Monogamy is rare among mammals, but the binding mechanisms in species that form lasting bonds with their mates might have parallels in reward learning and addiction. Indeed, previous studies have shown that dopamine signalling in the nucleus accumbens (NAc), part of the mesolimbic reward system, is required for pair-bond formation in prairie voles, which are characteristically monogamous. A new study in *Nature Neuroscience* reports that differential signalling through certain dopamine receptors is also important for the maintenance of pair bonds by promoting selective aggression towards strangers.

After 24 h of cohabitation and mating with a female, sexually naive male prairie voles come to prefer the contact of their mating partner to that of a novel female. This partner preference requires signalling through D2-like dopamine receptors in the NAc, and Aragona et al. show that this signalling specifically occurs in the rostral shell of the NAc, a region that is associated with appetitive conditioning in other animals. By contrast, a D1-like receptor agonist infused into the NAc blocked mating-induced partner preference, indicating differential effects of dopaminergic signalling through these two types of receptor.

Partner preference is an initial prerequisite for lasting pair-bond formation, but complete transition to a pair bond also requires that stranger conspecifics, including potential new mates, be actively rejected. Given the opposing actions of D1- and D2-like receptors in partner preference formation, Aragona and co-workers asked whether dopaminergic signalling in the NAc was also important for the development of selective aggression towards novel females. They found that fully pair-bonded male prairie voles had higher levels of D1-like receptors in the rostral core and shell of the NAc compared with naive males. Furthermore, blocking these receptors with a D1-like receptor antagonist blocked aggressive behaviour towards novel females.

The authors therefore suggest that a reorganization of dopaminergic signalling in the NAc contributes to the transition from an affiliative approach towards novel females observed in naive males to selective aggression in bonded males, a behaviour that helps to maintain an established partnership. Interestingly, similar opposing regulation by D1 and D2-like receptors also occurs in drug-seeking behaviour.

The monogamous pair bonds of prairie voles are unusual, even among vole species. Meadow voles are less social overall and have more promiscuous mating habits, and Aragona and colleagues show that male meadow voles have higher basal levels of D1-like receptors in the NAc. Blocking D1-like receptors increased affiliative behaviour in these voles, consistent with a role for this species difference in determining their naturally asocial ways, and a more general role for dopaminergic signalling in the organization of social behaviour.

*Cara Allen, Associate Editor, Nature Neuroscience*
**NEURODEGENERATIVE DISORDERS**

**Proof of delivery**

Treating any disorder of the brain poses a special challenge owing to the difficulty of getting drugs across the blood–brain barrier. New work shows that implanting the brains of animal models with genetically engineered neural progenitor cells (NPCs) reduces some symptoms of Parkinson’s disease, and might benefit other neurodegenerative disorders.

Parkinson’s disease affects ~1.5 million people in the United States and is caused by the irreversible loss of dopaminergic neurons, which coordinate muscle movement and balance. We know that some molecules — such as glial cell line-derived neurotrophic factor (GDNF) — can promote the regeneration of lost neurons, but delivering these agents to the brain by using viruses as carriers, or by injecting the molecule straight into the brain, could pose a risk to health or be inefficient. The group led byoshana Behrostock and Clive Svendsen has hit on a different strategy of modifying cells to express GDNF. The engineered cells — human NPCs derived from fetal brains — were transferred into the area of the brain in which GDNF was needed in parkinsonian rats and aging rhesus monkeys.

Remarkably, the protein produced by the cells remained active for up to 3 months and was transported to the substantia nigra, the brain region that degenerates in Parkinson’s disease. In addition, the cells migrated across the affected region and led to increased fibre sprouting and survival of the host neurons.

Given that the effects of GDNF are not specific to the cells that are damaged in Parkinson’s disease it is likely that these same cells could be used to treat other disorders, such as Huntington’s disease and amyotrophic lateral sclerosis (ALS). Whether this therapy can be attempted in humans will depend on our devising a way to control the expression of GDNF in the engineered cells — in particular, to shut it off. The authors accomplished protein regulation in culture, but shut-off in animals proved more difficult and is being addressed in new experiments. Nevertheless, this work provides convincing evidence that stem cells are a valid vehicle for targeting drugs to less accessible tissues such as the brain in a safe and efficient way.

*Tanita Casci, Senior Editor, Nature Reviews Genetics*

**SYNAPTIC PLASTICITY**

**MeCP2 and memory mechanisms**

Methyl-CpG-binding protein 2 (MeCP2) is an X-linked transcriptional repressor and a regulator of RNA splicing. Loss of function of this protein is a frequent cause of Rett syndrome, a progressive neurological developmental disorder and one of the most common causes of mental retardation in females. New work in mice shows that MeCP2 is necessary for learning and memory, and reveals that its loss of function causes functional and ultrastructural abnormalities in synapses.

Using three hippocampus-dependent behavioural paradigms, Moretti and co-workers describe deficits of spatial memory and contextual fear conditioning in mice expressing a truncated allele of MeCP2. These mice also show impairment of social interaction and long-term social memory, consistent with phenotypes observed in Rett syndrome.

Electrophysiological analysis of the CA1 region of the hippocampus in MeCP2 mutant mice showed increased postsynaptic depolarization and attenuated paired-pulse facilitation, a simple, short-term form of synaptic plasticity. Together, these data indicate an enhancement of basal synaptic transmission in this region.

Two mechanistically distinct forms of long-term potentiation (LTP) were impaired in the hippocampus of MeCP2 mutant mice, and LTP was also impaired in primary motor and sensory regions of the cortex. Measures of long-term depression (LTD) that rely entirely on postsynaptic mechanisms for the induction and expression of LTD were normal in MeCP2 mutant mice. Interestingly, paired-pulse low-frequency stimulation, a measure of LTD that is absolutely dependent on the presynaptic terminal for its induction, revealed an impairment in this form of synaptic plasticity in the CA1 region of mutant mice, which suggests the presence of alterations at the presynaptic terminus.

In addition, electron microscopy revealed changes at an ultrastructural level. Mutant mice showed a reduction in the average length of postsynaptic densities, despite there being no change in their density or the number of docked vesicles. Therefore, the authors speculate that the close correlation between presynaptic active zone and postsynaptic density size observed in normal synapses is perturbed in these mice.

Together with previous work showing an enhancement of plasticity due to MeCP2 overexpression, these findings suggest an important role for MeCP2 in the regulation of synaptic function. Analysis of the molecular targets of this protein will improve our understanding of its role in synaptic function. As dysfunction of MeCP2 is associated with mental retardation, mild learning disability and autism, such an understanding might also provide us with insight into the aetiology of a range of neurodevelopmental disorders.

*Daniel McGowan*


**WEB SITE** Clive Svendsen’s laboratory: http://www.waisman.wisc.edu/scrp/svendsen.html
In the news

**DAMAGE LIMITATION**

Nerve damage occurring as a result of injury or disease is generally irreversible, and the development of drugs with the capacity to prevent at least some of this damage could improve the quality of life for millions of people worldwide. Now, scientists in the United States and Japan have taken what could be an important step towards this goal.

Stuart Lipton, at the Burnham Institute, La Jolla, California, USA, and his colleagues showed that neurite outgrowth-promoting prostaglandin (NEPP) compounds, which are known to be neuroprotective, stimulate the production of natural antioxidants that protect against oxidative stress in a mouse model of stroke. The free radicals responsible for the excitotoxicity are also thought to play a part in the pathology of neurological disorders such as Alzheimer’s disease and Parkinson’s disease, so the potential utility of NEPPs could extend far beyond the treatment of stroke.

There are, of course, other compounds that can stimulate antioxidant production, but, says Professor Lipton, “...the very exciting finding here is that nerve cells are specifically targeted by the new drugs, avoiding other cell types” (BBC News Online, 9 January 2006).

Moreover, he adds, “These drugs may be much less toxic than prior drugs in this class because they are only low to moderately effective” (The Guardian, 10 January 2006). More effective drugs can actually be damaging to cells, because they disrupt their normal functions. The lower efficacy of NEPPs, combined with their preferential uptake by neurons, could contribute to a lower incidence of side effects.

The results so far are promising, but whether they can be replicated in humans in injury or disease, or used to develop safe and effective clinical treatments remains to be seen.

**NEUROECONOMICS**

**Decisions, decisions**

Standard decision theory postulates that ambiguity about probabilities of winning should not affect choices. However, experiments show that many people are more willing to bet on risky outcomes than on ambiguous ones. This empirical aversion to ambiguity prompted Ming Hsu and colleagues to search for neural distinctions between risk and ambiguity using functional MRI (fMRI).

Decision-making under risky and ambiguous uncertainty is best illustrated by what is known as the Ellsberg paradox. Imagine one deck of 20 cards composed of 10 red and 10 blue cards (the risky deck), and another of 20 red and blue cards in which the composition of red and blue cards is unknown (the ambiguous deck). A bet on a colour pays

**REPAIR**

**Talking about regeneration**

The adult brain’s ability to generate new neurons in circumscribed regions indicates the potential for exploiting intrinsic mechanisms for neuronal repair following degeneration or injury. Despite this, there has been a failure to generate new neurons in other regions following brain injury. So, are there factors that suppress neurogenesis in these non-neurogenic regions following brain injury? Magdalena Götz and colleagues set out to address this question, and showed that the basic helix–loop–helix transcription factor Olig2 (oligodendrocyte transcription factor 2) is a restricting factor.

Götz and colleagues investigated the effects of several neurogenic transcription factors — including Pax6, Ngn2, Mash1 and Gsh2 — on neurogenesis in mice following stab wounds or focal ischaemia, and in mice with amyloid plaque deposition. All of these transcription factors are involved in specifying neuronal fate during development, and are found in precursor cells in the subependymal zone. As expected, they were not present in injured cells, in line with the absence of neurogenesis. However, Olig2, but not Olig1, was abundant in a range of glial cell populations following injury, but not in intact regions.

This elevated number of Olig2-positive cells was apparent in all three injury paradigms, although the mechanisms that prompted this increase differed according to injury type. Stab wounds led to a rise in proliferation of Olig2-positive cells, whereas amyloid plaque deposition resulted in upregulation of Olig2 at the transcriptional level.

Next, these researchers looked specifically at the action of Olig2 following stab wounds by disrupting its function through injection of retroviral...
a fixed sum if a card of the chosen
colour is drawn. Which deck of cards
would participants prefer to bet on?
Interestingly, most people prefer to
bet on a card from the risky rather
than the ambiguous deck, even
though there is a 50–50 chance of
winning in both cases.

Using similar experimental treat-
ments, the researchers show that the
brain in fact treats the two decks of
cards differently. Twenty-four areas
in the brain are more active under
conditions of ambiguity than risk.
Among these regions are the amyg-
dala, the orbitofrontal cortex (OFC)
and the dorsomedial prefrontal
cortex. By constrast, the dorsal stria-
tum is preferentially activated during
the risky condition. As the dorsal stria-
tum is implicated in reward
prediction, the result indicates that
ambiguity lowers the anticipated
rewards.

To confirm the fMRI results, Hsu
et al. conducted similar behavioural
tests using patients with focal brain
lesions. They found that patients
with OFC lesions did not distinguish
between risky and ambiguous uncer-
tainty — an observation that was
not seen in control patients who had
temporal lobe damage.

Therefore, different areas of the
brain are activated when we evaluate
ambiguous and risky choices. This
might underlie a general process of
how organisms explore their environ-
ment, which often contains risky and
ambiguous uncertainty. In addition,
understanding the neural basis of
choice under uncertainty has impor-
tant social implications because it is
a fundamental activity at every level
of society — from the personal to the
political.

Jane Qiu

ORIGINAL RESEARCH PAPER
Hsu, M. et al.
Neural systems responding to degrees of
FURTHER READING
Sugrue, L. P. et al. Choosing
the greater of two goods: neural currencies for
WEB SITE
Camerer’s laboratory: http://www.hss.caltech.edu/~camerer/camerer.html

vectors containing a dominant-
negative form of Olig2 into the injured
region. Crucially, preventing Olig2
activity triggered the generation of
cells that acquired the hallmarks of
immature neurons. This suggests that
glial cells have the potential to generate
neurons following injury in adulthood.
Interestingly, PAX6 was seen in some
cells in which Olig2 function had been
suppressed, which indicates that Olig2
normally prevents the action of PAX6
after injury. Transduction of cells with
a PAX6-containing retrovirus led to a
further increase in neurogenesis from
cells that typically do not generate
neurons.

Only a relatively small number of
these cells differentiated into
mature neurons, so future studies
need to focus on mechanisms to
promote survival and differentiation.
Nevertheless, this work offers
vital clues towards a potential
therapeutic avenue for the induction
of neurogenesis in the adult brain
following even severe injuries.

Alison Rowan

ORIGINAL RESEARCH PAPER
Buffo, A. et al.
Expression pattern of the transcription factor
Olig2 in response to brain injuries: implications
for neuronal repair. Proc. Natl Acad. Sci. USA 102,
18183–18188 (2005)

Wnt–Ryk signalling mediates medial–lateral
retinotectal topographic mapping.

The complex connections of the vertebrate nervous system
are topographically highly organized. Order is achieved by
establishing an appropriate balance of opposing morphogens
that guide axons to their targets. A new study of the cues that
establish the topographic map for retinotectal projections
in the chick and mouse reveals WNT3 as a lateral mapping
force that acts in opposition to the medial-directed cue
provided by ephrins. Contributing a further degree of spatial
‘awareness’ to axons, the strength of the WNT3 effect varies
along the dorsoventral axis depending on the particular
receptor that it binds: an axon-repulsive WNT–RYK axis
competes with an attractive WNT–frizzled interaction,
which, together with ephrins determine the topographical
connections of axons.

A single vesicular glutamate transporter is sufficient
to fill a synaptic vesicle.

Neurotransmitter is released as packets, or quanta, which
correspond to one synaptic vesicle. Vesicles are filled with
neurotransmitter by vesicular neurotransmitter transporters,
and the postsynaptic response to the release of a synaptic
vesicle, known as the quantal size, depends on the amount of
transmitter within a particular vesicle. However, the minimum
number of transporters needed to fill a vesicle has so far not
been documented. Daniels et al. created a series of Drosophila
mutants in which there was graded expression of the vesicular
glutamate transporter (VGLUT) at the neuromuscular junction.
They found that, in the mutant flies, there was a reduction
in the frequency of spontaneous quantal release that varied
according to the level of VGLUT. Importantly, quantal size
remained normal, and, according to probabalistic calculations,
even when the number of transporters was restricted so
that each synaptic vesicle was thought to contain only one
functional unit of VGLUT, all synaptic vesicles were still filled
to the same level as they were in wild-type flies. These findings
were taken to indicate that a single vesicular glutamate
transporter is sufficient to fill each synaptic vesicle.

Declarative memory consolidation in humans:
a prospective functional magnetic resonance
imaging study.

In a prospective study, Takashima et al. used functional MRI
over the course of 3 months to monitor the effects of memory
consolidation on brain activity. Hippocampal activity declined,
whereas activation in the ventral medial prefrontal cortex
increased over repeated testing. Moreover, the duration of
slow-wave sleep was positively correlated with recognition
memory performance and negatively correlated with the
strength of changes in hippocampal activity. These findings
support a model in which memory consolidation is facilitated
by slow-wave sleep and a gradual shift of retrieval processes
to the neocortex.
Dynamic networking

Whether external inputs from the thalamus or the internal circuitry of the cortex has the greater role in determining the activity of primary sensory cortices has been a topic of discussion for many years, as it reflects the larger philosophical issue of to what extent our minds are driven internally or by the outside world. Results reported by MacLean, Yuste and colleagues in Neuron go some way to resolving this issue, suggesting that intracortical connections govern the cortical response to thalamic stimulation.

It has previously been shown that the thalamus is not essential for spontaneous activity in the cortex, as spontaneous activity arises in brain slices that have no intact thalamic inputs. However, it has yet to be resolved how, if at all, spontaneous activity and activity that is triggered by external thalamic inputs are linked.

Using mouse thalamocortical slices in which connections from the thalamus to the cortex are intact, MacLean and colleagues investigated cortical activity arising spontaneously and compared it with activity generated by thalamic stimulation. Calcium imaging of layer 4 cortical neurons in these brain slices showed that spontaneous activity, as reported by imaging, was coincident with a transition from a DOWN state (hyperpolarized potential) to an UP state (prolonged depolarization) in patch-clamped neurons. How does the response to thalamic input compare with this activity? The authors found that the cortical activity triggered by stimulation of the thalamus (>10 Hz) could not be differentiated from spontaneous activity. Moreover, the same neuronal population was activated in a specific spatiotemporal pattern in both spontaneous and thalamically triggered activity.

The authors went on to explore whether the thalamus is the source of the spontaneous activity in the cortex. Spontaneous activity, and the accompanying intracellular UP states, was observed in thalamocortical slices in which the connection between the thalamus and cortex was disrupted. It has previously been shown that the activity in layer 4 of the thalamus is spontaneously generated by stimulation of the thalamus.

By patch-clamping the thalamus and recording from layer 4, the authors observed a transition from a DOWN state to an UP state, suggesting that the spontaneous activity observed in the cortex is generated by the thalamus. This finding has important implications for the treatment of pain, in which the thalamus appears to be a key site of pain modulation.

Their study evaluated both healthy volunteers and patients with chronic pain, and real-time functional MRI (rtfMRI) was used to provide information about rACC activation as it occurred. Participants were shown line chart and video images to represent rtfMRI measurements of their levels of rACC activation. Through the feedback provided by these images, the healthy participants were trained to increase and then decrease their rACC activation over two consecutive minutes, with a 30 s application of a noxious heat stimulus beginning 10 s into each minute. Patients with chronic pain were also trained to increase and decrease their rACC activity, but were not subjected to the external stimulus.

After training, healthy participants reported increased pain perception during test periods in which they were controlling increases in rACC activation compared with when they controlled decreases. Control groups that had undergone similar training procedures without the images representing their rACC activation reported significantly less control over pain perception and smaller variations in pain intensity.

The patients with chronic pain all reported an improvement in baseline pain levels after the training procedure, in some cases of more than 50%, whereas a control patient group, in which autonomic rather than rACC activation feedback had been given, experienced much smaller decreases in pain.

Controlling pain through real-time imaging may be a clinical possibility for the future. Whether similar control can be exerted over other brain areas, and what other applications this technique might have remain to be discovered.


thalamus and the cortex had been severed, which suggests that spontaneous activity originates not from the thalamus but from the cortex as a result of intrinsic cortical dynamics and/or connectivity. In addition, spontaneous cortical activity seems to be neither maintained nor influenced directly by the thalamus.

This finding, when coupled with the observation that the thalamus can trigger intrinsic cortical dynamics, led MacLean and colleagues to suggest that the thalamus serves to activate the internal circuitry dynamics of the cortex. Taken together, the results reported by these authors indicate that internal dynamics dominate the cortical response to thalamic stimulation and, therefore, that the cortex sits in the driver’s seat of sensory perception.

Samantha Barton

**ORIGINAL RESEARCH PAPER**

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**RESEARCH HIGHLIGHTS**

**NMDA receptors on oligodendrocytes**

The prevailing view that white matter oligodendrocytes lack NMDA (N-methyl-D-aspartate)-type glutamate receptors seems to have been wrong, according to three papers published recently in *Nature*. The reports provide compelling evidence for the involvement of oligodendrocyte NMDA receptors in glutamate-mediated damage to these cells in injury and disease.

Damage to oligodendrocyte processes — the structures responsible for myelination — leads to functional impairments in a wide range of conditions, including cerebral palsy, spinal cord injury, multiple sclerosis and stroke. Unlike neurons, which are susceptible to NMDA receptor-mediated damage, white matter oligodendrocytes were previously thought to be damaged by glutamate acting on AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid) and kainate receptors alone. Three groups now challenge this view by showing that a distinct form of NMDA receptor is present on the processes of oligodendrocytes.

Káradóttir et al. recorded from rat precursor, immature and mature oligodendrocytes in the white matter of the cerebellum and the corpus callosum. These cells showed glutamate- and NMDA-evoked inward currents that were inhibited by NMDA receptor antagonists. Oligodendrocyte NMDA receptors were less susceptible to Mg2+ block than neuronal receptors, allowing significant current to be generated even at the cell resting potential. Simulating ischaemia generated inward currents that were mediated, in part, by an action of glutamate at oligodendrocyte NMDA receptors.

Salter and Fern looked at developing oligodendrocytes in the mouse optic nerve by specifically expressing green fluorescent protein (GFP) in these cells. Oxygen and glucose deprivation led to a rapid Ca2+-dependent loss of cell bodies, but had no effect on the detachment and disintegration of oligodendrocyte processes, whereas a selective NMDA receptor antagonist largely prevented injury to processes.

Micu et al. measured changes in the concentration of Ca2+ in the cytoplasm of compact myelin in the adult rat optic nerve. Shortly after the onset of chemical ischaemia, the fluorescence of a Ca2+ indicator rose in myelin regions and in the cell bodies of oligodendrocytes. The researchers showed that whereas blocking AMPA and kainate receptors could prevent the Ca2+ rise at the cell body, NMDA receptors were responsible for ischaemic Ca2+ influx in the myelin sheath: NMDA receptor antagonists blocked the rise in cytosolic Ca2+ and subsequent damage to myelin.

Oligodendrocyte NMDA receptors could be targeted therapeutically to prevent white matter damage in a range of conditions.

All three research groups confirmed the presence of NR1, NR2 and NR3 NMDA receptor subunits — including NR1, NR2A, NR2B, NR2C, NR2D and NR3A — in developing oligodendrocyte processes or adult myelin, where the small intracellular space could allow large, toxic increases in intracellular ion concentrations.

These studies highlight NMDA receptors of unusual subunit composition as a potential therapeutic target for preventing white matter damage in a range of conditions, and suggest a new mechanism of signalling from axon to myelin under physiological conditions.

Rebecca Craven

**ORIGINAL RESEARCH PAPERS**
GLIA

Essential assemblies

Nodes of Ranvier are important for rapid, saltatory nerve conduction. Although the molecular constituents of the nodes and paranodes are well established, how they are assembled is still a mystery. Now, a study shows that two isoforms of neurofascin, Nfasc155 and Nfasc186, have distinct and crucial roles in the formation of functional nodes of Ranvier.

The nodes contain clusters of protein complexes, which consist of sodium channels, Nfasc186 and neuronal-glial-related cell adhesion molecule (NRCA), as well as structural proteins such as βIV-spectrin and ankyrin G. The distinct functions of Nfasc155 and Nfasc186 in nodal and paranodal assemblies are intriguing.

SYNAPTIC PLASTICITY

Capturing the signal

Late-phase long-term potentiation (L-LTP) refers to LTP that persists for more than 2 h and results in changes in strength at excitatory synapses. When L-LTP is triggered by suprathreshold stimulation it can be ‘captured’ by other synapses that are subject to subthreshold stimulation. Synaptic capture has been described in apical dendrites, which arise from the apex of pyramidal cells, and Alarcon and colleagues now show that L-LTP can also be captured in basal dendrites, which emerge from the base of a pyramidal cell. Moreover, they report that this phenomenon can occur between these two types of dendritic compartment.

The initiation of L-LTP depends on the regulation of many biochemical signalling pathways that control several processes that are crucial for synaptic plasticity, including gene expression. The products of gene expression (mRNAs and proteins) are delivered throughout the cell, but it is thought that they can be captured and thereby influence increases in synaptic strength only at synapses that have been ‘tagged’ by previous synaptic activity.

Alarcon et al. studied L-LTP in CA1 pyramidal neurons of mice and reported that, despite differences in the mechanisms that underlie the induction and expression of LTP in basal and apical dendrites, capture of L-LTP in the basilar compartment could be induced in response to the same stimulation protocol — a single train of high-frequency (100 Hz) stimulation — that was used for capture in apical compartments. Capture of L-LTP in both compartments was blocked or reduced by inhibition of protein kinase A and protein synthesis, respectively, suggesting that the tagging mechanism was the same in basilar as in apical dendritic compartments.

These researchers then investigated whether capturing can take place across the two dendritic compartments. The stimulation protocol used to induce within-compartment capture was not sufficient to drive capture between the two compartments in either direction. Varying the intensity of the priming stimuli, the time interval between stimuli delivered to each dendritic compartment, and the distance between the nucleus and the capture site did not allow cross-compartment capture. However, this could be triggered following stronger activation, such as two trains of tetanic stimulation.

Alarcon and colleagues propose that, although the tagging signal is the same in basilar and apical compartments, the synaptic tag is compartment restricted after only one train of stimulation; heightened stimulation is thought to trigger synaptic tagging over a wider area, allowing cross-compartment capture to take place. This, they say, would allow hippocampal neurons to process dendritic signals differently depending on the level of activation. However, further work will be necessary to confirm this model and unravel the principles that govern activity-mediated synaptic capture between different dendritic compartments.

At the paranodal axonal–glial junctions on either side of the node, Nfasc155, which is expressed by myelin-forming glial cells, binds to CASPR (contactin-associated protein) and contactin on the axon.

In this study, Sherman and colleagues found that in mice lacking neurofascin, the myelin sheath is grossly normal, but the velocities of nerve conduction are remarkably reduced compared with those of control animals. Close examination of myelina ultrastructure in these mice show that CASPR and contactin are absent from the paranodal junctions, and that sodium channels, NRCAM, βIV-spectrin and ankyrin G are no longer concentrated at the nodes. As the expression and localization of these molecules are normal in mutant mice, these data indicate that neurofascin is crucial for proper assembly of nodal and paranodal complexes. Transgenic expression of Nfasc155 in the myelinating glia of neurofascin-deficient mice rescues the axonal–glial adhesion complex by recruiting CASPR and contactin, but has no effect on the assembly of nodal complexes.

The distinct functions of Nfasc155 and Nfasc186 in nodal and paranodal assemblies are intriguing. Differential expression of neurofascin in glia and neurons might have a fundamental role in the evolution of saltatory nerve conduction in vertebrates.

Jane Qiu


Alison Rowan


... heightened stimulation is thought to trigger synaptic tagging over a wider area, allowing cross-compartment capture to take place.