.

About half of all recorded neurons in the VMHvl responded initially to both a male and a female intruder, but many of these ultimately continued firing during only one of the two behaviour patterns. The dual activation of some neurons during the earliest stages of both encounters indicates that they share some types of input; in other words, the interaction of the two outcomes is deeply rooted in the basic architecture of the brain.

Lin *et al.*[1] provide another line of evidence for the interaction between sexual behaviour

50 Years Ago

The Tobacco Manufacturers' Standing Committee has as a declared aim the assistance of research into questions concerned with the relationship between smoking and health. That this object is being fulfilled is evident from its report for the year ended May 31, 1960, which summarizes investigations carried out during the year under the auspices of the Committee or with its financial support ... Fractions of cigarette smoke condensate prepared in the laboratories of the Committee have been found by several workers to have carcinogenic or tumour-promoting properties, but as the report points out, these results, obtained by application of smoke fractions to animal tissues, are not necessarily reliable guides to the possible response of human lung tissue to tobacco smoke.
From *Nature* 11 February 1961

100 Years Ago

The terrible intensity of the outbreak of pneumonic plague now raging in Manchuria, and the presence of plague-infested animals within our own borders, have called forth recently a number of communications on plague in the daily press. A special correspondent in *The Times*, in two well-informed articles … summarises the situation, and gives an admirable sketch of the principal facts concerning the modes of spread of plague. Dr. L. W. Sambon has also contributed two letters on the subject … He remarks, for example, that in his belief transmission from man to man is probably more frequent than from rat to man. If Dr. Sambon bases this statement upon personal experience of epidemics of bubonic plague, it must be said that his observations are directly opposed to the experience of many competent plague workers.
From *Nature* 9 February 1911

and violence by activating the VMHvl — using the technique of optogenetic stimulation — during encounters with intruders. The male mice rapidly attacked animals of either sex; most would even attack an inflated glove if it was moved. Intriguingly, however, when the authors stimulated the VMHvl at the same level during sexual intercourse, they saw no attack. This suggests that neurons mediating aggression are actively suppressed during mating, even in mice that are made hyperaggressive by optogenetic stimulation.

Can hypothalamic neurons be manipulated to curb aggressive behaviour? Lin and colleagues used a viral vector to cause VMHvl neurons to express inhibitory chloride channels that are regulated by ivermectin — an antibiotic that can be given systemically and that penetrates the brain. Following ivermectin administration, 25% of animals that previously showed normal attack rates did not attack at all, and the rest showed increased latency and decreased duration of attacks on male intruders. Eight days after ivermectin injection, the responses had returned to normal levels.

Clearly, much more must be learned about how hypothalamic neurons that mediate sex and violence operate, and how they can be productively controlled. But the possibility of using this information to change human behaviour may not be far from the minds of those who live with the challenge of dealing with violent sexual offenders. In *A Clockwork Orange*, social engineers used Pavlovian conditioning of the protagonist to induce an aversion to both sex and violence. Could — and should — the behaviour of sex offenders or violent criminals be similarly controlled by genetic therapy to induce expression of ion channels in the VMHvl followed by pharmacological or optogenetic stimulation? It would be particularly valuable to decipher the chemical features of neurons with specific firing patterns. With this information in hand, researchers could potentially design vectors to introduce foreign ion channels only in a specific group of neurons — a way to differentially modify sexual or violent behaviours.

It is noteworthy that this work[1] was done entirely in male mice. Although among humans, men commit a larger proportion of both sex offences and violent crimes, women commit their own distinct patterns of sexual and violent crimes. The same parts of the brain exist in both sexes, and presumably similar circuitry controls behaviour in females. Exploring sexual differentiation of the circuitry that regulates sex and violence might provide an exciting chapter in understanding some of the most basic components of our personalities. ■

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PALAEOCLIMATOLOGY

Core data from the Antarctic margin

Sediments at the edge of Antarctica are a largely unexploited source of information about climate change. They have now provided a valuable local record of sea surface temperatures for the past 12,000 years. SEE LETTER P.250

JAMES BENDLE

The coastal areas of Antarctica are sites of strong air–sea–ice interactions that can affect the entire globe, but they remain the least-studied region on Earth with respect to climate variability. The paper by Shevenell *et al.* (page 250 of this issue[1]) is a good start in addressing that deficiency.

The western Antarctic Peninsula is warming five times faster (3.4 °C per century[2]) than the global mean increase during the twentieth century. The consequences are evident in the changing distribution of plants and animals, and in the retreat and sometimes dramatic disintegration of ice shelves. But there are all too few data to assess the causes of this warming, and to judge how unusual it is in recent Earth history. Satellites have been continuously monitoring sea surface temperatures (SSTs) and ice extent on the Antarctic Peninsula for only the past three decades. Globally, the instrumental record covers just the past few hundred years, with notably sparse data coverage for the Southern Ocean and Antarctica.

It is against this background that the paper by Shevenell *et al.*[1] appears. The authors report a proxy record of SSTs on the inner continental shelf of the western Antarctic Peninsula for the Holocene epoch — the most recent, relatively warm and stable 12,000 years of geological time. They reconstruct SSTs using measurements of biological molecules extracted from ocean-sediment cores collected by the Ocean Drilling Program (ODP Leg 178), from Site 1098, at 1,010 metres water depth in the Palmer Deep, a prominent basin on the inner shelf. Figure 1a of the paper (page 251) shows the region concerned.

Over the interval 12,000–2,000 years ago, the reconstructed SSTs exhibit a cooling trend of 3–4 °C, which broadly tracks the decline of spring solar radiation at 65° S (a function of cyclical changes in Earth's orbit). Superimposed on the longer trend are temperature variations of 2–4 °C on the centennial to millennial scales. The longer-term cooling trend and many of the millennial-scale events can be found in other palaeoclimate records[3], but in comparison with other locations the temperature variations are remarkably high.

Thus, the absolute values should be treated with caution, but perhaps are not unexpected. Because of its position in the seasonal sea-ice zone, models predict that temperature changes at ODP 1098 should be amplified by the albedo effect (for example, dark, sunlight-absorbing open water warms up more readily than white, sunlight-reflecting sea ice)[4]. The temperatures between 11,800 and 9,000 years ago are especially warm and may also reflect intense spring/summer warming of surface waters, stratified by glacial meltwater. Interestingly, independent geological evidence indicates that the neighbouring George VI Ice Shelf collapsed around 9,600 years ago, following the 2,000 years of warm temperatures recorded at ODP 1098.

Most intriguingly, Shevenell and colleagues' work supports evidence that, during the Holocene, SSTs off the western Antarctic Peninsula were directly linked to westerly wind strengths in the Southern Hemisphere and to the El Niño–Southern Oscillation (ENSO; a roughly periodic, trans-Pacific pattern of climate fluctuation). A clearer mechanistic understanding of these connections will be essential. ENSO and the southern westerlies are predicted to strengthen further with future climate warming; if they are indeed a strong controlling factor on the temperature of the oceans around Antarctica, there are implications for ice-sheet stability and sea-level changes.

But what about the recent rapid warming of the western Antarctic Peninsula? What has the