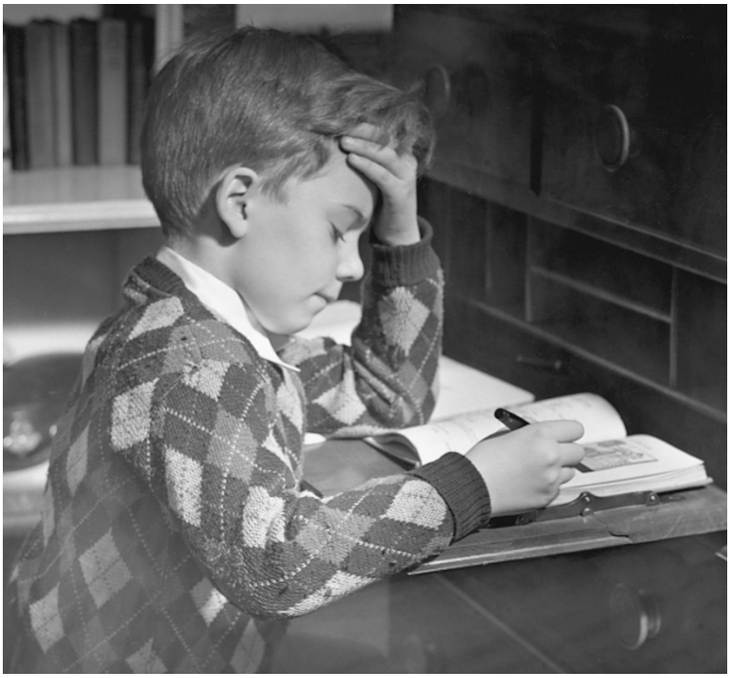
FUNCTIONAL IMAGING

Learning by the rules



For many years, learning theorists have known how animals — or humans — learn that one thing leads to another. The Rescorla–Wagner learning rule states that the likelihood of learning about an association on a particular trial depends on an error signal, which arises from the difference between what the subject expects to happen and what actually happens. At the beginning of training, before an association has been learned, any outcome is unexpected and learning will occur quickly. After many training trials, on the other hand, the association will have been learned so well that the outcome of a given trial is completely predicted and no further learning occurs, because there is no error signal.

It seems that neuroscientists are only now catching up with the behaviourists in learning about learning. First came the demonstration that the responses of midbrain dopamine neurons in primates followed precisely the predictions of formal learning theory, as published by Waelti *et al.* earlier this year (see 'Trial and error' in the August issue of *Nature Reviews Neuroscience*). And now Fletcher and colleagues have shown that responses in the human dorsolateral prefrontal cortex (DLPFC), as observed by functional magnetic resonance imaging (fMRI), do exactly the same thing.

People lying in an fMRI scanner were shown images of drugs followed by images representing syndromes; their task was to learn which drugs would cause which syndromes. During the first few training trials, activity in the DLPFC was high, but then it decreased as the subjects were increasingly able to predict the outcome of a trial.

After learning, unexpected outcomes (for example, when a drug that had previously been associated with a syndrome did not give rise to that syndrome) produced increased activity in DLPFC, just as predicted by learning theory. The Rescorla–Wagner rule also states that different outcomes will have different effects on learning, depending on salience or other factors; so another prediction was that the DLPFC would be more sensitive to surprise outcomes if they

DEVELOPMENT

Nerves are brought to heal

Healing of a skin wound can be a long and complicated process, and it seems that the problem is made even worse if the cutaneous nerve supply is impaired. In conditions such as diabetic neuropathy, complications associated with skin wounds have even led to amputation in extreme cases. Do nerves play an active role in the healing process? The fact that skin often becomes hyperinnervated after wounding would certainly support such a theory. However, some people have argued that the loss of pain sensation after denervation makes tissue more susceptible to further injury, thereby slowing the healing process.

As reported in *Developmental Biology*, Harsum *et al.* have set out to resolve this conundrum by studying the relationship between innervation and wound healing in the developing chick embryo. The skin of the early embryo shows a remarkable capacity for wound healing, and wounds made at embryonic day 4 (E4) heal within 24 hours, leaving no scar. However, the rate of healing becomes progressively slower as development proceeds, and the skin becomes increasingly prone to scarring, indicating that the mechanisms of wound healing change with time.

By irradiating the E2 neural tube between somites 12 and 20, Harsum *et al.* generated chick embryos with nerveless wings. At E4, the skin healed normally in these embryos, but around the time that the skin would normally become innervated (E7), healing became impaired, and was significantly slower than in wild-type skin at the same stage. The effects of continual injury due to lack of sensation could be ruled out, because the embryos were grown in a liquid environment, which was unlikely to cause damage.

The results of this experiment indicate a role for nerve-derived signals in wound healing, but only from the time that the skin normally becomes innervated. Dependence on these signals is acquired during development and, as it also seems to be acquired by nerveless skin, it clearly does not require contact with nerves. Interestingly, wounded fetal skin does not become hyperinnervated, so this does not seem to be a prerequisite for healing. Rather, the authors argue that hyperinnervation is a consequence of the inflammatory response, which does not occur in fetal tissue.

The next step will be to identify the signals released by nerves that are beneficial for tissue repair. Substance P and fibroblast growth factors are likely candidates, and both have been shown to be released by damaged nerves. It will also be important to understand why the response of the skin to these signals changes during development. With this knowledge, it should be possible to devise ways to improve the efficiency of wound healing in adult skin.

Heather Wood

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involved occurrence of the syndrome than if they did not. As predicted, surprise events where the outcome was 'syndrome' produced more DLPFC activation than those where the outcome was 'no syndrome' — and these events were also more likely to produce learning (that is, to change the subjects' subsequent predictions).

This study provides further evidence that neural activity — across whole brain regions as well as in individual neurons — reflects the specific predictions that arise from formal learning theory. Further collaborations between behavioural theorists and neuroscientists might give us similar insight into the neural bases of other types of learning or behaviour.

Rachel Jones

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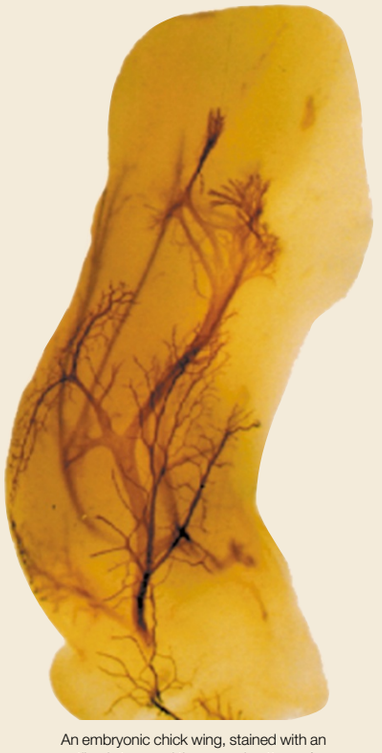

An embryonic chick wing, stained with an antibody to reveal the normal pattern of innervation. Courtesy of Jonathan Clarke and Paul Martin, University College London, UK.

VISUAL PROCESSING

A roving eye

As we view the world around us, our eyes frequently make ballistic movements from one point of gaze to another. These 'saccades', which can occur several times per second, are usually automatic and go unnoticed. This is somewhat surprising. After all, when the image of a fast-moving object sweeps across the static retina, we are normally aware of its motion. So why is it that we fail to detect the comparable motion of images as they sweep across the retina during saccades? This apparent paradox has previously been explained by the intrasaccadic suppression of visual sensitivity. But as García-Pérez and Peli report in the *Journal of Neuroscience*, it seems that we might have underestimated our capacity for visual perception during saccades.

Traditionally, intrasaccadic suppression has been studied by presenting a range of visual stimuli to subjects, and comparing their performance during saccades with that in fixation trials. But because the stimulus differs in these situations — the image falls onto a single retinal location in the latter case, but is spread across the retina in the former — this approach does not answer the question of whether lower sensitivity during saccades is actually the result of a deterioration in visual processing. García-Pérez and Peli adopted a different approach. They isolated intrasaccadic perception in human volunteers by presenting them with high-speed visual stimuli that are invisible under fixation (because fast temporal oscillations are filtered out by the mammalian visual system), but which can be detected by executing saccades. In this way, they removed the potential complications of pre- and postsaccadic perception of the visual stimulus.

Subjects viewed gratings (patterns made up of alternating bright and dark stripes) that differed in their spatial resolution (the number of repeats of the pattern per degree of the subject's visual angle) and in the speed at which they drifted. The fact that fast-drifting gratings can be seen during saccades shows that intrasaccadic suppression does not eliminate the perception of high-contrast stimuli. But how much are we able to perceive during saccades? As has been reported previously, García-Pérez and Peli found that intrasaccadic processing allows the conscious perception of motion. But interestingly, whereas motion perception during saccades has previously been ascribed to the magnocellular pathway, the authors found that it did not occur for stimuli that are optimal for processing by this system (those with low spatial and high temporal frequencies). They went on to show that a number of other complex visual tasks can be performed during saccades; for example, direction-of-motion discrimination, contrast discrimination and contrast matching. Moreover, they were able to show that, in theory at least, a filtering process of the type that accounts for the invisibility of fast-moving gratings under fixation might also operate during saccades.

The analysis presented by García-Pérez and Peli indicates that, rather than being degraded, visual processing during saccades shares many of the characteristics of processing under fixation. These findings argue against the idea of intrasaccadic suppression, so how is it that our view of the world remains stable as we execute saccades? The authors concur with others in suggesting that, under normal circumstances, the answer might lie in visual masking by pre- and postsaccadic perception.

Rebecca Craven

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WEB SITE

Eli Peli's lab: http://www.eri.harvard.edu/faculty/peli/index.html