authors' models predict that, at some times in the breeding season, mating with a pied male may actually be the best choice for a collared female — and the data confirm this[1].

Veen *et al.*'s results show that, in vertebrates, sophisticated mechanisms may have developed to counteract the negative consequences of apparent hybridization. Such mechanisms might evolve rapidly in a location where two related species overlap. Alternatively, it is possible that these mechanisms did not evolve to cope with hybridization, but rather are a side-effect of existing female preferences.

For example, in the collared flycatcher, males that have a large white patch on the forehead are more successful in siring extra-pair young[5]. In other words, genetically speaking, it is better for collared females to mate with collared males with large forehead patches. However, socially it might be better for them to form pair bonds with collared males with slightly smaller patches if those males had better territories, and then to compensate for this by extra-pair mating. This might also explain why collared females occasionally (particularly late in the season) form pair bonds with pied males, as these males might provide better territories. As pied males have smaller forehead patches than collared males (Fig. 1), collared females in heterospecific pairs might then apply their normal mate-choice rule and engage in extra-pair matings with collared males.

Although not explicitly discussed by Veen *et al.*[1], their study has implications for speciation. Hybridization can oppose the effects of speciation — two closely related species that hybridize may eventually merge into a single species. But it may also enhance species divergence. For example, the negative outcomes of hybridization may put pressure on the two species to evolve better ways of distinguishing between each other[6]. This would increase the differences between the species. Alternatively, the mixing of genes that occurs during hybridization might create new combinations of genes (from gene combinations that have already been shaped by considerable evolutionary pressure in the parental species), allowing a third species to evolve[3,7]. Regardless of which of these mechanisms applies, the longer two species come into contact, mixing and exchanging genes, the more likely it is that rapid and major evolutionary changes will occur[2].

It is not yet known how important hybridization is to the speciation of birds. But, with the rapid development of new molecular methods for analysing DNA[8], studies of the histories of closely related species are now possible[9]. Such studies might yield astonishing new insights into speciation, in particular revealing the involvement of hybridization. ■

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Neurobiology

Dopamine receptors get a boost

Francis J. White

A protein that controls the growth and survival of neurons is now shown to have another task: boosting the expression of a molecule that allows neurons to respond to the neurotransmitter dopamine.

Nerve cells in many parts of the brain communicate using the neurotransmitter dopamine, and dopamine-dependent neuronal pathways are thought to be defective in several brain disorders, including Parkinson's disease, schizophrenia and drug addiction. Much of the diversity in dopamine's effects can be explained by the fact that it works through five different types of receptor molecule. Of these, the D_1 and D_2 receptors are the most common and have been investigated most thoroughly, but the D_3 receptor, too, has received much attention since its discovery just over a decade ago[1]. A few definitive roles for this receptor have now emerged[2–4]. It is unusual in being expressed in just a few brain regions. On page 86 of this issue, Guillin and colleagues[5] provide evidence for another odd characteristic. They find that expression of the D_3 receptor is regulated by brain-derived neurotrophic factor (BDNF) — a protein that was once thought to be needed simply for the proliferation, maturation and survival of neurons.

Guillin *et al.*[5] looked first at the expression of D_3 receptors in rats that have been experimentally altered to provide a 'model' of Parkinson's disease. In these rats, dopamine-releasing neurons on one side of the midbrain are destroyed by infusion of a chemical, 6-hydroxydopamine. The out-

100 YEARS AGO

The improvement in distance over which it is possible to signal has been very marked. The empirical law put forward by Mr. Marconi that, other things being equal, the distance over which signalling would be possible was proportional to the product of the heights of the masts at the two ends seems to be fairly well established as a working rule. But the improvements in transmitting and receiving apparatus have been so great that it is now possible to signal over much greater distances with the same heights of masts than was the case in 1898. For example, in 1898 Mr. Marconi was only able to cover 15 miles with vertical wires 120 ft. high, whereas to-day, according to the recent announcement made by Prof. Fleming, a distance of 200 miles from the Lizard to St. Catherine's, Isle of Wight, has been signalled over with masts only 160 ft. high… across land such great distances have not been attained, but here again we think the credit of having signalled over the greatest distance must be given to Mr. Marconi, who established in 1899 communication between Dovercourt and Chelmsford, a distance of more than 40 miles.
From *Nature* 2 May 1901.

50 YEARS AGO

It is in the tradition of British natural history that the only monograph on the water-mites of this country — the Ray Society's three volumes on "The British Hydracarina" — should have been written by two amateur naturalists, C. D. Soar and William Williamson. Williamson, born in Leith in June 1869, was during practically the whole of his working life a clerk, and latterly chief clerk, in the Scottish American Mortgage Company in Edinburgh. His interest in natural history began fortuitously, on account of his discovery, in the course of miscellaneous reading, of a series of articles describing British water-mites which appeared in *Science Gossip* in 1899 and 1900. The author was C. D. Soar, and Williamson, finding that he could easily identify from the detailed descriptions the water-mites he began to collect, got in touch with Soar, so commencing a friendship which lasted until Soar's death, almost forty years later. The contact was in a way a turning-point in his life, for the enthusiasm of one amateur stimulated the other, and Williamson's spare time now became devoted to collecting, identifying and recording hydrachnids.
From *Nature* 5 May 1951.

come is that the rats show many of the symptoms of humans with Parkinson's disease.

The D_3 receptor is normally expressed largely in an area of the brain called the nucleus accumbens, particularly in the so-called shell, which forms the deepest portions of this area. Guillin *et al.* find that the destruction of dopamine-releasing neurons in the rat model of Parkinson's disease reduces the amount of D_3-receptor messenger RNA in neurons in the nucleus accumbens shell, and increases the amount of mRNA encoding a BDNF receptor called TrkB. Receptor levels generally increase when levels of their binding partner decrease. The authors also show that infusion of BDNF into the shell restores the expression of D_3 receptors. The implication is that the reduced expression of D_3 receptors is caused by a reduction in BDNF levels, rather than a loss of dopamine.

To find out how BDNF might be involved in regulating D_3 receptors throughout development, the authors then used mice that had been engineered to lack functional BDNF. They show that this protein is needed for the normal increase in D_3-receptor expression that occurs shortly after birth. They also find that BDNF regulates D_3 receptors but not D_1 or D_2 receptors. Moreover, BDNF shows remarkable regional specificity: in both the BDNF-deficient mice and the rat model of Parkinson's disease, expression of D_3 receptors within the islands of Calleja — which lie beneath the shell and express the highest concentration of D_3 receptors — was normal.

Neurons produce dopamine from a precursor compound called levodopa (which is in fact the most frequently prescribed treatment for Parkinson's disease). As mentioned above, in the rat model of Parkinson's disease, dopamine-releasing neurons on only one side of the brain are damaged. When these rats are injected with levodopa, the expression of D_3 receptors in the nucleus accumbens shell increases. The animals also continuously turn away from the side of the damage, because the injection of levodopa causes dopamine receptors on the side of the damage to be activated more than those on the other side. With repeated injections, this behaviour becomes more pronounced (sensitizes), and increased expression of D_3 receptors occurs not only in the nucleus accumbens shell, but also within the region of the dorsal striatum in which the dopamine-releasing neurons are also damaged[3]. This suggests that the induction of D_3-receptor expression might be responsible for behavioural sensitization to levodopa.

Guillin *et al.*[5] investigated the involvement of BDNF in this response to levodopa. They infused soluble, antibody-labelled TrkB, which blocks BDNF, into the rats' striatum during repeated treatment with levodopa. They found that both the expression of D_3 receptors and sensitized movements were reduced. This suggests that BDNF is required for sensitization, presumably by inducing the expression of D_3 receptors. The source of the BDNF was the frontal cortex — removal of this area impaired D_3-receptor expression and sensitization in response to levodopa.

So the authors turned their attention to the frontal cortex. They find that a single injection of levodopa induces the expression of BDNF mRNA in the frontal cortex, mainly on the side of the brain in which dopamine-releasing cells had been damaged. Moreover, the authors then show that levodopa works through D_1 or D_5 receptors in the frontal cortex to induce the expression of BDNF there. Finally, Guillin *et al.* show that, in response to repeated administration of levodopa, TrkB is expressed in the striatum even more than in the rats that are not injected with levodopa. The implication is that levodopa — which is converted to dopamine — activates D_1 or D_5 receptors in neurons of the frontal cortex. These activated receptors then stimulate the production of BDNF, which in turn acts on its receptor (TrkB) in striatal neurons to lead to the increased expression of D_3 receptors there (Fig. 1).

This comprehensive set of studies has revealed a new function for BDNF: regulating the expression of dopamine D_3 receptors by certain neurons. In essence, BDNF thereby controls the responsiveness of those neurons to dopamine, and so is involved in long-lasting neuronal adaptations in dopamine-dependent pathways. Given that these pathways have so many roles in neurological and psychiatric disorders, the implications of these findings may be extensive. Guillin *et al.* speculate compellingly about how the regulation of D_3 receptors by BDNF could be involved in the effects of levodopa on people with Parkinson's disease, and in processes that might underlie drug addiction. Such speculation seems warranted because molecules that bind preferentially to D_3 receptors are effective in treating Parkinson's disease[6] and in reducing cocaine-seeking behaviour in animal models of cocaine addiction[4].

Interestingly, another neurotrophic factor — astrocytic basic fibroblast growth factor — has also been implicated in the development of behavioural sensitization, in this case to psychostimulant drugs such as cocaine[7,8]. Continued study of the interactions between neurotrophic factors and the dopamine system will surely reveal much about how drugs affect the brain. ■

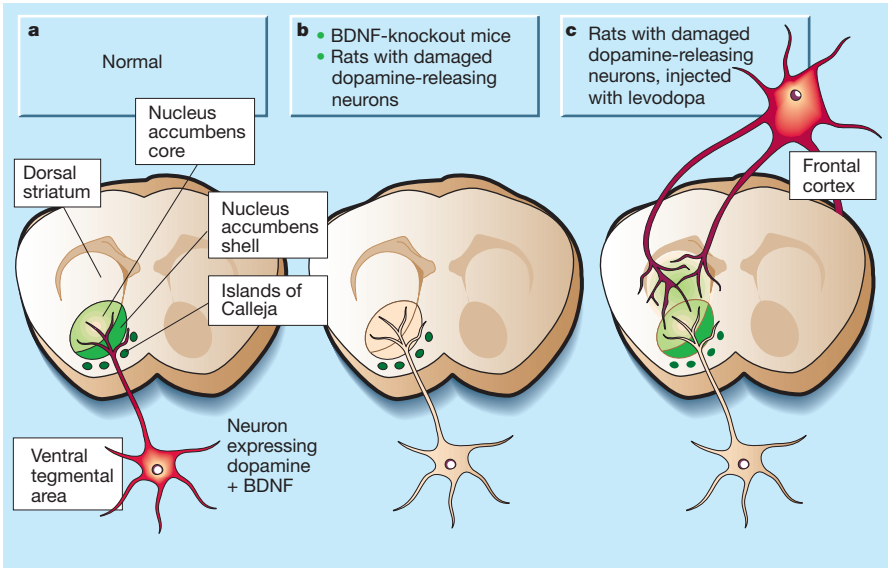

Figure 1 **A neuronal growth factor broadens its scope. Brain-derived neurotrophic factor (BDNF) was once thought to be needed only for the proliferation and survival of neurons, but more of its functions have since been discovered. Guillin *et al.*[5] now reveal that BDNF regulates the expression of the dopamine D_3 receptor.** a, **In the brains of normal rats and mice, D_3 receptors (green shading) are expressed in the shell of the nucleus accumbens region and the islands of Calleja (and, to a lesser extent, in the nucleus accumbens core). Neurons from the ventral tegmental area (VTA), which produce both dopamine and BDNF, connect to neurons in the nucleus accumbens.** b, **As Guillin *et al.* discover, in mice that lack BDNF or in rats in which dopamine-releasing neurons in the VTA are damaged, D_3 receptors are not expressed in the nucleus accumbens shell, but remain in the islands of Calleja.** c, **When the rats with damaged dopamine-releasing neurons are injected repeatedly with levodopa (the precursor of dopamine), D_3 receptors are expressed in both the dorsal striatum and the nucleus accumbens; expression of the BDNF receptor TrkB is simultaneously increased (not shown). This requires the release of BDNF from frontal-cortex neurons that express the D_1 receptor.**

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Earth science

Hard-cored continents

Andrew A. Nyblade

Each continent contains pockets of ancient crust that appear to have been unaffected by tectonic forces since they formed billions of years ago. Why? There's now a fresh twist on the usual explanation.

The existence of the small, ancient cores of continents, known as cratons, has long been a puzzle. Cratons were created during the Archaean eon, more than 2.5 billion years ago, and form the oldest parts of Earth's tectonic plates. Yet they have somehow remained largely unmodified by tectonic forces. By contrast, younger parts of the continents bear the geological scars \of repeated tectonic buffeting, and appear to be weaker and less stable. So, why are cratons tectonically stable? Lee and co-workers (page 69 of this issue[1]) provide new insight into this question.

Not much is known about the processes that formed cratons in the Archaean. But it has been suspected for some time that their tectonic longevity derives from 'keels' — as on sailing vessels — that extend deep into the Earth (Fig. 1). These keels are made of lithospheric mantle more than 2.5 billion years old and more than 200 km deep. The lithosphere is Earth's outermost rigid layer, and consists of the crust and uppermost mantle. The chemical composition of craton keels is thought to stem from their depletion of the basaltic constituents (Al_2O_3, FeO, CaO) and volatile molecules (H_2O, CO_2) compared with the 'fertile' mantle that is the source of basaltic volcanism along mid-ocean ridges[2,3].

According to theory, a combination of the loss of basalt and volatiles makes the keels strong enough to resist wholesale destruction by tectonic forces. This is because extraction of basaltic constituents during volcanism removes iron from the remaining mantle, making it more buoyant than its surroundings. In addition, removal of volatiles from the mantle during mantle melting increases the melting temperature and stiffness of the remaining material, making it even more resistant to tectonic forces.

Lee *et al.*[1] show that depletion of basaltic constituents does indeed influence the strength of lithospheric mantle, mainly by controlling the thickness to which the keel can grow. But they find that the degree of depletion is not always a function of age. Their evidence is geochemical, and comes from two regions of southwestern United States where small pieces of lithospheric mantle, called xenoliths, have been brought rapidly to the surface by volcanoes. One location is in the southern Basin and Range province, where crust 2.0–2.6 billion years in age is being deformed by tectonic forces. The other is in the Colorado plateau, a tectonically stable region of crust 1.6–2.0 billion years old that borders the Basin and Range province to the east (see map on page 70.)

By measuring the abundance of rhenium and osmium isotopes in the xenoliths, Lee and co-workers show that the lithospheric mantle beneath the sampling localities is similar in age to the overlying crust. The bulk composition of the xenoliths, together with the pressure and temperature conditions under which some of their component minerals formed, also reveal that the lithospheric mantle beneath the Basin and Range province is thinner and less depleted of basaltic constituents — that is, more fertile — than it is beneath the Colorado plateau. So it seems that it is not the age of the lithospheric mantle that correlates with its tectonic stability. Rather, given the greater basaltic depletion and thicker lithospheric mantle found under the younger yet more stable crust of the Colorado plateau, it is depletion and in turn thickness that are the determining factors.

The authors next turn to the question of how this loss of basalt controls the thickness of the lithosphere. Here they draw upon the observation that cratonic keels must in fact be neutrally buoyant, even though they contain less basalt, because they are not associated with significant perturbations in Earth's gravity field. According to the isopycnic (equal-density) condition proposed by Jordan[2], the negative buoyancy resulting

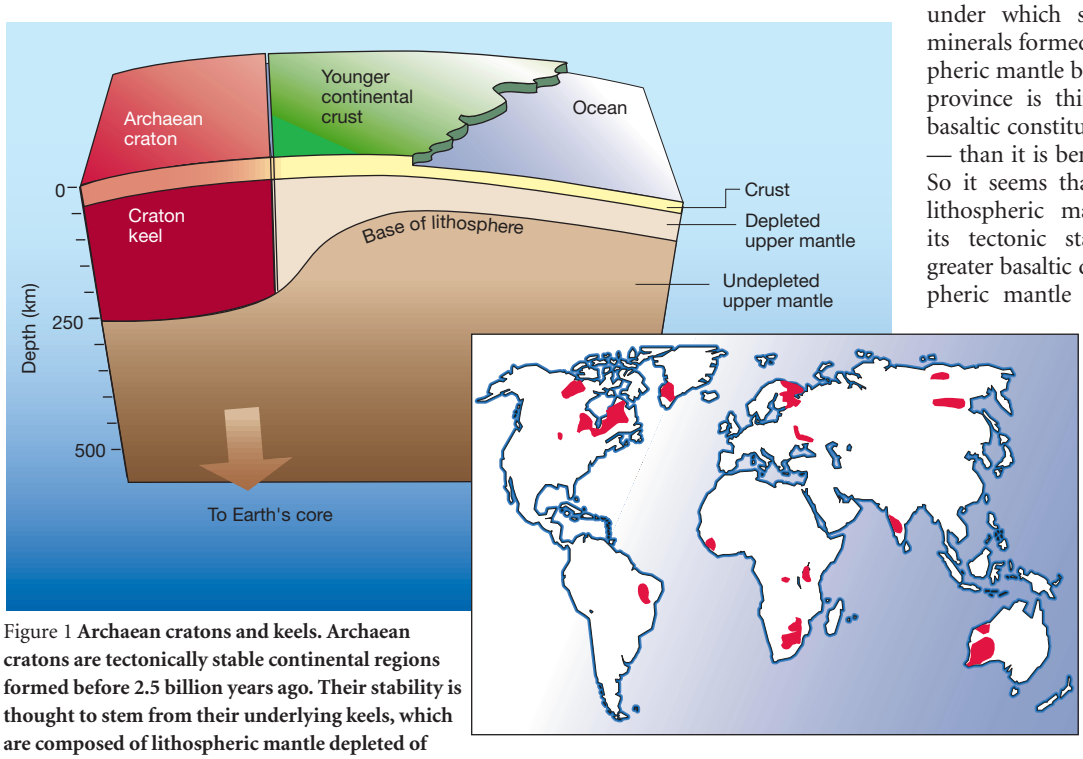

Figure 1 **Archaean cratons and keels. Archaean cratons are tectonically stable continental regions formed before 2.5 billion years ago. Their stability is thought to stem from their underlying keels, which are composed of lithospheric mantle depleted of basaltic components and are at least twice as thick as the lithospheric mantle beneath younger parts of the continents and oceans. As reported by Lee *et al.*[1], the thickness of the keel is controlled by the degree of basalt depletion in the lithospheric mantle. The inset map shows the global distribution of Archaean cratons. (Main graphic modified from ref. 2.)**