PERCEPTION

Linking perception to neural activation

The relevance of linking neural activity patterns to perceptual tasks — a core objective of cognitive neuroscience — is highlighted by a new study in the honeybee *Apis mellifera*. Reporting in *PloS Biology*, Guerrieri, Schubert and colleagues show that odours that are encoded as physiologically similar are also perceived to be similar by bees.

To determine the perceptual similarity of odours, Guerrieri *et al.* adopted the olfactory conditioning of the proboscis extension response, a classical conditioning paradigm in which an olfactory stimulus (the conditioned stimulus, or CS) is paired with a sucrose feed until extension of the proboscis is evoked by the CS alone. They used 16 odours that varied in two chemical features: functional group and carbon-chain length. Each bee was conditioned to one of the odours and tested for generalization responses — in which different but similar stimuli are treated as equivalents — to four odours, one of which could be the trained odour.

The researchers found that all the odorants could be learned, and that generalization depended on functional group (for example, generalization was high from ketones to alcohols and aldehydes) and chain length (generalization was higher between long-chain than between short-chain odorants). They went on to build an olfactory perceptual space for the honeybee by principal components analysis (PCA), in which the relationships between odours were represented in a limited number of dimensions. The PCA showed a clear organization of odours depending on their chemical characteristics — functional group and chain length being 'inner dimensions' of the bees'

PAIN

Yin and yang of acupuncture

Acupuncture, which is rooted in a 3,000 year-old Chinese tradition of yin and yang, is believed to cure diseases by re-establishing the 'energy balance' in organs when it goes awry. Although the practice of acupuncture is becoming increasingly mainstream in Western countries, whether acupuncture has a real therapeutic effect beyond placebo is the subject of heated debate. This debate is highlighted by two recent studies, although the answer remains elusive.

In a randomized controlled trial, Linde and colleagues tested the value of acupuncture for the treatment of migraines. They divided 302 patients with migraines into three groups. The first group received proper acupuncture treatment and the second a sham acupuncture treatment that did not follow the rules, whereas the third comprised an untreated control group. After 9–12 weeks, 15% of untreated patients reported a reduction of 50% or more in the number of days on which they had migraines.

In the acupuncture and sham groups, the percentage of patients who experienced a similar decrease was 51% and 53%, respectively. Therefore, acupuncture was no more effective than sham acupuncture in reducing migraines, although both interventions had some positive effects compared with no treatment.

In the second study, a team led by Lewith used position-emission tomography to investigate whether acupuncture has a specific demonstrable effect on the brain. The study group, which consisted of 14 patients with arthritis, was subjected, in random order, to three treatments. In one treatment, the patients were jabbed with blunt needles that did not penetrate the skin, having been told in advance that the procedure should not have any therapeutic value. In another treatment, they received sham acupuncture with placebo needles that retracted into their shafts like stage daggers, thereby tricking patients into believing that they were being treated. The third treatment was genuine acupuncture. Interestingly, both sham and real acupuncture activated the dorsolateral prefrontal cortex, anterior cingulate cortex and midbrain — regions of the brain that are associated with belief and expectation. In addition, real acupuncture activated the insula, which is thought to be involved in pain modulation. The authors conclude that acupuncture has a real physiological effect that might underlie its ability to relieve pain.

The discrepancy between these studies highlights the importance of well-defined placebo controls in clinical trials. It will be interesting to determine whether acupuncture at unorthodox positions can also activate the insula, and whether different brain activities can be detected as a result of acupuncture using sham and real acupuncture needles at those positions.

Jane Qiu

References and links

ORIGINAL RESEARCH PAPER Linde, K. *et al.* Acupuncture for patients with migraine: a randomized controlled trial. *JAMA* **293**, 2118–2125 (2005) | Pariente, J. *et al.* Expectancy and belief modulate the neuronal substrates of pain treated by acupuncture. *Neuroimage* **25**, 1161–1167 (2005)

FURTHER READING Colloca, L. & Benedetti, F. Placebos and painkillers: is mind as real as matter? *Nature Rev. Neurosci.* **6**, 545–552 (2005)

olfactory space. Distances between odours in this perceptual space correlated with physiological distances — a measure of the similarity of odours based on neural activation patterns — obtained in optical imaging experiments of antennal lobe activity.

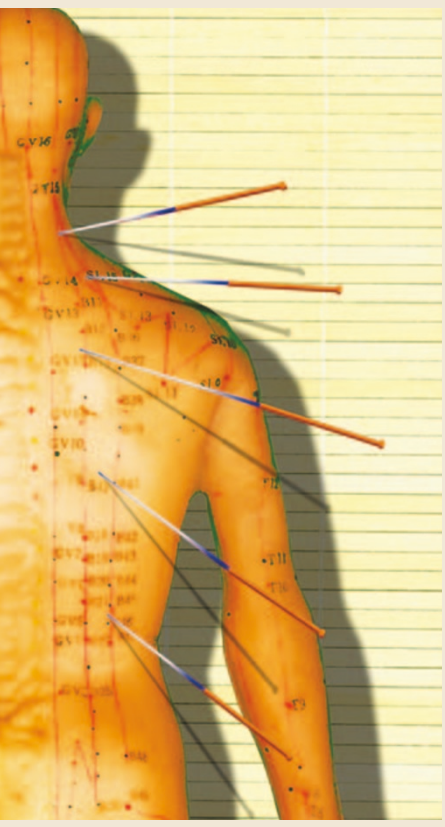
This study confirms that olfactory neural activity corresponds to olfactory perception, and shows how invertebrate models such as the honeybee can be used to answer fundamental questions about the neurobiology of perception. As this line of enquiry is pursued with more odours, comprising a range of molecular features, we will gain a more complete description of the honeybee's olfactory perceptual space, and a better understanding of how perceptual measures relate to patterns of neural activity.

Rebecca Craven

References and links

ORIGINAL RESEARCH PAPER Guerrieri, F. *et al.* Perceptual and neural olfactory similarity in honeybees. *PLoS Biol.* **3**, e60 (2005)

FURTHER READING Sachse, S. *et al.* The spatial representation of chemical structures in the antennal lobe of honeybees: steps towards the olfactory code. *Eur. J. Neurosci.* **11**, 3970–3982 (1999)



DEVELOPMENT

MicroRNAs and brain morphogenesis

Hundreds of microRNAs (miRNAs) have been identified in a range of organisms, from plants to fish to humans. These small, non-coding RNAs function as negative regulators of gene expression at the post-transcriptional level. Now, Schier and colleagues have used a zebrafish model to bring to light an important role for miRNAs in brain development.

The development of precurser miRNAs into mature miRNAs involves sequential cleavage events that are catalysed by two ribonuclease III (RNaseIII) enzymes, Drosha and Dicer. One strand of the resulting processed duplex is incorporated into a silencing complex, which acts on its target through either translational inhibition or mRNA cleavage.

Schier and colleagues generated *dicer* mutant zebrafish in which this process was disrupted and mature miRNAs were absent. In early-developing zygotes, maternally-derived Dicer is still active, so mature miRNAs are generated even if the zygotic *dicer* is mutated. The authors therefore used a germ line-replacement technique to abolish the maternal and zygotic functions of *dicer* in zebrafish.

In these mutant zebrafish, anterior–posterior and dorsal–ventral neural patterning occurred normally, and all principal subregions and cell types were present. This indicates that early patterning and fate specification were unaffected by the absence of miRNAs. However, there were major disruptions to morphogenesis during gastrulation, somitogenesis, and heart and brain development. The mutant zebrafish also developed at a reduced speed compared with their wild-type counterparts.

Specifically, abnormalities in neural development involved impairments in the positioning of neurons, in the defasciculation of longitudinally projecting axons and in touch-induced escape behaviour. Most strikingly, although the neural plate gave rise to a normal neural rod, the formation of the neural tube and neurocoel was disrupted. Normal ventricles did not form, and some boundaries that subdivide the brain into cell-tight compartments, such as the midbrain–hindbrain boundary, were missing. There were also defects in retinal development. So, miRNAs seem to be crucial for normal brain morphogenesis, neural differentiation and neural function during zebrafish development.

Further investigations revealed that the miR-430 family of miRNAs is ubiquitously expressed and especially active during early stages of development. Importantly, injection of miR-430 miRNAs into the mutant zebrafish rescued specific abnormalities in brain development, including the ventricle and boundary formation defects, although it had no effect on the heart and circulation abnormalities. This finding indicates that mature miRNAs are crucial for normal development and that the miR-430 family of miRNAs is responsible for the morphogenic defects seen in this study.

This work provides an important step in our understanding of the roles of miRNAs in brain development. More detailed knowledge of the molecular mechanisms that underlie brain morphogenesis — including neural tube and ventricle formation — could be gained through the study of the miR-430 miRNA family and its downstream targets. Moreover, the method used in this study — to prevent the generation of mature miRNAs in zebrafish — is just as noteworthy as the results, and could prove invaluable in future studies of the role of miRNAs in development.

Alison Rowan

References and links

ORIGINAL RESEARCH PAPER Giraldez, A. J. *et al.* MicroRNAs regulate brain morphogenesis in zebrafish. *Science* **308**, 833–838 (2005)

FURTHER READING He, L. & Hannon, G. J. MicroRNAs: small RNAs with a big role in gene regulation. *Nature Rev. Genet.* **5**, 522–531 (2004)