LEARNING AND MEMORY

LTP makes dendrites excitable

Since the pioneering work of Hebb, models to explain how memory traces are established have focused predominantly on plasticity at the synapse. However, it is becoming clear that changes in conductivity within the neuron are also important features of memory storage. It has already been shown that the induction of long-term potentiation (LTP) at a synapse can increase the intrinsic excitability of the postsynaptic neuron. Now, in *Nature Neuroscience*, Frick and colleagues propose a molecular mechanism to explain a link between LTP and dendritic excitability.

Frick *et al.* used a combination of calcium imaging and dendritic patch-clamp recording to measure the activity of CA1 pyramidal neurons in slices of rat hippocampus. To gauge the excitability of individual dendrites, they measured the amplitude of action potentials that backpropagated from the soma into the dendritic tree. Before LTP was induced, the amplitude of the backpropagating action potential declined rapidly as it travelled towards the distal end of the dendrite. However, if LTP was induced at synapses within a dendrite, the propagation of the backpropagating action potential in that dendrite was enhanced.

The attenuation of the backpropagating action potential that normally occurs along the dendrite has been attributed to a transient outward K^+ current known as I_A, which is mediated by A-type K^+ channels. The authors asked whether the effect of LTP induction on backpropagating action potential amplitude was related to a change in I_A, and they found that this current was indeed reduced around the potentiated synapses. The number of A-type K^+ channels was unchanged, so Frick *et al.* concluded that LTP somehow brings about a change in the channel properties.

What is the functional significance of this increase in dendritic excitability? Apart from the obvious effect of facilitating the transmission of information, it has been suggested that it might also prime the postsynaptic neuron to undergo subsequent plasticity — a phenomenon that is often referred to as metaplasticity. These findings illustrate that neuronal plasticity is a highly complex process that affects numerous aspects of neuronal activity, and the task of unravelling these complexities is set to keep researchers occupied for years to come.

Heather Wood

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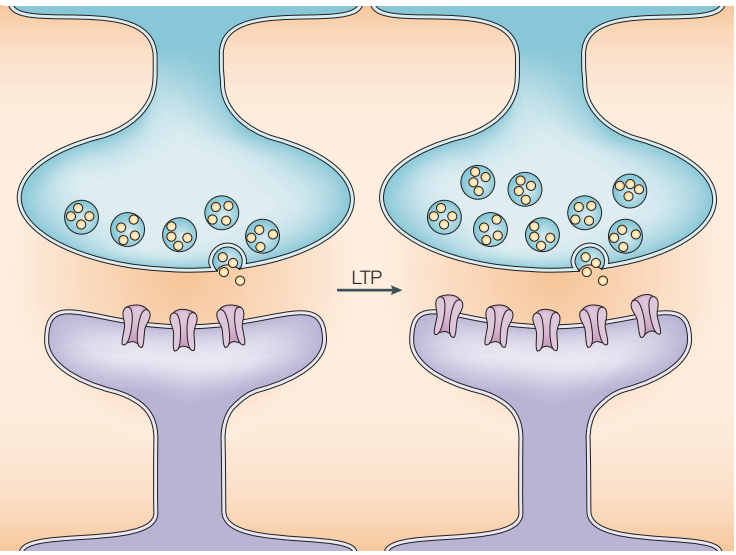
WEB SITES

Encyclopedia of Life Sciences:
http://www.els.net/
Long-term potentiation

Courtesy of D. Johnston, Baylor College of Medicine, USA.

SYNAPTIC PHYSIOLOGY

Putting receptors in their place



The protein postsynaptic density 95, or PSD95, has been implicated in the control of receptor trafficking during synaptic plasticity. In *The Journal of Neuroscience*, Ehrlich and Malinow show that PSD95 controls the incorporation of AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid) receptors into the postsynaptic membrane during plasticity both *in vitro* and *in vivo*.

It was previously shown that expression of PSD95 in hippocampal neurons in slice culture could mimic long-term potentiation (LTP) by increasing the recruitment of AMPA receptors to the synapse, and that it also prevented the induction of further LTP, indicating that the two phenomena probably shared a mechanism. Now, Ehrlich and Malinow have confirmed these findings and taken them further by showing that PSD95 is also important for a different form of plasticity *in vivo*.

The authors investigated whether PSD95 was involved in experience-driven plasticity in the barrel cortex of young rats. At synapses between layer IV and layer II/III pyramidal neurons in neonatal rats, sensory experience from the whiskers causes an increase in AMPA receptors and consequently strengthens synaptic transmission. When the rats are deprived of sensory experience because their whiskers are trimmed, this recruitment process is reduced. Ehrlich and Malinow found that expression of a PSD95–GFP (green fluorescent protein) construct in barrel cortex neurons in rats with trimmed whiskers mimicked the AMPA receptor recruitment that is normally induced by sensory experience. Expression of PSD95 also occluded experience-dependent recruitment of AMPA receptors to synapses, and a dominant-negative form of the protein blocked receptor recruitment.

It is unclear how PSD95 drives the recruitment of AMPA receptors to the synapse. The authors found that mutations that prevented either its association with the cell membrane or its binding to proteins with PDZ

STEM CELLS

Matrix revolutions in 3D

Three-dimensional bioactive scaffolds hold great promise as substrates for generating tissue from stem cells *in vitro* and for promoting tissue regeneration *in vivo*. As reported in *Science*, Silva and colleagues have developed a remarkable new nanofibre matrix that assembles spontaneously when it comes into contact with cells, and can be engineered to promote neuronal differentiation.

The authors constructed a molecule called IKVAV-PA, which included the five-amino-acid motif IKVAV (isoleucine–lysine–valine–alanine–valine). This motif occurs in the extracellular matrix component laminin, and it has been shown to induce and direct the growth of neurites. The IKVAV-PA molecules carried a net negative charge, and mutual repulsion prevented them from aggregating in solution at pH 7.4. However, when they were exposed to positive ions — for example, in living tissue — they formed nanofibres and assembled into a gel-like matrix.

The authors added mouse neural progenitor cells to a solution of IKVAV-PA, prompting the formation of a matrix that encapsulated the cells. The resulting scaffold had a high water content, which allowed efficient diffusion of nutrients. A high proportion of the progenitors differentiated rapidly into neurons, as indicated by the expression of specific marker genes and neurite outgrowth. By contrast, there was little evidence of astrocytic differentiation. A control molecule — EQS-PA — in which the laminin motif was replaced by the non-physiological sequence glutamic acid–glutamine–serine (EQS), was also capable of self-assembly, but failed to induce neuronal differentiation.

Interestingly, the IKVAV-PA nanofibres were also effective at promoting neuronal differentiation when they were presented to neural progenitors as a two-dimensional substrate on a culture dish. The authors proposed that the key to the success of the matrix is the high density of IKVAV epitope that is presented to the cells, rather than the three-dimensional conformation. A soluble IKVAV peptide added to an EQS-PA matrix was far less efficient at stimulating neuronal differentiation than the IKVAV-PA scaffold, indicating that the epitope needs to be integrated into the nanofibres to be appropriately presented.

Silva *et al.* found that the matrix could also be induced to assemble if it was injected into tissue, raising the tantalizing possibility that it could be used to stimulate the regeneration of injured nerves *in vivo*. As the matrix assembles on contact with tissue, it could be injected as a fluid at the injury site, which would be far less invasive than implanting a pre-formed scaffold. Also, because the IKVAV-PA scaffold seems to suppress astrocytic differentiation, it is unlikely to exacerbate the injury by inducing glial scar formation. Further investigations should uncover the full potential of this intriguing material.

Heather Wood

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ligands reduced the ability of PSD95 to potentiate synaptic transmission in hippocampal slice cultures, and proteins containing both mutations had no potentiating effect. Pharmacological experiments also showed that neither the calcium/calmodulin-dependent protein kinase II (CaMKII) cascade, which is involved in LTP, nor the mitogen-activated protein kinase (MAPK) signalling pathway, elements of which interact with PSD95, was needed for the effects of PSD95. It seems likely that PSD95 acts downstream of these signalling pathways, through a mechanism that requires it to associate with the membrane and to bind to other proteins through its PDZ domains.

Rachel Jones

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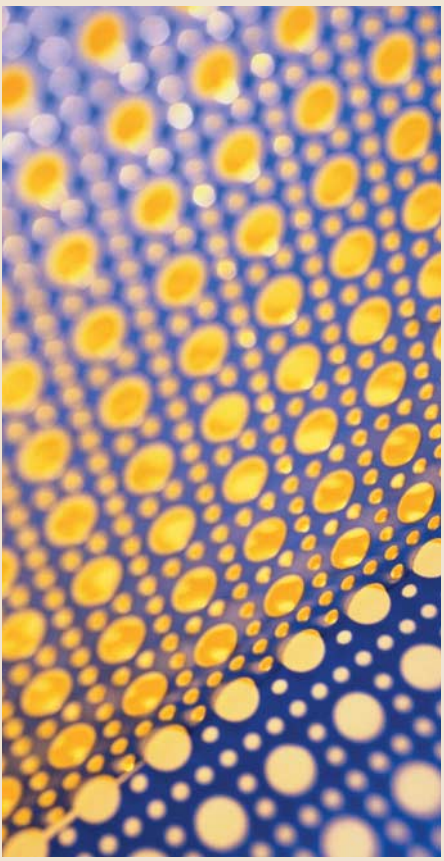


IN THE NEWS

Where now for primate research?

The decision to scrap plans to build a primate research centre in Cambridge, UK, is a severe blow for research into brain disease, according to leading scientists. Colin Blakemore, the chief executive of the Medical Research Council, said "current research in primates is offering hope of treatments for Alzheimer's, Parkinson's, Huntington's disease and strokes" (*Daily Telegraph*, UK, 28 January 2004). Mark Walport, the director of the Wellcome Trust, agreed "research using primates will continue to be essential if we are to conquer many diseases. Without facilities such as those planned for the Cambridge University site this kind of medical pioneering work will be severely hampered" (*Daily Telegraph*).

Although rising costs were cited as the main reason for abandoning the project, the move was widely perceived as a victory for the animal rights movement. Cambridge is certainly no stranger to animal rights protestors — Huntingdon Life Sciences, a contract research facility that is based just outside the city, has been the target of a sustained campaign by such groups, including a physical attack on its managing director, Brian Cass. Cass was quoted as saying "we in the research community have been assured of the support of the Government … but this decision is saying that violence and illegal protest works" (*Daily Telegraph*).

Not surprisingly, animal rights groups welcomed the decision. Andrew Tyler of Animal Aid said, "it would have been a factory to mutilate the brains of monkeys and then dispose of them. It would have made Cambridge University the monkey torture capital of Europe" (*Daily Telegraph*). In the *Guardian* (UK, 28 January), Wendy Higgins, the campaigns director at the British Union for the Abolition of Vivisection, wrote "despite attempts to convince us most animals suffer nothing more than a pin prick, there is growing public disquiet about vivisection. We too want to see cures for human diseases but making animals suffer is not the most credible way of reaching that goal."

Nevertheless, the national press in the UK largely supported the view that primate research should continue. A *Guardian* leader article argued "what would have made the public more uncomfortable was the use of monkeys. But this places emotion before reason. Colin Blakemore … is right to point to the many medical breakthroughs which would not have been achieved without them."

The *Independent* (UK, 28 January), however, took a different line: "the right decision has been taken … but for the wrong reasons. To keep animals so similar to ourselves in laboratory conditions is an unacceptable cruelty, and to experiment on them is a violation of rights that should be extended to these, our near relatives." However, the article went on to say that the University's decision to abandon the project was "born out of fear: of the unreasonable violence of animal rights campaigners," and that scientists "should stop violating the rights of the higher primates because they are persuaded it is wrong, not because they are intimidated by baseball bats and bricks."

Blakemore, who has frequently been targeted by anti-vivisection groups himself, refuses to be deterred: "They will not win. We will try to make sure [the research] goes on in Cambridge but, if not, it will go on elsewhere in the world eventually and it will be patients who benefit" (*Times*, UK, 28 January).

Heather Wood

SENSORY SYSTEMS

Sight versus sound

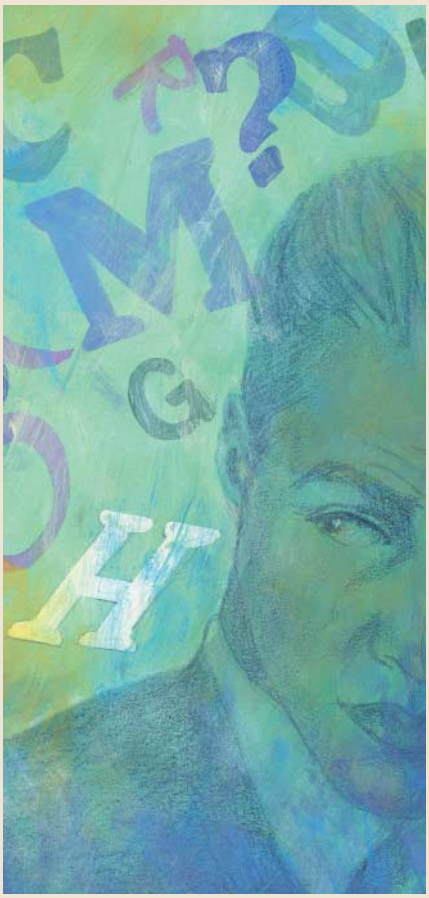
A new study of spatial localization of audio-visual stimuli has shown that the 'ventriloquist effect' is a function of near-optimal integration of visual and auditory inputs.

Ventriloquism is a phenomenon whereby we inaccurately perceive a voice as emanating from a spatially displaced source; for example, from the lips of a ventriloquist's dummy rather than from those of the ventriloquist. The effect was originally thought to be the product of voice projection techniques perfected by the performer, but recent hypotheses have suggested that it results from the domination of hearing by vision.

Alais and Burr tested this assertion by having observers localize visual and audio stimuli — brief 'blobs' of light or 'clicks' of sound — in space. Unimodal thresholds were established by presenting these stimuli separately and asking observers to indicate which of the two stimuli appeared more to the left. Subsequently, blobs and clicks were presented simultaneously in one of two modes. In 'conflict' mode, blobs and clicks were spatially displaced from each other; in 'non-conflict' mode, the stimuli were equally displaced to the left or right of centre.

The ability of subjects to localize the stimuli depended on the size and clarity of the blobs. When visual localization was good, vision 'captured' sound, as in the classic ventriloquist effect. However, the reverse was true when visual stimuli were blurred and therefore poorly localized. In this case, the subjects perceived the blob as closer to the correct location of the click, rather than vice versa. In all six subjects, bimodal localization was more precise than either form of unimodal localization. Based on these data, the authors propose a model in which visual and auditory inputs are optimally combined to minimize variance and improve spatial localization.

Suzanne Farley



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NEUROLOGICAL DISORDERS

A convergence point in MS pathology

The enzyme cytosolic phospholipase A_2 ($cPLA_2$) may have a key role in the pathogenesis of multiple sclerosis (MS), according to a new study published in *Neuron*. The findings, made by Kalyvas and David in an animal model of the condition, could lead to better treatments for MS patients.

MS is an inflammatory, demyelinating disease of the central nervous system (CNS). It is thought to involve an autoimmune response in which myelin-reactive cells enter the CNS and initiate the disease. Although the aetiology and pathogenesis of the disorder are still not fully understood, it seems that various causative factors trigger a common mechanism, resulting in the classical pathology of MS — immune cell infiltration into the CNS, a complex inflammatory cascade, and demyelination and axonal damage.

Kalyvas and David looked for a convergence point in the induction of these stereotypical pathologies. They focused on $cPLA_2$ for two main reasons: first, because many pro-inflammatory chemokines and cytokines produced in the early stages of MS can induce PLA_2; and second, because metabolic products of PLA_2, including arachidonic acid (AA) and lysophosphatidylcholine (LPC), can mediate inflammation and demyelination.

The researchers examined mice with experimental autoimmune encephalomyelitis (EAE), an inflammatory, demyelinating condition induced by immunizing animals against myelin antigens. They found that $cPLA_2$ was expressed at high levels in endothelial cells and immune cells at EAE lesions. Blocking the enzyme with an AA analogue led to a dramatic reduction in the onset and progression of EAE. The authors showed that $cPLA_2$ was present at much reduced levels in mice treated with this inhibitor. What's more, they found that inhibiting $cPLA_2$ in mice with EAE led to a decrease in the expression of many mediators of inflammation, including chemokines and cytokines that are known to induce the expression of $cPLA_2$ or to be induced by LPC.

These results suggest that $cPLA_2$ could serve as the common link by which various factors trigger the inflammatory and axonal pathologies characteristic of EAE and MS. Studies of potent and specific inhibitors of $cPLA_2$ as potential treatments for MS are now warranted.

Rebecca Craven, Senior Subeditor, Nature

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PAIN

The pain of integrins

Although chronic pain is a common problem, progress in treating it has been relatively slow. Advances in our understanding of neuropathic and inflammatory pain are important if new therapeutic targets are to be identified. In the *European Journal of Neuroscience*, Dina and colleagues describe a potential role for integrins in mediating this kind of pain.

Integrins are adhesion molecules that are expressed on primary afferent neurons. They bind to elements of the extracellular matrix (ECM) and interact with signalling systems that are known to mediate hyperalgesia. Inflammation and nerve injury cause changes in the ECM around peripheral nerves that might provide important signals to integrins. So, the authors investigated whether integrins were involved in the sensitization of nociceptors that leads to hyperalgesia in animal models of inflammatory and neuropathic pain.

Dina *et al.* used several methods to interfere with normal integrin signalling in rats, and found that by doing so they could block the development of hyperalgesia. However, there seems to be more than one pathway through which integrins can influence pain.

Fragments of laminin, or antibodies against the integrin subunits that are involved in binding to laminin, blocked hyperalgesia induced by injection of prostaglandin E_2 (PGE_2), but not that induced by injection of adrenaline (epinephrine). The laminin peptides also blocked the induction of hyperalgesia in a slower-acting model of inflammatory pain, the injection of carrageenan. On the other hand, fragments of fibronectin, or antibodies against the subunits of integrin that are needed for bindng fibronectin, prevented the induction of hyperalgesia by adrenaline, but not by PGE_2 or by carrageenan.

The β_1 integrin subunit is involved in the binding of both laminin and fibronectin. When rats were treated with antibodies against this subunit, neither adrenaline nor PGE_2 induced hyperalgesia. The same effect was obtained by treatment with antisense oligodeoxynucleotides that knocked down the expression of the β_1 subunit. The knockdown also prevented hyperalgesia in a model of neuropathic pain caused by the chemotherapeutic drug taxol, and could reverse hyperalgesia if given after taxol treatment.

This evidence that specific integrin subunits are involved in pathways that cause pain when stimulated by different substances should add to our growing understanding of the mechanisms of chronic pain. It might also lead to the development of new therapies for the many patients who are affected by inflammatory or neuropathic pain.

Rachel Jones

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IN BRIEF

SENSORY PHYSIOLOGY

$K_V1.3$ channel gene-targeted deletion produces 'super-smeller mice' with altered glomeruli, interacting scaffold proteins, and biophysics.

Fadool, D. A. *et al. Neuron* **41**, 389–404 (2004)

Mice with a targeted deletion of the voltage-dependent K^+ channel $K_V1.3$ are found to have a heightened sense of smell, with a threshold for odour detection that is 1,000- to 10,000-fold lower than the wild type. Anatomically, they have smaller olfactory glomeruli than wild-type mice, and more of them. Potassium currents in olfactory bulb neurons from the $K_V1.3^{-/-}$ mice have slower inactivation and a modified voltage dependence, and are not modulated by activators of receptor tyrosine signalling cascades.

NEUROLOGICAL DISORDERS

Diffusion tensor MRI of early upper motor neuron involvement in amyotrophic lateral sclerosis.

Sach, M. *et al. Brain* **127**, 340–350 (2004)

It is difficult to assess the involvement of upper motor neurons during the early stages of amyotrophic lateral sclerosis (ALS). Sach and colleagues show that diffusion tensor imaging can identify changes that are related to upper motor neuron involvement in patients with ALS before they show clinical symptoms related to corticospinal tract lesions.

NEURAL MODULATION

Selective D2 receptor actions on the functional circuitry of working memory.

Wang, M. *et al. Science* **303**, 853–856 (2004)

D2 dopamine receptors have been implicated in various cognitive and motor functions. To clarify the functions of these receptors, Wang *et al.* recorded from prefrontal cortical neurons in monkeys performing an oculomotor task while applying selective D2 agonists and antagonists through iontophoresis. They found that D2 receptors modulate saccade-related activity, whereas D1 receptors modulate memory-related activity.

GENE EXPRESSION

Stochastic yet biased expression of multiple *Dscam* splice variants by individual cells.

Neves, G. *et al. Nature Genet.* 1 February 2004 (10.1038/ng1299)

The *Drosophila* homologue of *Dscam* is essential for axon guidance and undergoes alternative splicing to generate 38,016 possible isoforms. Neves *et al.* used single-cell RT-PCR to investigate the expression of *Dscam* in single photoreceptors. The authors find that individual photoreceptors express 14–50 mRNAs from the possible range of *Dscam* isoforms, and that populations of photoreceptor subtypes express broad but distinctive subsets of *Dscam*. They propose that the *Dscam* repertoire of a cell could provide a mechanism for generating unique cell identity in the nervous system.

IN THE NEWS

Juggling boosts the brain

When people spend three months learning to juggle, according to a paper published in *Nature*, parts of their brains grow. "Researchers in Germany split 24 students into two groups, one of which was given three months to learn a classic three-ball cascade juggling routine. Brain scans were then carried out on both sets of volunteers." (*The Scotsman*, 22 January 2004). The brains of the jugglers and non-jugglers were scanned before and after the three-month learning period.

According to *BBC News Online* (22 January 2004), "Jugglers had more grey matter — which consists largely of the nerve cells — in the mid-temporal area and the left posterior intraparietal sulcus, which both process visual motion information."

Arne May, of the University of Regensburg, Germany, led the group that carried out the research. May said, "Our results challenge our view of the human central nervous system. Human brains probably must be viewed as dynamic, changing with development and normal learning." (*CNN*, 22 January 2004).

When the same groups were scanned again after another three months, the increase in grey matter had reduced. Talking to *BBC News Online*, Vanessa Sluming of the University of Liverpool, UK said, "It would be interesting to know at what point this acquired grey matter can be retained. Does it mean you need to continuously practise the acquired skill to retain it, or at some point have you done enough to retain it?"

Rachel Jones

SENSORY SYSTEMS

The flavour of long life

In the nematode *Caernorhabditis elegans*, mutations in genes that are required for sensory transduction can dramatically extend lifespan. Writing in *Neuron*, Alcedo and Kenyon use laser ablation of individual neurons to identify a subset of sensory neurons that interact to regulate longevity, and find that the sensory control of lifespan is surprisingly complex.

Mutations that inhibit sensory function in *C. elegans* are thought to extend lifespan in adults by decreasing signalling through a pathway that involves DAF-2, a homologue of the insulin/IGF-1 receptor. Lifespan can also be increased by mutations in *daf-2*, and this effect depends on the transcription factor DAF-16. Early in life, this pathway also mediates the formation of a specific larval state called the dauer that is specialized for survival in unfavourable conditions.

To investigate the relationship between sensory input, DAF-2 signalling and longevity, the authors killed specific pairs of sensory neurons by laser ablation. Three pairs of gustatory neurons, called ADF, ASI and ASG, inhibit dauer formation — ablation of these neurons causes the worms to form dauers. Alcedo and Kenyon found that ablation of either the ASI or the ASG neurons significantly extended lifespan, but that ablation of the ADF neurons did not. There are also neurons that promote dauer formation, called the ASJ and ASK neurons, but ablating these did not reduce lifespan. However, if either of these pairs of neurons was killed, it suppressed the longevity induced by ASI ablation. So, some neurons promote longevity, whereas others inhibit it.

Although it seems that regulation of lifespan and dauer formation might have overlapping mechanisms, the authors also found that lifespan can be regulated independently. If they ablated a pair of olfactory neurons, called AWA, lifespan was extended, and this effect was amplified if another pair of olfactory neurons (the AWC neurons) were also killed. But ablation of these neurons has no effect on dauer formation. A mutation in the *odr-7* gene, which is specifically required for AWA function, also induced longevity.

The gustatory neurons seem to act through the DAF-2 pathway to regulate longevity, as the effect of ablating these neurons depends on DAF-16. However, the lifespan extension that is caused by ablating the olfactory neuron AWA depended only partly on DAF-16, indicating that the olfactory and gustatory neurons act through partially independent pathways to regulate longevity.

So how do these neurons interact to regulate longevity? Among the gustatory neurons, it seems that some inhibit longevity — such as ASI and ASG — whereas others, including ASK, promote it. Given that ablation of ASK alone had no effect on lifespan, it is most likely that ASI and ASG inhibit some

longevity-promoting effect of ASK. In this model, ablation of ASI or ASG lifts the inhibition, allowing ASK to promote longevity. However, when ASK is also ablated, the effect is reversed.

Presumably, specific environmental cues that are detected by these gustatory and olfactory neurons can influence longevity. One attractive model had been that the pheromone that induces dauer formation in juvenile animals induces longevity in adults. However, the authors showed that this was not the case. It is possible that the signals include food-related substances.

The AWC and ASI neurons express a putative chemosensory G-protein-coupled receptor, STR-2, and the study showed that reductions in levels of this receptor also extended lifespan, supporting the idea that specific cues are involved in longevity.

Insulin/IGF-1 signalling pathways can also influence lifespan in flies and mammals, and there is evidence that food-related sensory input can alter insulin levels in humans. So it is possible that sensory inputs can work through neuroendocrine mechanisms to alter longevity in organisms other than *C. elegans*. Further work should investigate this intriguing possibility.

Rachel Jones

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WEB SITE

Kenyon laboratory: http://wormworld.ucsf.edu/labhomepage.html

SENSORY SYSTEMS

Regulating olfactory receptors

Two new studies provide evidence that the monoallelic expression pattern of olfactory receptors (ORs) in mammals is regulated by a negative feedback mechanism.

The exquisite sensitivity of the mammalian olfactory system depends on functionally distinct neuronal populations that project to precisely defined glomeruli in the olfactory bulb (see figure). Establishment of these discrete populations is a function of the 'one neuron–one receptor' rule. This rule describes how each olfactory neuron expresses only one allele of one OR gene from the more than 1,000 in the mouse genome. In an effort to enhance our understanding of how this process is regulated, two research groups tested the hypothesis that the product of an expressed OR gene prevents activation of its counterparts.

Sakano and colleagues used transgenic constructs in yeast artificial chromosomes to manipulate expression of the *MOR28* gene in mice. Transformation of mice with enhanced green fluorescent protein (EGFP)-tagged *MOR28* from which the entire coding sequence had been deleted resulted in co-expression of EGFP and endogenous *MOR28* in many cells. Other EGFP-positive neurons of the olfactory epithelium expressed different endogenous OR genes, indicating that a product of the *MOR28* coding sequence is required to prevent the expression of other ORs.

Lewcock and Reed extended these findings by showing that it is the protein product of OR genes that activates the negative regulatory loop. To distinguish between possible transcriptional and translational activation of inhibition, the authors used an OR-promoter-driven transgene in which the coding sequence was present but untranslatable. The presence of this transgene did not prevent the expression of other OR alleles — strong evidence that it is OR protein rather than messenger RNA that directs the selective expression of a single OR allele.

Sakano *et al.* also identified a *cis*-acting regulatory element upstream of the *MOR28* gene cluster that is necessary for gene expression. These authors suggest a model in which a transcription-activating complex is formed in this regulatory region. This complex would then interact with the promoter of just one gene in the cluster, expression of which would feed back to prevent the induction of other OR genes.

Suzanne Farley

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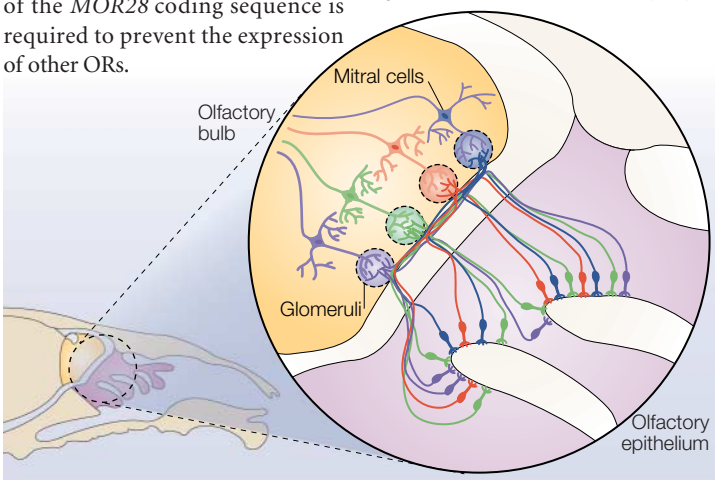

IN BRIEF

COGNITIVE NEUROSCIENCE

Shrinkage of the entorhinal cortex over five years predicts memory performance in healthy adults.

Rodrigue, K. M. & Raz, N. *J. Neurosci.* **24**, 956–963 (2004)

In a five-year longitudinal study, Rodrigue and Raz tested whether shrinkage of the entorhinal cortex, hippocampus or prefrontal cortex of healthy adults could predict episodic memory performance. Although none of the regional volumes was associated with memory performance, greater shrinkage in the entorhinal cortex was associated with poorer memory performance at the end of the study. The shrinkage of the hippocampus and prefrontal cortex did not predict memory performance.

SENSORY PHYSIOLOGY

Mustard oils and cannabinoids excite sensory nerve fibres through the TRP channel ANKTM1.

Jordt, S.-E. *et al. Nature* **427**, 260–265 (2004)

Isothiocyanate compounds, such as the active ingredients in mustard, produce pain, inflammation and hypersensitivity when applied to the skin. Jordt and colleagues show that the application of mustard oil depolarizes the same primary sensory neurons as are activated by capsaicin, the 'hot' ingredient in chilli peppers, and by Δ^9-tetrahydrocannabinol (THC), the active ingredient in marijuana. Both allyl isothiocyanate and THC activate a TRP (transient receptor potential) ion channel called ANKTM1.

DEVELOPMENT

Paraxial mesoderm specifies zebrafish primary motoneuron subtype identity.

Lewis, K. E. & Eisen, J. S. *Development* **131**, 891–902 (2004)

Signals from the paraxial mesoderm specify distinct populations of motor neurons in vertebrates. Lewis and Eisen show that the paraxial mesoderm is also the origin of signals that control the more precise patterning of primary motor neurons in the zebrafish, giving rise to a segmentally repeated pattern of two subtypes of motor neuron. In the absence of paraxial mesoderm-derived signals, primary motor neurons seem to have a hybrid identity.

GLIA

Astrocyte-mediated activation of neuronal kainate receptors.

Liu, Q.-S. *et al. Proc. Natl Acad. Sci. USA* 6 February 2004 (10.1073/pnas.0306731101)

To test whether glutamate released by astrocytes in rat hippocampal slices activates kainate receptors on neighbouring neurons, Liu *et al.* used *o*-nitrophenyl-EGTA to uncage Ca^{2+}. Increases in intracellular Ca^{2+} in astrocytes increased action-potential-driven spontaneous inhibitory postsynaptic currents in nearby interneurons. The effect was blocked by kainate receptor antagonists but not by antagonists of other glutamate receptor subtypes. Astrocytes might therefore be an important modulator of neuronal function in the hippocampus.