VISUAL SYSTEM

Catch a shooting star

New work by Jancke and colleagues, using voltage-sensitive dyes to image neuronal activity *in vivo*, shows how activity in the early visual cortex can account for our perception of a classic visual illusion.

Visual illusions, in which we perceive something that differs from the physical stimulus, are often used to investigate perception. For example, in the line-motion illusion, a small square is flashed on a screen, immediately followed by a bar, one end of which is at the same point as the square. Rather than seeing a square followed by a stationary bar, subjects report that they see a bar being gradually drawn across the screen (rather like the tail of a shooting star; see http://www.nature.com/nature/journal/v428/n6981/extref/line-motion-examples.html for examples).

Psychophysical experiments have provided some evidence that this illusion involves the influence of higher cortical areas, but other studies point towards early processing stages. Jancke *et al*. used optical imaging of area 18 of the cat cortex (an early area in visual cortical processing) to investigate whether 'bottom-up' activity in the early visual cortex could lead to the illusory perception of movement.

Although they found that either a flashed square or a flashed bar alone produced a stationary patch of spiking activity in the cortex, a square followed by a bar — as in the illusion — produced a different effect . Spiking activity began in the area of cortex corresponding to the position of the square, but when the bar was presented, the activity spread steadily along the cortex, from the position of the square to the other end of the bar (shown as a movie at http://www.nature.com/nature/journal/v428/n6981/extref/line-motion-examples_2.html). This activity pattern was identical to that produced by a visual stimulus in which the square moved at the same speed as the perceived movement in the illusion.

The initial spreading response to a bar presented after a square was faster than the response to a bar presented alone. When a square is presented alone, the area of spiking activity is surrounded by a spreading field of sub-threshold activity. This 'primes' the surrounding cortex so that any subsequent visual stimulus can produce a spiking response more quickly. Because the subthreshold activity is greatest near the area of spiking activity, and falls off with distance, the response to the stationary bar would be fastest in the cortex that immediately surrounds the area that responded to the square, and slower further away. This could explain the spreading activity and, the authors propose, the perception of motion — without the need for 'top-down' influences from higher areas of cortex.

Rachel Jones

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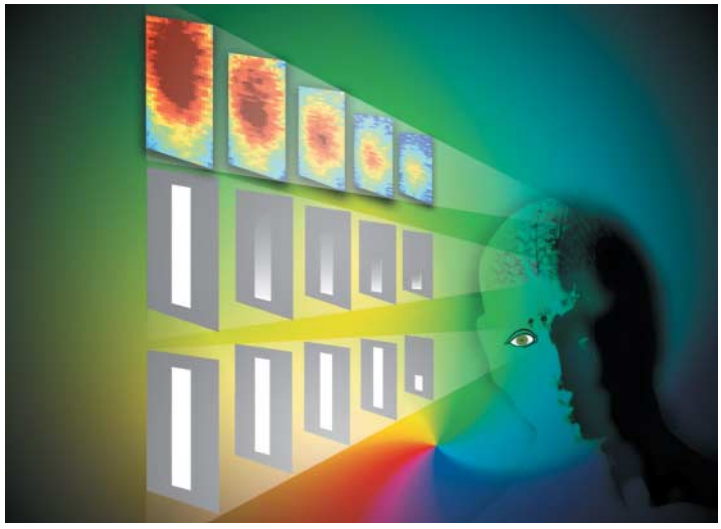

The bottom row of panels represents the visual stimulus. The middle row represents the subject's perception of the stimulus, and the top row shows recordings of activity from the cat visual cortex, showing how the activity (red) spreads across the cortex. Image courtesy of A. Grinvald, The Weizmann Institute of Science, Israel.

IN THE NEWS

How tickled am I?
When we ponder the really big questions in neuroscience, it's unlikely that the first one that springs to mind is "Why can't I tickle myself?" Yet researchers at the University of Wales in Swansea claim that the answer to this question could have important ramifications for the study of consciousness.

The research team, led by Dr Mark Blagrove, used a "2-foot long, electronically-controlled 'tickler'" (icwales.icnetwork.co.uk, 5 April 2004) to test the ability of volunteers to tickle themselves when they were fully awake, or had just woken from rapid eye movement (REM) or non-dreaming sleep. They found that if the volunteers used the machine to tickle themselves just as they were waking from REM sleep, the sensation was as intense as if someone else was doing the tickling, but this was not the case if they were awake or had just woken from non-dreaming sleep.

Blagrove compares the dream state to the hallucinatory state in schizophrenia: "People with schizophrenia can successfully tickle themselves because they produce hallucinations, but think that what they see is real … not actually produced by them. REM sleep allows you to believe that the events of the dream are real, that you are not producing them, and this … carries over for a few minutes when you are awake" (*BBC News Online*, 5 April).

So, other than giving hope to people who have a burning desire to be able to tickle themselves, what are the implications of this research? Blagrove says: "It is quite an important thing in terms of when do people feel in control of what they are doing, and when do they think things are being done to them. It is all to do with whether you can monitor what you are doing to yourself" (*BBC News Online*).

Heather Wood

PRIONS

Proteins go it alone

Two recent papers published in *Nature* provide the strongest evidence yet to support the protein-only hypothesis for the transmission of prion diseases. In addition, these studies — one by King and Diaz-Avalos, and the other by Tanaka and colleagues — confirm that distinct 'strains' of prion arise in the absence of genetic alterations owing to differences in protein conformation.

Although it is generally accepted that proteins are the sole infectious agents in prion diseases, this has been difficult to prove. In the new studies, the authors used a yeast system to demonstrate this principle. Sup35 is a *Saccharomyces cereviseae* prion that is required in normal cells for the termination of translation. Similar to the events that occur in prion diseases, Sup35 can be converted into an 'infectious' form that can propagate itself and form aggregates — known as amyloids. Cells in which this has occurred are known as [*PSI*$^+$] cells, and can be distinguished from their normal counterparts, [*psi*$^-$] cells, by alterations in their colour under certain conditions. The authors used *Escherichia coli* to overexpress a region of Sup35 that is sufficient to stimulate amyloid formation and purified aggregates of this protein. Expression in a bacterial system ensured the absence of any virus from the yeast cells that might be responsible for infectivity. They then used novel methods to deliver the aggregates into [*psi*$^-$] cells and showed that this resulted in conversion to the [*PSI*$^+$] state. Protease treatment greatly decreased the infectivity of the aggregates, whereas nuclease treatment had no effect, providing the strongest evidence so far that prion proteins, in the absence of genetic material, are sufficient for infectivity.

Another contentious issue in prion research is the existence of different 'strains' of the same prion protein that vary in their infective properties. How can these distinct characteristics arise if a single protein-only agent is responsible for transmission? Both groups showed that the generation of various conformations of the same protein underlies the existence of different prion strains. In *S. cereviseae*, several [*PSI*$^+$] strains can be distinguished on the basis of differential levels of Sup35 aggregation. Both groups found that when Sup35 aggregates from a specific strain were used to infect [*psi*$^-$] cells, the recipient cells were converted to the [*PSI*$^+$] strain from which the aggregates were derived. They also showed that Sup35 amyloids with distinct conformations are generated *in vitro* at various temperatures and that these distinct forms induced different infective characteristics when introduced into [*psi*$^-$] cells.

So, a prion protein folded in a specific way can induce the stable propagation of that conformation, with different strains being more or less efficient at converting the normal form of the protein. How this conversion takes place at the molecular level will be a key question for future investigation.

Louisa Flintoft, Assistant Editor,
Nature Reviews Microbiology

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SYNAPTIC PLASTICITY

Spiny problems in MRX

Cases of nonspecific X-linked mental retardation (MRX) in humans have been attributed to mutations in 11 different genes. Three of these genes code for molecules that interact with the Rho signalling pathway, which is known to regulate the actin cytoskeleton. So, how might Rho pathway dysfunction lead to the cognitive deficits that are associated with MRX? In a new study reported in *Nature Neuroscience*, Govek and colleagues provide some answers to this question.

In one family, MRX was found to be associated with a mutation in the gene that encodes a Rho-GTPase activating protein called oligophrenin-1 (OPHN-1). Govek *et al.* showed that in the rat brain, puncta of oligophrenin-1 were present at both presynaptic and postsynaptic sites, perhaps indicating a role in synaptic development and/or function. In the postsynaptic compartment, the protein was co-localized with F-actin, which is a key component of the dendritic spine cytoskeleton.

The authors used two approaches — antisense RNA and RNA interference — to knock down *Ophn-1* gene function in hippocampal slices from rats at postnatal day 4. They found that the mean dendritic spine length was significantly reduced on neurons that had been transfected with an *Ophn-1* antisense construct or small interfering RNAs. This knock-down phenotype could be mimicked by overexpression of RhoA, but not by overexpression of the other Rho family members Rac1 and Cdc42. In addition, the Ophn-1 knock-down phenotype was rescued by inhibiting Rho-kinase, a downstream target of RhoA that was previously shown to be involved in neurite retraction.

These findings indicate that Ophn-1 normally maintains dendritic spine length by negatively regulating the RhoA/Rho-kinase signalling pathway. Govek *et al.* also showed that Ophn-1 contains a binding site for Homer, an adaptor protein that provides a link between glutamate receptor activation and cytoskeletal rearrangements. Therefore, Ophn-1 might be part of a pathway that stabilizes spines in response to synaptic activity. This points towards a model for MRX, in which the defects in spine morphogenesis and stabilization that result from loss of Ophn-1 function impair the brain's capacity for synaptic plasticity, which in turn leads to deficits in learning and memory.

Heather Wood

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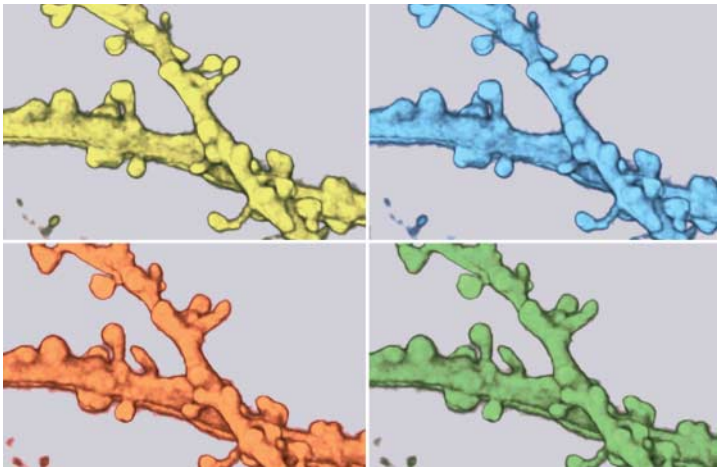


IN BRIEF

GENES AND BEHAVIOUR

Parallel *FoxP1* and *FoxP2* expression in songbird and human brain predicts functional interaction.

Teramitsu, I. *et al. J. Neurosci.* **24**, 3152–3163 (2004)

FoxP2 expression in avian vocal learners and non-learners.

Haesler, S. *et al. J. Neurosci.* **24**, 3164–3175 (2004)

FOXP2 is a forkhead gene that was identified as the gene that is mutated in a family with an autosomal-dominant speech and language disorder. These two papers provide evidence that it might also be involved in learned vocalisation in birds. Teramitsu *et al.* show that *FoxP2* and the forkhead family member *FoxP1* are expressed in an overlapping pattern in the songbird, in a corticostriatal pattern that reflects that structural abnormalities seen in the human patients and that is similar to the localization of *FOXP1* and *FOXP2* in the human fetal brain. Haesler *et al.* find that *FoxP2* expression in songbirds varies seasonally, being stronger at times when vocal learning occurs in brain structures that are associated with song learning.

NEURAL DEVELOPMENT

A role for ligand-gated ion channels in rod photoreceptor development.

Young, T. L. & Cepko, C. L. *Neuron* **41**, 867–879 (2004)

Taurine is present in the developing vertebrate CNS and has been shown to potentiate the development of rod photoreceptors. Young and Cepko now show that this effect is probably mediated by glycine α2 and $GABA_A$ (γ-aminobutyric acid, subtype A) receptors. Strychnine (a glycine receptor antagonist) and bicuculline (a GABA receptor antagonist) inhibited the ability of taurine to induce the production of rod photoreceptors, and a gain-of-function study showed that signalling through glycine α2 receptors caused cells to leave mitosis and increased the number of rods. Consistent with this, a targeted knockdown of glycine α2 receptors led to a decrease in the number of rods but an increase in other retinal cells.

SYNAPTIC PHYSIOLOGY

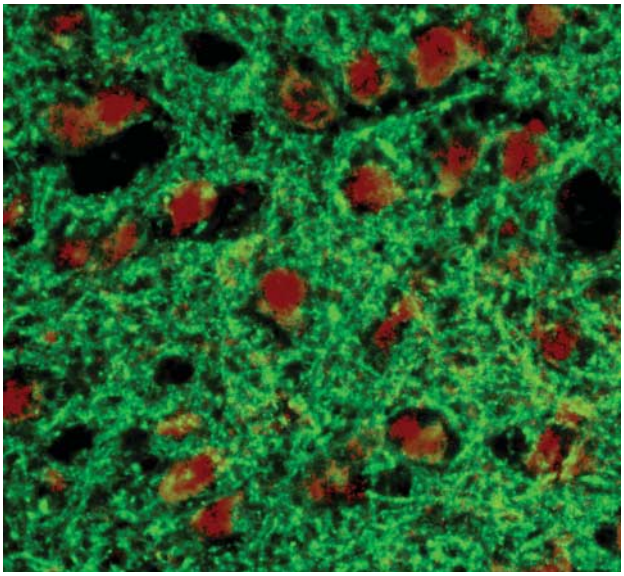
The structural organization of the readily releasable pool of synaptic vesicles.

Rizzoli, S. O. & Betz, W. J. *Science* **303**, 2037–2039 (2004)

The authors labelled the readily releasable pool (RRP) — those vesicles that are recruited first during neuronal activity — with a fluorescent dye, FM1-43, that is taken up by recycling vesicles. Although it might be expected that the RRP would consist of those vesicles closest to the presynaptic membrane, Rizzoli and Betz found that the labelled vesicles were scattered throughout the nerve terminal, except for the centre of the cluster of vesicles. So, it seems that vesicle recruitment does not depend on proximity to the release sites, but instead involves a different mechanism of mobilization.

NEUROBIOLOGY OF ADDICTION

The rewards of tPA



Immunohistochemical localization of MAP2 (green) and tPA (red) in morphine-treated mice. Image courtesy of K. Yamada, Kanazawa University Graduate School of Natural Science & Technology, Japan.

The tissue plasminogen activator (tPA)–plasmin system, which degrades extracellular matrix proteins, regulates the brain's response to morphine, according to new work by Nagai *et al.* Writing in *The Proceedings of the National Academy of Sciences of the USA*, they show that this system regulates the morphine-induced release of dopamine in the nucleus accumbens, which is thought to be involved in morphine's rewarding effects.

The extracellular protease tPA converts plasminogen into plasmin, and is expressed throughout the CNS. The tPA–plasmin system is thought to be important for various neuronal functions, including plasticity, migration and neurite outgrowth. Nagai and colleagues investigated the response of this system to treatment with morphine in rats and mice, and found that morphine treatment led to an increase in the expression of tPA in the nucleus accumbens, and that this effect was blocked by naloxone (an opioid receptor blocker).

They then investigated the effects of morphine in mice that lacked either tPA or plasminogen. Although the anti-nociceptive effects of morphine were normal in these mice, they showed much less morphine-induced hyperactivity than wild-type mice. This deficit could be partly reversed by injecting tPA or plasmin into the nucleus accumbens. In addition, the mutant mice failed to develop normal conditioned place preference following morphine treatment, and this is generally considered to be a measure of the rewarding properties of morphine. However, the interpretation of this finding is complicated by the fact that tPA-knockout mice also show deficits in other measures of learning.

If the tPA–plasmin system is necessary for the rewarding effects of morphine, what is its role? Normally, morphine causes a release of dopamine in the nucleus accumbens, and this is related to the rewarding effects of morphine. In mice that lacked tPA or plasminogen, the amount of

DEVELOPMENT

RNA snippets specify cell fate

A new study in *Cell* shows that multipotent stem cells are committed to a neuronal lineage through the novel regulatory action of small, double-stranded RNAs (dsRNAs).

Small RNAs have received a lot of attention recently owing to their involvement in RNA interference, the process by which snippets of RNA bind specifically to target mRNAs and prevent their translation into protein. Now, Fred Gage and colleagues have discovered a new mode of action of dsRNAs — activating gene expression by interacting directly with proteins and DNA.

The discovery was made while investigating the molecular mechanisms that regulate neuron-specific gene expression. In a screen for small, non-coding RNAs that might participate in the differentiation of neurons, Gage's team isolated a short dsRNA whose sequence matched that of *neuron restrictive silencer element/RE1* (*NRSE/RE1*) from adult hippocampal neural stem cells. *NRSE/RE1* is a conserved DNA response element that is present in genes that code for neuronal proteins, including ion channels and neurotransmitter receptors. In non-neuronal cells, expression of neuronal genes is prevented when the *NRSE/RE1* element in their promoters binds to neuronal restricted silencing factor/RE1 silencing transcription factor (NRSF/REST). This zinc finger protein mediates its repressive effect on gene expression by recruiting negative transcriptional regulators such as histone deacetylases.

The authors used viral vectors to introduce *NRSE/RE1* dsRNAs into adult hippocampal stem cells. This transfection caused morphological changes consistent with the differentiation of neurons, such as the extension of processes. The expression of neuron-specific genes that contain *NRSE/RE1* in their promoters (including *synapsin 1* and *mGluR2*) increased in these cells. So *NRSE/RE1* dsRNAs seem to have a crucial role in the acquistion of neuronal cell fate by counteracting the repressive action of NRSF/REST.

Do *NRSE/RE1* dsRNAs exert their effect by silencing the *NRSF/REST* gene through RNA interference? As expression of NRSF/REST was unaffected in cells transfected with *NRSE/RE1* dsRNAs, the authors concluded that this was not the case. Support for an alternative mechanism came from experiments in which stem cell extracts were incubated with biotin-labelled *NRSE/RE1* dsRNAs. Immunoblots of biotin-positive conjugates and titration analysis revealed that *NRSE/RE1* dsRNA binds NRSF/REST in a highly-specific manner.

So, a model is emerging whereby cells that are to become neurons activate the transcription of genes that contain the *NRSE/RE1* sequence. These cells might then generate non-coding *NRSE/RE1* dsRNAs that interact with the *NRSE/RE1* DNA response element and NRSF/REST, switching this transcription factor from repressor to activator by disrupting its association with negative transcriptional regulators. No doubt many more examples of transcriptional regulation by other small modulatory RNAs of this type will come to light in the near future.

Suzanne Farley

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dopamine that was released in the nucleus accumbens in response to morphine was greatly reduced, and injection of plasmin into the nucleus accumbens in *tPA*$^{-/-}$ mice reversed this effect.

So, the authors propose that morphine causes an increase in tPA in the nucleus accumbens, which converts plasminogen to plasmin and thereby leads to an increase in the release of dopamine. The pathway that leads from plasmin production to dopamine release is unknown, but it could be related to the degradation of laminin (an extracellular matrix protein that regulates calcium channels at synapses) by plasmin. Future work should focus on elucidating this pathway.

Rachel Jones

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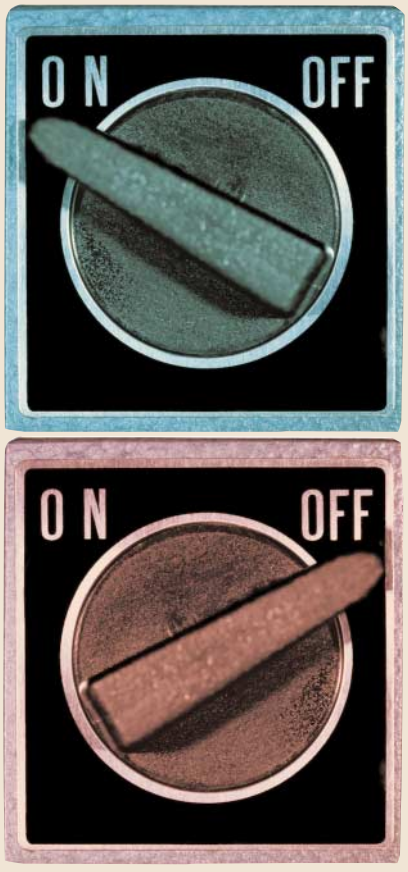

GLIA

Myelin made to measure

There is a precise and predictable relationship between the diameter of an axon and the thickness of the myelin that surrounds it. Writing in *Science*, Michailov, Sereda and colleagues describe evidence that the amount of neuregulin-1 (Nrg1) that is produced by an axon tells Schwann cells how thick the myelin sheath around that axon should be.

The speed at which action potentials are conducted along an axon depends largely on the diameter of the axon and the thickness of its myelin sheath — two factors that are closely related. Maintaining the precise control of conductance velocity is essential for the proper function of the nervous system, and it has been suggested that myelin thickness might be controlled by interactions between ligands produced by the axon and receptors on the myelinating glia. Michailov *et al.* tested the idea that the axonal ligand that is responsible — in the periphery, at least — is Nrg1, interacting with ErbB receptors on Schwann cells.

The *Nrg1* gene is expressed in neurons of the sciatic nerve in mice, and *ErbB2* and *ErbB3* are expressed by Schwann cells. If interactions between Nrg1 and ErbB receptors control myelin thickness, changes in the amount of ligand or receptor might alter the thickness of the myelin sheath. When the authors generated compound heterozygote mice that had reduced gene dosages of both *Nrg1* and *ErbB2*, they found that the myelin in the sciatic nerves of the mice was significantly thinner than usual. Although the mice seemed normal, the conduction velocity in their nerves was also reduced, even though the sizes of the axons were unchanged.

To narrow down the cause of the reduced myelination, the authors looked at mice with reduced dosages of just the *Nrg1* gene or the *ErbB2* gene. Mice that were heterozygous for *ErbB2* showed normal myelination, but in the *Nrg1* heterozygotes, the myelin was as thin as in the compound heterozygotes. So the expression of Nrg1 seems to control the thickness of myelin.

To test this theory further, the authors generated mice in which Nrg1 was overexpressed under the control of the murine Thy1.2 promotor, so that the excess Nrg1 was expressed specifically in post-natal motor neurons and dorsal root ganglion neurons. In these mice, the peripheral nerves showed hypermyelination when compared with wild-type mice.

There are three isoforms of Nrg1, and these effects seem to be specific for Nrg1 type III. Mice that overexpressed Nrg1 type III showed

hypermyelination, but mice that overexpressed Nrg1 type I did not (although they did show some myelin abnormalities in the CNS). A specific reduction in the expression of the Nrg1 type III isoform also produced hypomyelination, indicating that Nrg1 types I and II cannot compensate for the lack of the type III isoform.

These results support a model in which Nrg1 type III is produced as a function of axonal diameter. The amount of Nrg1 dictates the amount of signalling through the Schwann cell ErbB receptors, and this controls the degree of myelination of each axon. Important questions include how the production of Nrg1 is quantitatively controlled, and what signalling pathway is responsible for dictating myelin thickness as a result.

Rachel Jones

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WEB SITE

Nave laboratory: http://nave.em.mpg.de/root/

NEURODEGENERATIVE DISEASE

Metabolite-mediated misfolding

The three-dimensional conformation of a protein is specified by its amino-acid sequence, so mutations can lead to aberrant folding. But why do normal, mutation-free proteins become misfolded? Resolving this conundrum would improve our understanding of the sporadic form of Alzheimer's disease, in which wild-type amyloid β-peptides (Aβ) misfold and aggregate to form pathogenic plaques in the brain.

One possibility is that modification by abnormal metabolites causes wild-type Aβ to misfold. Recently established links between Alzheimer's disease, high cholesterol levels and inflammation prompted a team of investigators led by Jeffery Kelly to focus on the Aβ-modifying potential of metabolites that form through the reaction of cholesterol with ozone, which is generated during inflammation.

A key property of these cholesterol metabolites is that they possess an aldehyde group, which could covalently modify amines in Aβ. This attachment would markedly increase the hydrophobicity of Aβ, potentially increasing the likelihood of misfolding. To assess this possibility, several cholesterol metabolites were individually incubated with Aβ. Two such metabolites — dubbed compounds 1 and 2 — caused a concentration-dependent increase in the rate of amyloidogenesis and were shown to be present in human brains.

Once formation of aggregates in the *in vitro* assay had ceased, the authors measured the amount of soluble Aβ that remained in the reaction mixture. This provided an estimate of the 'critical concentration' for aggregation in the presence of compound 1 or 2. The derived maximal value of 90 nM is much lower than that for metabolite-free Aβ, which might explain how physiological concentrations of Aβ (typically in the nanomolar range) could form amyloid plaques in individuals that lack predisposing

mutations. The authors suggest that atherosclerosis-related inflammation causes ozonolysis of cholesterol, transiently increasing the concentrations of highly reactive metabolites that in turn initiate amyloidogenesis.

Suzanne Farley

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NEUROLOGICAL DISORDERS

Special agents provide early warnings

The early diagnosis of Alzheimer's disease — the most common cause of dementia in the elderly — remains problematic. Now, Nobuyuki Okamura and colleagues report a potential way to detect early changes in patients who are at risk of developing Alzheimer's disease through the non-invasive imaging of senile plaques — a pathological change that precedes the onset of cognitive deterioration.

Senile plaques contain amyloid-β (Aβ) peptide, levels of which are elevated in early dementia. The initial stages of Alzheimer's disease are characterized by extensive deposition of diffuse plaques and the formation of neurofibrillary tangles in the entorhinal cortex. An agent that can selectively recognize amyloid fibrils and that can permeate the blood–brain barrier might allow clinicians to visualize these initial pathological changes *in vivo* using positron emission tomography (PET) or single-photon emission computed tomography (SPECT).

Okamura *et al.* screened many derivatives of styrylbenzoxazole for those that that have a high binding affinity to amyloid fibrils. One of these derivatives, 6-(2-fluoroethoxy)-2-[2-(4-methylaminophenil) ethenyl]benzoxazole (BF-168), selectively recognized senile plaques and neurofibrillary tangles: *in vitro* binding assays showed that it had a high binding affinity with synthetic Aβ aggregates, and neuropathological staining showed evidence for binding of BF-168 to both neuritc and diffuse plaques in brain sections from patients with Alzheimer's disease.

The authors went on to test whether BF-168 could be used for *in vivo* imaging of amyloid deposits in the brain. In two transgenic mouse models of Alzheimer's disease, fluorescent microscopy and autoradiography showed that the compound bound selectively and specifically to both compact and, more importantly, diffuse Aβ deposits in the neocortex, hippocampus and entorhinal cortex. This, together with the high initial uptake of [^{18}F]BF-168 and fast brain washout, indicates that this agent might be an ideal imaging probe.

Further work is needed to demonstrate the safety and efficacy of BF-168 in humans. However, if it can be successfully used in the clinic, *in vivo* imaging of amyloid plaques using BF-168 offers hope for the identification of individuals who are at risk of developing Alzheimer's desease, and in turn, for the application of potential preventative treatments for pre-symptomatic patients.

Alison Rowan, Copy Editor,
Nature Reviews Genetics

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AXON GUIDANCE

Zic3 makes the gradient

During the development of the vertebrate eye, retinal ganglion cell axons converge on the optic disc, where they exit the eyeball to form the optic stalk. The mechanisms that guide these axons towards the optic disc are poorly understood — it was proposed that the disc itself might produce a long-range chemoattractant, but no such activity has been identified in this region. Now, Zhang and colleagues present evidence that graded expression of the transcription factor Zic3 induces the generation of a repulsive force, which channels retinal axons towards the optic disc.

Using *in situ* hybridization, the authors showed that the *Zic3* gene is normally expressed in a gradient within the retina, with the highest concentration at the periphery and the lowest at the centre. They disrupted this gradient by transfecting the embryonic chick retina with a Zic3-expressing retroviral vector. This caused various axon guidance defects, including stalling of growth cones within the sites of transfection, and, less frequently, axons turning 180° to project back towards the periphery of the retina.

Next, Zhang *et al.* presented retinal ganglion cells in culture with the choice of growing on retinal membrane fragments that were transfected with either a control green fluorescent protein-expressing retroviral construct or the Zic3-expressing construct. When they were faced with alternating stripes of these two tissues, the cells extended axons preferentially on the control stripes. Similarly, when the cells were presented with alternating stripes of membrane from the centre and the periphery of the retina, most of their axons grew along the stripes from the centre of the retina.

Taken together, these findings indicate that Zic3-expressing tissue releases a factor that repels the axons of retinal ganglion cells. Zic3 is not the first Zic family member to be implicated in axon guidance in the visual system — Zic2 was recently shown to be involved in controlling axon crossing at the optic chiasm. As the Zic proteins are transcription factors, they presumably act by inducing the expression of guidance cues. So, to understand their roles in axon guidance, it will be important to identify their downstream targets.

Heather Wood

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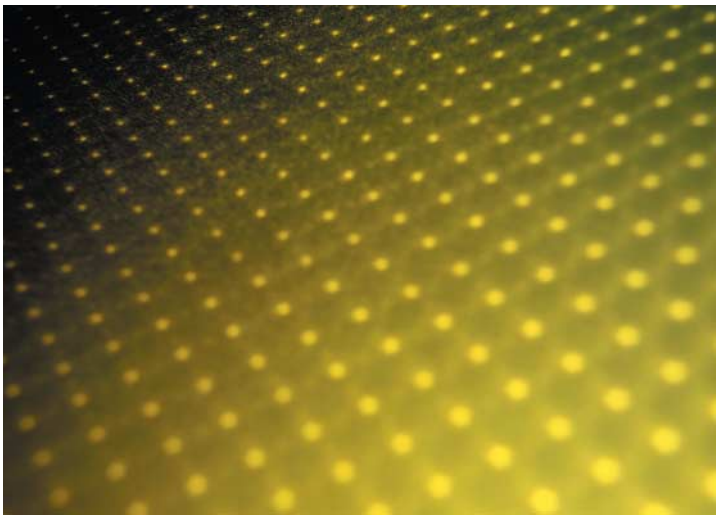

IN BRIEF

SYNAPTIC PHYSIOLOGY

Roles of glutamate transporters in shaping excitatory synaptic currents in cerebellar Purkinje cells.

Takayasu, Y. *et al. Eur. J. Neurosci.* **19**, 1285–1295 (2004)

The authors used a blocker of glutamate transporters, DL-*threo*-β-benzyloxyaspartate (DL-TBOA) to investigate the role of these transporters in cerebellar synapses. Blocking glutamate transporters prolonged excitatory postsynaptic potentials in cerebellar Purkinje cells. DL-TBOA seems to increase the time for which synaptically released glutamate is present and also induces glutamate spillover to neighbouring targets. The results indicate that glutamate transporters are an important influence on synaptic transmission at these synapses.

NEURAL DEVELOPMENT

Columnar architecture sculpted by GABA circuits in developing cat visual cortex.

Hensch, T. K. & Stryker, M. P. *Science* **303**, 1678–1681 (2004)

Specific $GABA_A$ circuits for visual cortical plasticity.

Fagiolini, M. *et al. Science* **303**, 1681–1683 (2004)

Two papers from Hensch and colleagues give important new insights into the development of ocular dominance columns in the visual cortex. In the first, Hensch and Stryker used benzodiazepines to modulate the inhibitory activity in the visual cortex of kittens. Diazepam, which potentiates inhibitory activity, caused the columns to become broader, whereas treatment with DMCM, which reduces inhibition, made the columns narrower. To investigate further how inhibitory inputs shape the development of cortical segregation in the visual system, Fagiolini *et al.* used a mouse knock-in mutation to make specific types of $GABA_A$ (γ-aminobutyric acid, subtype A) receptor insensitive to diazepam. They found that receptors containing the α1 subunit were needed for diazepam to be able to influence ocular dominance plasticity, indicating that this subtype of receptor is responsible for shaping ocular dominance columns in the developing visual cortex.

COGNITIVE NEUROSCIENCE

Your own action influences how you perceive another person's action.

Hamilton, A. *et al. Curr. Biol.* **14**, 493–498 (2004)

The authors tested the hypothesis that the motor system is responsible for decoding the observed action of others by asking subjects to judge the weight of a box being lifted by another person while they lifted or held a light or heavy box. Actively lifting a heavy box led to a perception of the observed box as being lighter, whereas lifting a light box meant that the observed box was judged to be heavier. The authors propose a model that can account for these results by using overlapping neural systems for motor control and action understanding to process multiple models of observed and performed actions.