100 YEARS AGO

An interesting instance of that adaptability to changing tastes and conditions which is the mainspring of progress in industry as well as in science is afforded by a note in the *Journal* of the Society of Arts (July 18). For some years the demand for claret has greatly diminished in favour of the wines of Champagne, and has seriously affected the wine industry in the Bordeaux region. Several proprietors in the Médoc have, however, now commenced the production of sparkling wines by the same process as champagne is made, and their action has been the means of developing practically a new industry. It may at first seem strange that white wine should be able to be made in the Médoc, where only black grapes are grown, but as a matter of fact champagne is almost entirely made from black grapes, and the most celebrated vineyards in the Champagne district are all planted with them… It is stated that to the ordinary taster there is nothing but the label to distinguish the sparkling médoc from the best brands of champagne.

From *Nature* 31 July 1902.

50 YEARS AGO

***The Psychology of the Occult.* This stimulating and highly provocative book is an attempt to describe and analyse the part "played by various types of psychological anomaly in the creation and perpetuation of occult beliefs and practices"… Mr. Rawcliffe is completely unmoved by the flood of modern propaganda in favour of the reality of so-called psychic phenomena… As for the physical phenomena of the séance room, Mr. Rawcliffe finds the evidence scarcely worth considering. To him the whole of the studies of the psychical research worker are mere examples of magic and superstition dressed up in modern garb and often presented behind a façade of statistical jargon which is intended to disguise the faulty character of the original data. In support of his position he has skilfully put together a mass of material in which the incompetence and credulity of not a few workers in this field are cruelly displayed. Yet he has omitted much that would have strengthened his case and, it must be added, a good deal that would have weakened it… however, this book remains a useful handbook for those who suspect that much of what passes for psychical research and which is often unfortunately supported by leading parapsychologists is scarcely worth the paper on which it is recorded.**

From *Nature* 2 August 1952.

surface, see inside the structure and sample the rocks. But exposed impact structures are typically incomplete, lacking their uppermost parts through the vagaries of erosion and deformation processes. The only way of 'seeing' virgin morphology is when a structure has been rapidly buried after it formed, and so has been preserved. Geophysicists then need to use seismic techniques to reveal the three-dimensional structure, as has been done for Silverpit. The development of multiple concentric rings at such a small diameter may not be unusual because, until recently, we have been unable to obtain images with this degree of detail in such a well-preserved example.

Finally, the real test that Silverpit was created by an impact will be to look for shock effects in the rocks that form it. Shock-generated features such as unusual microscopic mineral deformations and shatter cones (conical fracture systems formed by shock waves in rock) would be compelling evidence of an impact origin. Two wells that were drilled in the search for oil and gas do penetrate the structure, but unfortunately, few samples of the drill cuttings from them were taken. Given that impact structures are among the most productive hydrocarbon sites on the planet, we may get more rock samples if Silverpit shows exploration potential. ■

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Neurobiology

Never fear, cannabinoids are here

Pankaj Sah

Although we understand how fearful memories are stored in the brain, how they are extinguished remains a mystery. The answers may lie with the cannabinoid compounds our bodies produce.

Cannabinoids such as marijuana and hashish have been used for over a thousand years for medicinal and recreational purposes. The active 'ingredient' of these drugs is Δ^9-tetrahydrocannabinol, which produces effects on nerve cells in the brain by binding to a protein on the neuronal surface, the CB1 receptor[1]. But of course the receptor is not there simply to detect this externally derived compound: it also binds to 'endogenous' cannabinoids, which are produced naturally by the body. On page 530 of this issue, Marsicano and colleagues[2] propose a new role for this 'endocannabinoid' system — extinguishing fear-related memories in mice. The finding might have implications for treating anxiety disorders in humans.

We can form memories in several different ways, one of which is Pavlovian conditioning — the classic example being that of Pavlov's dogs, which learned to expect food whenever they heard a ringing tone. We all form these types of associations; for instance, we may associate a particular piece of music with our first love affair. But the connection need not always be pleasant. Imagine you are having a quiet walk in a park when you are threatened by an armed person. During the attack you are terrified; your heart races and your palms are sweaty. You run and escape. Later, you may find that entering the same park brings back in detail the memory of the attack, right down to the sweaty palms.

In the lab, the neuronal and molecular mechanisms underlying fearful memories are often studied in animals by using 'fear conditioning'. Here, a neutral — or conditioned — stimulus, which is typically a tone or a light, is paired with an aversive (unconditioned) stimulus, typically a small electric shock to the foot. After the two stimuli are paired a few times, the conditioned stimulus alone evokes the stereotypical features of the fearful response to the unconditioned stimulus, including changes in heart rate and blood pressure and freezing of ongoing movements. Repeated presentation of the conditioned stimulus alone leads to extinction of the fearful response — the animal learns that it need no longer fear a shock from the tone or light.

A large body of work has established that a small, almond-shaped region in the brain, the amygdala, is crucial in acquiring and, possibly, storing the memory of conditioned fear[3,4]. It is thought that, at the cellular and molecular level, this learned behaviour requires neurons in the basolateral part of the amygdala, and changes in the strength of their connection with other neurons ('synaptic plasticity') that depend on the NMDA receptor[5], which responds to the neurotransmitter glutamate.

The extinction of aversive memories also involves the basolateral amygdala, but the cellular and molecular details are less clear. Infusing antagonists of the NMDA receptor into this region blocks extinction, implying that these receptors are important here, too[6]. Yet their exact role is not known. It has been proposed that synaptic plasticity is

again involved[6], but the possible sites of plasticity and the underlying physiology are not known, and NMDA-receptor-dependent plasticity has not yet been correlated with extinction. Moreover, it has been suggested that there are also NMDA-receptor-independent mechanisms of extinction[7].

Marsicano *et al.*[2] now propose just such a mechanism, which involves the endocannabinoids anandamide and 2-arachidonylglycerol, and their CB1 receptors. These receptors are some of the most abundant neuromodulatory receptors in the central nervous system and are expressed at high levels in the limbic system, cerebellum and basal ganglia[8]. The classical behavioural effects of exogenous cannabinoids — such as sedation and memory changes — have been correlated with the presence of CB1 receptors in the limbic system and striatum.

It has been difficult, however, to pin down the physiological role of endocannabinoids and how they are released in these regions. In studies that were the first to reveal such a role, the depolarization of neurons by repetitive activity led to the release of endocannabinoids[9], which diffused to the terminals of other neurons and inhibited neurotransmitter release. This effect was transient in the hippocampus and cerebellum[9] and long lasting in the striatum[10]. Yet these changes in neurotransmission have not been connected to any specific behavioural effects. So the study by Marsicano *et al.*[2] represents a leap forward in two areas of neurobiology, in that it clearly implicates the release of endocannabinoids in a well-known, simple learning task. It also links endocannabinoid release to synaptic plasticity.

After engineering mice to lack the CB1 receptor, Marsicano *et al.* first showed that although these animals could learn and later recall the association of a tone with a foot shock, they could not extinguish the memory. A drug that antagonizes the CB1 receptor similarly prevented extinction in wild-type mice. The authors then found that during the extinction protocol (exposure to the tone alone), the levels of both anandamide and 2-arachidonylglycerol were raised in the basolateral amygdala in mutant and normal mice. This implies that a process involving activation of the CB1 receptors by endocannabinoids is essential in the extinction of conditioned fear.

Next, in experiments with slices of normal mouse brains, the authors looked at neurons in the basolateral amygdala that can release GABA (an inhibitory neurotransmitter). They found that low-frequency stimulation of these neurons leads to a long-term reduction in the release of GABA, which in turn leads to less inhibition of the connecting 'pyramidal' neurons. This long-term 'depression' — a type of synaptic plasticity — was completely blocked by the CB1-receptor antagonist, and absent in CB1-deficient mice. These findings suggest that the endocannabinoids reduce GABA release in the basolateral amygdala, thereby helping to extinguish the fear-conditioned response. In mammals, the neurons that release GABA are largely interneurons, which can be divided into several populations on the basis of their expression of certain proteins and peptides (such as cholecystokinin). The role of endocannabinoids in reducing GABA release fits with the finding that CB1 receptors in the basolateral amygdala are present on the terminals of cholecystokinin-containing interneurons[11,12].

This is an entirely new cellular and molecular mechanism for extinction. But how does it tie in with the NMDA receptors? There seems little doubt that activation of these glutamate receptors in the basolateral amygdala is somehow required for extinction[6]. But Marsicano *et al.*'s brain-slice experiments were performed with blocked glutamate receptors, showing that the endocannabinoid-mediated synaptic plasticity they report does not need the NMDA receptors. So we have yet to find out how these receptors are involved in extinction.

It has been argued that the neuronal circuitry underlying fear conditioning has similarities to that responsible for fear-related clinical conditions, such as post-traumatic stress disorder[4]. Behavioural therapies for these conditions — including systematic desensitization and imagery therapies — share features with extinction. The finding that the endocannabinoids contribute to extinction raises the possibility that drugs that target these molecules and their receptors could be useful new treatments for anxiety disorders. Finally, there is much anecdotal evidence of patients using cannabis heavily in the early stages of psychiatric illness. This has often been thought to contribute to acute illness. But it seems possible that it may instead be a form of self-medication for the sometimes extreme anxiety that these people experience. ■

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Earth science

Core values

John Brodholt and Francis Nimmo

Calculating the age of the Earth's solid inner core has proved to be a tricky business. But the suggestion that there is more potassium in the core than had been thought could help to reconcile differing estimates.

Potassium is a relatively insignificant element in the Earth, languishing in sixteenth place in the league table of chemical abundance. But, right now, radioactive decay of a potassium isotope, ^{40}K, is responsible for about 10% of the heat lost by the Earth. As ^{40}K has a half-life of 1.25 billion years, its decay would have produced much more heat in the past — just after the Earth formed, 4.6 billion years ago, daily decay of ^{40}K would have produced more heat than the present total daily heat loss of the Earth. Heat within the Earth drives processes such as convection in the mantle layer and the generation of the planet's magnetic field. So knowing how potassium and other radioactive elements are concentrated in different parts of the Earth is fundamental to understanding these processes.

There is a large concentration of potassium in the Earth's crust, and a significant proportion remains in the mantle below. What is not known is how much is in the Earth's core. Although experimental results have been ambiguous, it has generally been thought that, because of the relatively large radius of potassium ions, not much of this element could be absorbed in the core. But new results from Gessman and Wood[1], reported in *Earth and Planetary Science Letters*, show that the amount of potassium in the core depends on the core's sulphur and oxygen content, and on the structure of the coexisting silicate melt. Their findings help to explain some of the ambiguities in the earlier data, and also enable them to estimate the maximum concentration of potassium in the Earth's core — a number that has important bearing on the age of both the inner core and the Earth's magnetic field.

Although the magnetic field is generated by fluid flow in the liquid outer core, it is generally accepted that the solid inner core also plays a fundamental role. This is because